Urol Res (1992) 20:387–392

Urological Research

Changes in action potential kinetics following experimental bladder outflow obstruction in the guinea pig

N. Seki[1], O. M. A. Karim[2], and J. L. Mostwin[2]

[1]Department of Urology, Faculty of Medicine, Kyushu University, Fukuoka, Japan
[2]James Buchanan Brady Urological Institute, Johns Hopkins Medical Institutions, Baltimore, USA

Summary. The effect of experimental bladder outflow obstruction on membrane electrical activity of guinea pig detrusor smooth muscle was studied. Using an intracellular microelectrode technique, action potentials were recorded from single smooth muscle cells to determine the effect of outflow obstruction on action potential (AP) kinetics. Bladder outflow obstruction resulted in smooth muscle hypertrophy with bladder weight gain to 2.7 times control levels after 8–12 weeks' obstruction. The changes in the AP kinetics noted with obstruction-induced bladder hypertrophy were a prolongation of the AP duration and a decrease in the maximum velocity of depolarization and repolarization. The AP amplitude, after hyperpolarization and overshoot potential in addition to the resting membrane potential (RMP) did not change significantly with bladder outflow obstruction. The values of these AP parameters were not affected significantly by the application of atropine and guanethidine in smooth muscle tissue from either control or obstructed bladders. These results suggest that the active electrical properties of the detrusor smooth muscle membrane are changed significantly by obstruction-induced bladder hypertrophy. Furthermore, the results suggest that adrenergic and cholinergic neurotransmitters do not contribute to these changes in AP kinetics following obstruction. The changes in AP properties with outflow obstruction-induced bladder hypertrophy were compared with those previously reported for the hypertrophic myocardium and were discussed in relation to the known impaired contractile properties of obstructed bladder smooth muscle.

Key words: Action potential – Obstruction – Detrusor – Membrane potential – Hypertrophy

Bladder outflow obstruction results in major alterations in bladder structure and function, including detrusor hypertrophy, in vivo cystometric dysfunction and detrusor instability [21]. A number of investigators have previously demonstrated impaired contractility (decrease in active force production per unit muscle area, decrease in the maximum theoretical velocity and the maximum theoretical isometric force of the muscle) of smooth muscle tissue from bladders that have become hypertrophic secondary to outflow obstruction [3, 24] or volume overload [22]. Decreased maximal shorting velocity [2] and force per unit muscle area [23] have also been reported in hypertrophied venous smooth muscle, and it was suggested that these changes in contractile properties may be related to impairment of excitation-contraction coupling or the changes of contractile apparatus of the muscle fibers themselves [2].

The action potential is an electrical membrane event closely associates with smooth muscle cell signalling activity. Since it has been shown that the action potential plays a significant role in the regulation of tonic and phasic changes in bladder contractility [17], an understanding of how it might be altered by bladder outflow obstruction-induced detrusor hypertrophy might contribute to our understanding of the pathophysiological effects of bladder outflow obstruction on the detrusor. In addition, an analysis of the action potential in the hypertrophic bladder might provide us with a more precise method of describing and classifying abnormal states. This in turn might rationalize our approach to drug therapy in different cystometric disorders associated with bladder outflow obstruction. Previous electrophysiological studies of hypertrophic myocardium have suggested that structural changes in the heart are associated with functional electrical changes, including action potential properties [5]. There have been many reports dealing with changes in the action potential with hypertrophy in cardiac muscle, both in experimental animal models [4, 8, 20] and in human tissue [6]. A possible correlation with changes in mechanical properties has also been inferred. In contrast to the relatively frequent studies undertaken with cardiovascular tissue, there have been few studies on the cellular electrophysiological changes associated with smooth muscle hypertrophy in the obstructed bladder. In view of the changes in action potential properties induced by hyperthophy in cardiac tissue, it seems reasonable to

