Influence of temperature on activity of the isolated whole bladder preparation of neonatal and adult rats

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Sugaya, Kimio, and William C. de Groat. Influence of temperature on activity of the isolated whole bladder preparation of neonatal and adult rats. Am. J. Physiol. Regulatory Integrative Comp. Physiol. 278: R238–R246, 2000.—The temperature sensitivity of in vitro whole bladder preparations from neonatal and adult rats with or without chronic partial urethral obstruction was investigated. After the bladder was filled to a volume eliciting isovolumetric contractions, temperature was changed between 19 and 38°C. In all preparations, higher temperatures were associated with higher frequencies of spontaneous intravesical pressure waves (IVPW). In 1- to 2-wk-old neonates, IVPW amplitude increased as the temperature increased; however, in older neonates and normal adults, the opposite occurred. The transition period was at 3 wk of age when bladder volume also markedly increased. At this age as well as in adult rats with outlet obstruction, changing temperature had little influence on the amplitude of IVPW. Thus obstructed outlet bladders and 3-wk-old bladders had similar properties. It is concluded that the properties of bladder muscle are changed during postnatal maturation and that in 3-wk-old rats, when brain control of voiding is emerging, micturition is abnormal, leading to obstructive changes in bladder muscle.

In the neonatal rat, during the first 2–3 postnatal wk, micturition is activated by the mother licking the perineum, which induces a perineal-to-bladder reflex (3). This reflex, which is organized in the spinal cord, induces strong bladder contractions and efficient voiding; whereas bladder distension, which is the stimulus for voiding in adult animals does not elicit voiding in young neonates (3, 4, 13, 26). As the central nervous system matures during the postnatal period, the spinal perineal-to-bladder reflex is gradually replaced by a supraspinal bladder-to-bladder reflex that induces voiding in response to bladder distension (3, 26). This change in reflex mechanisms occurs during the third postnatal week (3).

Previously, we examined the central nervous control of the neonatal rat bladder using the in vitro brain stem-spinal cord-bladder preparation (25) and the spinal cord-bladder preparation (23). In unpublished pilot experiments, an analysis of the optimal temperature of the perfusion fluid in these preparations revealed that the amplitude of the intrinsic bladder contractions of the isolated whole bladder preparation was directly correlated with the temperature of the perfusion fluid between 19 and 38°C. On the other hand, the temperature characteristics of the adult rat bladder in vitro were inversely correlated with temperature; i.e., the amplitudes of the intrinsic contractions were larger at lower temperature.

This study was undertaken to determine when the temperature characteristics of isolated whole bladder activity in vitro change during postnatal development and whether the temperature characteristics of the adult rat hyperactive bladder with outlet obstruction are similar to those of the neonatal bladder.

METHODS

Observation of rat development. Developmental changes in seven litters of Sprague-Dawley rats (n = 8–15 pups/litter) were studied from 2 days to 6 wk after birth. Changes in feeding, micturition, and defecation behavior in the neonates and the interactions between mothers and their pups were observed for 2–5 h in the evening every week.

Isovolumetric cystometry of isolated whole bladder preparations at varying temperatures in normal neonatal and adult rats. After measurement of body weight, the animals were decapitated and the urinary bladders were isolated from 2-day-old, 1- to 6-wk-old (either sex), and adult (6 mo old) female Sprague-Dawley rats (n = 4 at each age). The bladder neck and both ureters were ligated to record isovolumetric...
bladder contractions. The isolated whole bladder was pinned down on a layer of Sylgard resin (Dow Corning) in a recording chamber perfused with Krebs solution. The pins were inserted in the urethra, and the anterior surface of the bladder dome was facing up. A 21-gauge needle was inserted through the dome, and the needle was connected via polyethylene tubing to an infusion pump and a pressure transducer via a three-way stopcock. The tubing was filled with saline. Bladder pressure was displayed on a chart recorder. The bladder was slowly filled (0.052 ml/min) with physiological saline to a volume sufficient to elicit spontaneous bladder contractions at 27°C. The saline contained 2% blue food coloring (McCormick) to check for leakage of fluid around the needle or through the urethral orifice. Bipolar silver electrodes (inter-electrode distance 1 mm) were positioned on the serosal surface of the bladder for electrical stimulation (ES) with trains of pulses (50 V, 1-ms pulse duration, 50-Hz intratrain frequency, 5-s train duration).