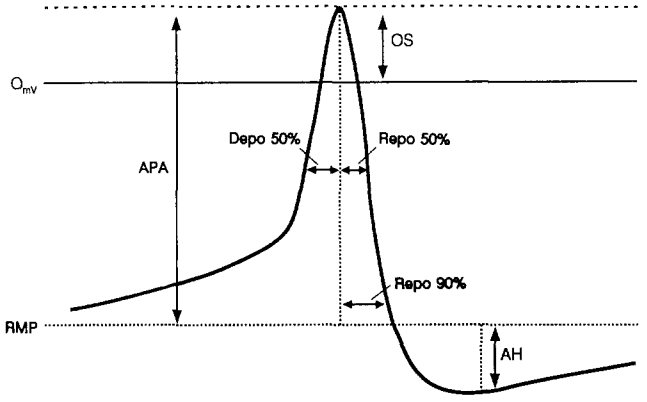

Fig. 1. Detail of measured action potential parameters. Action potential amplitude (*APA*, mV); overshoot potential (*OS*, mV); after hyperpolarization (*AH*, mV); resting membrane potential (*RMP*, mV); action potential duration, measured as the time from 50% depolarization to the point of maximal depolarization (*Depo 50%*, ms) and the time to 50% and 90% repolarization following the point of maximal depolarization (*Repo 50%*, ms) and 90% (*Repo 90%*, ms) respectively. The maximum velocity of depolarization (dV/dt, Vs^{-1}) and repolarization (dr/dt, Vs^{-1}) are the maximum values of the first derivatives of upstroke and downstroke segments in AP, respectively

suspect that similar changes in membrane electrical properties occur in bladder smooth muscle with outflow obstruction-induced detrusor hypertrophy. Using a recently described model of bladder outflow obstruction in the guinea pig, this study was undertaken to investigate the changes in action potential kinetics with obstruction induced detrusor hypertrophy. The model we have utilized results in a gradual onset bladder outflow obstruction similar to that which might occur in man with benign enlargement of the prostate [18].

Materials and methods

Animals and experimental procedure

Immature male albino guinea pigs (Hartley Strain, Charles River) weighing 280–320 g (4 weeks of age) underwent partial urethral obstruction as previously described [18]. In this model, urodynamic studies confirm that the onset of bladder outflow obstruction occurs by 4 weeks following placement of a silver ring around the urethra. Animals with the rings in situ 8 and 12 weeks after surgery are, therefore, obstructed. Age-matched guinea pigs from the same initial groups were used as non-operated controls.

Following 8–12 weeks of obstruction, animals were sacrificed by CO_2 inhalation and bladders were removed and placed in oxygenated Krebs solution at room temperature. After opening by a dorsal mid-line incision, the bladders were weighed. The luminal aspect of the bladder smooth muscle was exposed by careful removal of the mucosa and submucosa under a binocular dissecting microscope. For recording with microelectrodes, parallel longitudinal muscle bundles 10 mm in lenght and 1–2 mm in width were selected. These muscle strips were mounted with the mucosal side uppermost in a recording chamber (2.0 ml capacity). After being equilibrated for at least 1.5 h, the dissected tissue was immobilized using tiny pins on a silicon rubber plate (KE-66, Shin-Etsu Kagaku, Tokyo, Japan) covering the bottom of the chamber, and superfused with warmed (35–36°C) Krebs solution at a constant flow rate of 2–3 ml/min. Electrical responses of the bladder smooth muscle cell membrane were recorded using glass capillary microelectrodes (1.2 mm outer diameter) filled with 3 M KCl. Each electrode had a 0.1 μm tip diameter, with 40–60 Mohm tip resistance. The tissue was stimulated extracellularly by the application of square current, using a electric stimulator (S48-F, Grass) between Ag-AgCl plates 10 mm apart through which one end of the tissue passed [1].

The Krebs solution had the following composition (mM): Na^+, 137.0; K^+, 5.9; Ca^{2+}, 2.5; Mg^{2+}, 1.2; HCO_3^-, 15.5; $H_2PO_4^-$, 1.2; Cl^-, 134; glucose, 11.5. The solution was aerated with O_2 containing 3% CO_2, and the pH of the solution was maintained at 7.2. The solution was made hypertonic by addition of 12 g sucrose to 100 ml Krebs solution in order to reduce tissue movement. The drugs used were atropine sulfate and guanethidine sulfate (Sigma).

Data and statistical analysis

The APs thus recorded from the smooth muscle membrane were displayed on a cathode-ray oscilloscope (Tektronix 5113) and on a pen-writing recorder (Gould 220). The data was simultaneously digitized through an analog to digital converter (Data Acquisition A/D convertor AT-Codas Waveform scroller, Dataq Instruments) at a sample rate of 2 kHz (2000 per s and stored on magnetic disk (Dell 316SX) for subsequent analysis. A computer program in a highlevel scientific language (Asyst, Asyst Software Technologies) was written to analyze the constitutive components of the action potential (AP) as described previously [10]. The following AP parameters were measured: total action potential amplitude (APA), after hyperpolarization (AH), overshoot potential (OS), resting membrane potential, maximum velocity of depolarization (dv/dt), maximum velocity of repolarization (dr/dt), duration to 50% ($DEPO_{50}$) of complete depolarization, duration to 50% ($REPO_{50}$) and 90% ($REPO_{90}$) of complete repolarization (Fig. 1). The values recorded were expressed as mean ± standard deviation (SD) and statistical significant difference between the experimental group and respective age-matched control group was determined using Student's *t*-test. Probabilities of less than 5% ($P < 0.05$) were considered significant.

Results

Bladder weight

Guinea pigs with bladder outflow obstruction showed a marked increase in bladder weight compared with control animals. The control bladder weighted 0.39 ± 0.07 g ($n = 14$), the obstructed weighed 1.05 ± 0.31 g ($n = 8$) respectively ($p < 0.05$). The ratio of bladder weight to body weight also increased significantly in the obstructed bladder by 8–12 weeks (control ratio was 0.63 ± 0.11 g/kg, $n = 14$; obstructed ratio was 2.40 ± 0.79 g/kg, $n = 8$, $P < 0.05$).

Change of electrical properties associated with bladder hypertrophy

The RMP recorded from control and obstructed bladder smooth muscle was -39.1 ± 1.5 mV ($n = 78$) and -39.8 ± 1.7 mV ($n = 38$), respectively ($P > 0.05$). In 64.3% of muscle preparations (9 out of 14 tissues studied) set up for more than 1.5 h, all the cell membrane of detrusor smooth muscle tissue from control guinea pigs showed spontaneous electrical activity that was generally in the form of simple APs of regular frequency. This electrical activity continued for more than 6-8 h. In contrast, the smooth

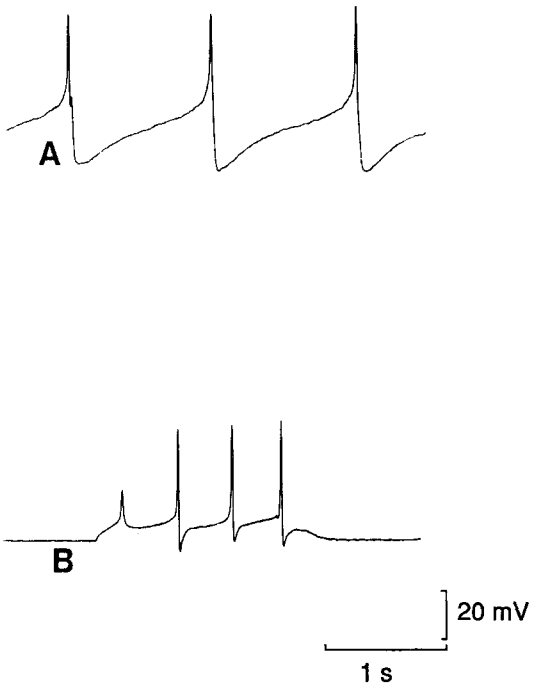

Fig. 2A, B. Examples of action potentials recorded from control bladder smooth muscle. A Spontaneously generated AP; B current-induced AP. Constant outward current (2.0 V intensity, 1.5 s duration) was applied to generate AP

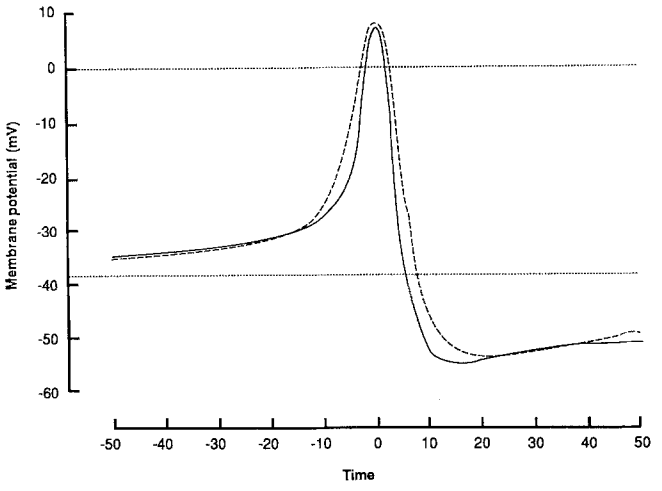

Fig. 3. Configuration of representative spontaneously generated AP recorded from smooth muscle of control and obstructed bladders. Traces represent the mean of 15 APs recorded from three animals. The *abscissa* shows time (ms) from the point of maximum depolarization. *Horizontal dotted lines* show zero potential and mean RMP. —— = Control; – – – = obstructed

muscle cell membrane obtained from obstructed bladders was almost totally electrically quiescent. Only 25.0% of the tissues studied (2 out of 8 preparations) showed spontaneous APs. Depolarizing current pulses (2.0 V intensity, 2.0 s duration) applied to these electrically quiescent cell membranes gave rise to current-induced APs in tissues from both control and obstructed animals with little change in the resting membrane potential. Figure 2 shows fairly typical APs recorded in bladder smooth muscle from a control animal. These APs were composed of an upstroke and a downstroke each of 5–10 ms duration. There was no plateau phase, but a pronounced after-hyperpolarization with long duration. In both control and obstructed bladder smooth muscle, there were no significant difference in the AP parameters between spontaneous or current-induced APs (not shown).

Table 1 summarizes the parameters of spontaneous APs obtained from control and obstructed bladder smooth muscle. The most obvious difference in the AP parameters between control and obstructed bladder smooth muscle tissue was the AP duration. The AP duration for 50% depolarization, 50% and 90% repolarization were consistently and significantly prolonged in tissue from obstructed animals. Furthermore, both the dv/dt and dr/dt were significantly reduced in the obstructed bladder. In contrast, the AP amplitude, after hyperpolarization and overshoot potential did not change significantly with bladder outflow obstruction.

Representative traces of spontaneous APs recorded from control and obstructed bladders are shown in Fig. 3. The marked prolongation in duration during both upstroke and downstroke, and the reduction in dv/dt and dr/dt is apparent in obstructed bladder.

Table 1. Action potential parameters in control and obstructed bladder smooth muscle

	APA (mV)	AH (mV)	OS (mV)	Depo 50% (ms)	Repo 50% (ms)	Repo 90% (ms)	dv/dt (V/s)	dr/dt (V/s)
Control	46.2 ± 6.3	14.5 ± 3.1	7.8 ± 6.0	5.0 ± 1.0	4.0 ± 1.0	5.9 ± 1.5	7.1 ± 1.9	11.5 ± 3.4
Obstructed	45.4 ± 5.5	13.6 ± 4.3	8.2 ± 5.9	6.5* ± 2.0	4.7* ± 1.1	7.6* ± 1.8	5.8* ± 1.7	8.7 ± 1.9

Values are means ± SD

APA, action potential amplitude; AH, after hyperpolarization; OS, overshoot potential; Depo 50%, Repo 50% and Repo 90%, action potential duration (time to 50% depolarization, 50% and 90% repolarization); dv/dt, velocity of repolarization; dr/dt, velocity of repolarization

* $P < 0.05$, control vs obstructed. Numbers of observations: 189 from 14 animals (control) and 137 from 8 animals (obstructed)

Table 2. Effect of atropine (1 μM) and guanethidine (5 μM) on AP parameters recorded from control bladder smooth muscles

	APA (mV)	AH (mV)	OS (mV)	Depo 50% (ms)	Repo 50% (ms)	Repo 90% (ms)	dv/dt (V/s)	dr/dt (V/s)
Krebs	46.7 ± 6.8	14.7 ± 3.1	7.8 ± 6.4	5.1 ± 1.1	4.0 ± 1.0	6.0 ± 1.7	7.1 ± 1.9	11.3 ± 3.7
Atropine + guanethidine	47.9 ± 4.3	13.8 ± 3.8	8.5 ± 4.7	5.1 ± 1.0	4.0 ± 1.1	6.1 ± 1.9	7.0 ± 1.1	11.4 ± 3.1

Values are means ± SD. Numbers of observations: 148 from 4 animals (Krebs) and 117 from 4 animals (atropine with guanethidine)

Table 3. Effect of atropine (1 μM) and guanethidine (5 μM) on AP parameters recorded from obstructed bladder smooth muscles

	APA (mV)	AH (mV)	OS (mV)	Depo 50% (ms)	Repo 50% (ms)	Repo 90% (ms)	dv/dt (V/s)	dr/dt (V/s)
Krebs	45.9 ± 6.3	10.3 ± 4.2	8.5 ± 6.1	6.7 ± 1.2	4.9 ± 1.1	7.7 ± 1.9	5.7 ± 1.8	8.3 ± 1.7
Atropine + guanethidine	45.2 ± 4.8	11.7 ± 3.6	8.1 ± 5.0	6.5 ± 1.0	5.0 ± 1.0	8.1 ± 2.1	5.9 ± 1.1	8.1 ± 1.6

Values are means ± SD. Numbers of observations is 79 from 4 animals (Krebs) and 47 from 4 animals (atropine with guanethidine)

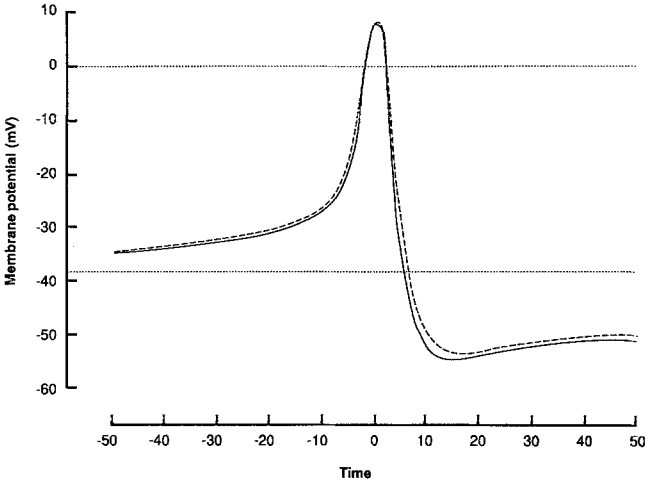

Fig. 4. Effects of atropine (10^{-6} M) and guanethidine (5×10^{-6} M) on spontaneously generated AP recorded from smooth muscles of control bladders. Traces represent the mean of 15 APs recorded from three animals. The *abscissa* shows time (ms) from the point of maximum depolarization. *Horizontal dotted lines* show zero potential and mean RMP. —— = Control; – – – = + atropine guanethidine

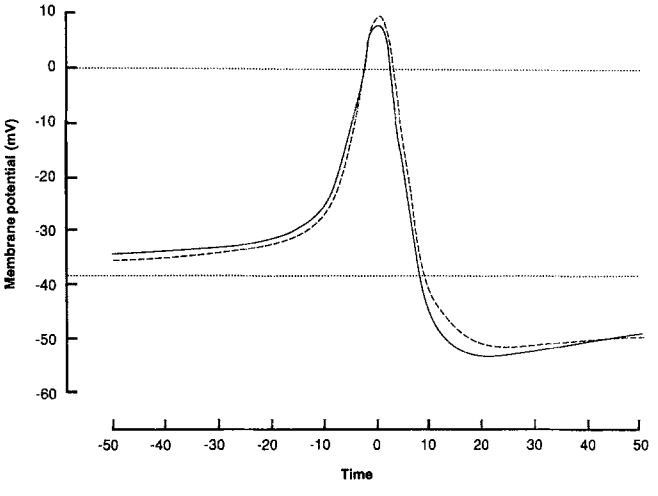

Fig. 5. Effects of atropine (10^{-6} M) and guanethidine (5×10^{-6} M) on spontaneously generated AP recorded from smooth muscles of obstructed bladders. Traces represent the mean of 15 APs recorded from three animals. The *abscissa* shows time (ms) from the point of maximum depolarization. *Horizontal dotted lines* show zero potential and mean RMP. —— = Obstructed; – – – = + atropine guanethidine

Effects of adrenergic and cholinergic antagonists on electrical properties

The effects of atropine and guanethidine on the AP were investigated to determine whether there is modification of membrane electrical properties (AP kinetics and RMP) by neurotransmitters in control and obstructed bladder smooth muscle tissue. Tissue was pretreated for 15 min with atropine (10^{-6} M) and guanethidine (5×10^{-6} M) before recording of the APs. The RMP did not change in the presence of either atropine or guanethidine (−39.3 mV, $n=24$ in control and −40.1 mV, $n=19$ in obstructed animals). The results of these experiments are summarized in Tables 2 and 3. No significant changes in AP parameters were observed following application of either atropine or guanethidine to either control or obstructed bladder smooth muscle. Representative tracings from these experiments are shown in Fig. 4 and 5. The characteristics of the APs recorded from control and obstructed bladders did not change significantly following

treatment with atropine or guanethidine. This implies that there is no significant background modification of the AP by neurotransmitter release from either adrenergic or cholinergic nerves.

Discussion

The results presented in this paper demonstrate that outflow obstruction-induced bladder hypertrophy results in significant prolongation of the bladder smooth muscle action potential duration with a concomitant decrease in the rate of depolarization (dv/dt) and repolarization (dr/dt). In contrast, the values for resting membrane potential (RMP), AP amplitude, after-hyperpolarization and overshoot potential did not change significantly with bladder outflow obstruction, despite the changes in the kinetic properties of the action potential. The RMP and APs recorded from both control and obstructed tissue were not affected significantly by the application of atropine or guanethidine. This suggests, that, the electrical properties of control and obstructed detrusor smooth muscle are not modified by adrenergic or cholinergic neurotransmitter under the experimental condition used. This might, furthermore, imply that the changes in AP kinetics in the obstructed bladder might not be due to prejunctional modification, but result from a change in intrinsic properties of the smooth muscle membrane itself. In this context, it is of interest to note that, though myocyte hyperplasia is an early event in the response of the detrusor musculature to outflow obstruction in this model, by 8 weeks of obstruction myocyte hypertrophy appears to be a significant contributing factor to the weight gain associated with bladder outflow obstruction (O. M. A. Karim, unpublished results).

The membrane electrical properties recorded in control guinea pig detrusor were almost identical with those reported previously [13, 17]. Although there have been few previous investigations of membrane electrical properties in hypertrophic detrusor smooth muscle with which to compare the results of the present investigation, these changes in cellular electrical activity obtained from hypertrophic guinea pig detrusor smooth muscle are qualitatively similar to those observed in previous studies of cardiac hypertrophy using multicellular cardiac preparations. Most studies in the rat model of left ventricular hypertrophy, induced gradually by renal hypertension or spontaneous hypertension, have reported prolongation of the AP duration without changes in the RMP, AP amplitude or overshoot potential [4, 9]. Studies on the mechanical properties of the rat left ventricle during hypertrophy induced by aortic constriction have shown a decrease in force development and velocity of shortening [15]. Furthermore, in cats with right ventricular hypertrophy, active force was reduced and velocity of shorting and maximal rate of tension development were decreased [7, 8]. These mechanical changes were generally associated with depression of the AP amplitude during the plateau phase, a reduction in the dr/dt and a prolongation of the AP duration [19, 20]. A decrease in active force development and a reduction in maximum shorting velocity has, similarly, been reported in obstruction-induced detrusor hypertrophy and overload-induced venous smooth muscle hypertrophy [2, 14, 24].

The contribution of these abnormalities in AP properties (increased AP duration, reduced dv/dt and dr/dt) to mechanical impairment of hypertrophic detrusor smooth muscle is less clear. It might be reasonable to suggest that an abnormality of the slow inward Ca current (I_{si}) might be involved in the mechanical and electrophysiological changes of hypertrophied bladder smooth muscle, since it is thought to play important roles in the genesis of the AP and in excitation-contraction (E-C) coupling of most smooth muscle including the bladder. In hypertrophic cardiac muscle, several reports have shown abnormalities of the slow Ca inward current [4, 19], and more conclusive evidence using patch clamp analysis has shown a delayed inactivation time course of I_{si} in hypertrophic feline ventricular myocytes [11], suggesting a possible involvement of abnormal I_{si} in the prolongation of the AP duration. Furthermore, the possible contribution of abnormal kinetics in the delayed rectifier K current (I_k) to the prolongation of AP duration has recently been proposed in hypertrophic feline myocytes [12]. Since it has been demonstrated that Ca inward current and K outward current are involved in the AP production in detrusor smooth muscle [13, 16, 17], a decrease in dv/dt and dr/dt in addition to the increase in the AP duration during both upstroke and downstroke in obstructed bladder might suggest that these transmembrane Ca and K currents are both altered in the hypertrophic bladder. The nature of the relationship between contraction and membrane depolarization is complex and varies with species and experimental conditions. It is, however, not unreasonable to speculate that such an increase in the AP duration might well play a role partially in producing the prolonged duration of shorting in hypertrophic smooth muscle. In contrast, the decreased magnitude of contraction observed in hypertrophic detrusor cannot be easily explained, since if the increase in the AP duration is a result of the delayed inactivation of I_{si}, it might be expected to increase contractility with increased transmembrane influx of Ca. There are numerous possible explanations for the diminished contractile response in the face of increased Ca influx. The cellular defects responsible for diminished contractility of hypertrophied detrusor muscle might be distal to the Ca influx step in the E-C coupling process. A likely possibility is abnormal Ca handling in intracellular Ca store site or decreased sensitivity of contractile protein to intracellular Ca. Prolongation of AP duration may represent a compensatory mechanism for preserving the contractile strength of hypertrophied smooth muscle by providing a larger signal for acitvation of contraction.

In conclusion, we have shown that smooth muscle hypertrophy associated with gradual onset bladder outflow obstruction in the guinea pig results in significant prolongation of the AP duration with decreases in the velocities of depolarization and repolarization. These findings seem to offer a partial explanation for the decreased velocity of contraction seen in hypertrophic detrusor smooth muscle.

Acknowledgement. This work was supported by funding from PHS grants D538466-03 and AM19300. O. M. A. Karim was supported by a King Edward VII Hospital Fund Travel Bursary and an Ethicon Foundation Travel grant from the Royal College of Surgeons of Edinburgh.

References

1. Abe Y, Tomita T (1968) Cable propertis of smooth muscle. J Physiol (Lond) 196:87–100
2. Arner A, Malmqvist U, Uvelius B (1985) Effects of Ca^{2+} on force-velocity characteristics of normal and hypertrophic smooth muscle of the rat portal vein. Acta Physiol Scand 124:525–533
3. Arner A, Malmqvist U, Uvelius B (1990) Metabolism and force in hypertrophic smooth muscle from rat urinary bladder. Am J Physiol 258:C923–C932
4. Aronson RS (1980) Characteristics of action potentials of hypertrophied myocardium from rats with renal hypertension. Circ Res 47:443–454
5. Cameron JS, Myerburg RJ, Wong SS, Gaide MS, Epstein K, Alvarez TR, Gelband H, Guse PA, Bassett AL (1983) Electrophysiologic consequences of chronic experimentally-induced left ventricular pressure overload. Am J Cardiol 2:481–487
6. Coltart DJ, Meldrum SJ (1970) Hypertrophic cardiomyopathy: an electrophysiological study. Br Med J IV:217–218
7. Cooper G 4th, Tomanek RJ, Ehrhardt JC, Marcus ML (1981) Chronic progressive pressure overload of the cat right ventricle. Circ Res 48:488–497
8. Gelband H, Bassett AL (1973) Depressed transmembrane potentials during experimentally induced ventricular failure in cats. Circ Res 32:625–634
9. Gulch RW (1980) The effect of chronic loading on the action potential of mammalian myocardium. J Mol Cell Cardiol 12:415–420
10. Karim OMA, Seki N, Mostwin JL (1992) Analysis of the detrusor smooth muscle action potential. Urol Res 20:173–176
11. Kleiman RB, Houser SR (1988) Calcium currents in normal and hypertrophied isolated feline ventricular myocytes. Am J Physiol 255:H1434–H1442
12. Kleiman RB, Houser SR (1989) Outward currents in normal and hypertrophied feline ventricular myocytes. Am J Physiol 256:H1450–H1461
13. Klockner U, Isenberg G (1985) Action potentials and net membrane currents of isolated smooth muscle cells (urinary bladder of the guinea pig). Pflugers Arch 405:329–339
14. Mattiasson A, Uvelius B (1982) Changes in contractile properties in hypertrophic rat urinary bladder. J Urol 128:1340–1342
15. Meerson FZ, Kapelko VI (1972) The contractile function of the myocardium in two types of cardiac adaptation to a chronic load. Cardiology 57:183–199
16. Montgomery BSI, Fry CH (1992) The action potential and net membrane currents in isolated human detrusor smooth muscle cells. J Urol 147:176–184
17. Mostwin JL (1986) The action potential of guinea pig bladder smooth muscle. J Urol 135:1299–1303
18. Mostwin JL, Karim OMA, Van Koeveringe G, Brooks EL (1991) The guinea pig as a model of gradual urethral obstruction. J Urol 145:854–858
19. Ten Eick RE, Bassett AL, Robertson LL (1983) Possible electrophysiological basis for decreased contractility associated with myocardial hypertrophy in the cat: a voltage clamp approach. In: Alpert NR (ed) Perspectives in cardiovascular research, myocardial hypertrophy and failure. Raven Press, New York, pp245–259
20. Tritthart H, Leudcke H, Bayer R, Stierle H, Kaufmann R (1975) Right ventricular hypertrophy in the cat: an electrophysiological and anatomical study. J Mol Cell Cardiol 7:163–174
21. Turner-Warwick R (1984) Bladder outflow obstruction in the male. In: Mundy AR, Stephenson TP, Wein AJ (ed) Urodynamics: principles, practice and application. Churchill Livingstone, New York, pp183–204
22. Uvelius B (1980) Relation between mechanical and morphological characteristics in urinary bladder smooth muscle. Acta Physiol Scand Suppl 483:1–51
23. Uvelius B, Arner A, Johansson B (1981) Structural and mechanical alterations in hypertrophic venous smooth muscle. Acta Physiol Scand 112:463–471
24. Van Koeveringe G, Mostwin JL, van Mastrigt R, Van Koeveringe BJ (1990) Effect of partial obstruction on force development in guinea pig bladder muscle (abstract). J Urol 143:355A

Narihito Seki, MD
Department of Urology
Faculty of Medicine
Kyushu University
Fukuoka
812 Japan