Isovolumetric bladder contractions occurring spontaneously or induced by ES were recorded on a rectilinear paper recorder while varying the temperature of the perfusion fluid. The movements of the bladder wall were observed using a stereomicroscope. TTX was administered in some preparations to determine if bladder activity was dependent on neural mechanisms.

Chemical sympathectomy. To examine the effect of the sympathetic innervation on the changes in intrinsic bladder activity, neonatal Sprague-Dawley rats (n = 4) were injected with 6-hydroxydopamine hydrochloride (6-OHDA, 100 mg/kg ip, for 10 days), which induces a complete sympathectomy (6, 22, 27). TTX was administered in some preparations (in mM): 113 NaCl, 4.7 KCl, 2.5 CaCl₂, 1.2 MgSO₄, 25 NaHCO₃, 1.2 KH₂PO₄, and 1.5 glucose. The solution was buffered to pH 7.4 and equilibrated with 95% O₂ and 5% CO₂. The solution in the recording chamber was also bubbled with the same gas mixture. The solution was preheated or pre-cooled by passage through a heat exchanger before entering the recording chamber and was maintained at first at 27°C. After spontaneous bladder contractions became stable, the temperature of the perfusion solution was changed to 19°C and then increased in 1°C increments to 38°C (n = 2 for each age) or changed to 38°C and decreased in 1°C increments to 19°C (n = 2 for each age). It required 1–10 min to change the temperature of the perfusion fluid in the recording chamber by 1°C. Once the temperature stabilized, each temperature was maintained (±0.3°C) in the recording chamber for a constant time ranging from 3 min at high temperatures to 45 min at low temperatures. The bath was drained by gravity or suction with the drainage flow rates adjusted to match inflow rates.

When bladder activity stabilized 30–45 min after setup of the preparation in the recording bath, the intravesical pressure and frequency of spontaneous bladder contractions were measured for 4–10 contractions. The amplitudes of ES-evoked bladder contractions were also measured at each temperature. Results are reported as means ± SE. Student’s t-test for paired or nonpaired data, linear regression, ANOVA was used for statistical data analysis. A level of P < 0.05 was considered statistically significant.

RESULTS

Behavior of neonatal rats. Body weight, which increased continuously during the postnatal period (Fig. 1), as well as the general behavior of neonatal animals were monitored during the first 6 postnatal wk. During the first 2 wk of age before opening of the eyelids, the rat pups were usually huddled together in one part of the cage. The mother nursed the pups and licked the perineum to induce micturition and defecation (26). The eyelids opened between postnatal day 15 and 16. Three-week-old pups moved freely about the cage, ate solid food, but also nursed. During the third postnatal week, it was rare to observe the mother lick the perineum of the pups, because the pups were more active. Pups at 4–6 wk of age ate solid food, did not nurse, and the mothers did not lick the perineum.

![Graph A: Rat body weight (A) and threshold bladder volume (B) sufficient to elicit spontaneous bladder contractions at 27°C in isolated whole bladders of 2-day-old (2D), 1 (1W), 2 (2W), 3 (3W), 4 (4W), 5 (5W), and 6-wk-old (6W) and 6-mo-old (6M, adult) rats. Body weight gradually increased with age (A). Threshold bladder volume of 3-wk-old rat bladder was significantly (P < 0.05) greater than those of 2-day-old and 1-, 2-, 4-, 5-, and 6-wk-old rats. Each value is mean ± SE of 4 animals (in A) or preparations (in B).](http://ajpregu.physiology.org)
Temperature characteristics of isolated whole bladder activity in normal neonatal and adult rats. Isolated whole bladders from rats of every age exhibited spontaneous bladder contractions when the bladder was filled with saline. The threshold bladder volume to elicit rhythmic contractions at 27°C was not significantly different (0.13–0.17 ml) at 2 days or 1 and 2 wk of age (Fig. 1). However, the threshold volume of the 3-wk-old rat bladder (0.62 ± 0.07 ml) was extremely large even when compared with 5- to 6-wk-old bladders (0.21 ± 0.03 and 0.37 ± 0.05 ml, respectively). Therefore, the increase during postnatal development in the threshold volume for inducing spontaneous bladder activity did not parallel the increase in body weight.

When the temperature of the perfusion fluid was changed between 19 and 38°C, the magnitude of the spontaneous and ES-evoked contractions also changed but the direction and the magnitude of the change was different in preparations of different age (Figs. 2 and 3). The maximal spontaneous contraction pressures were recorded at 38°C in 2-day-old (20 ± 1 cmH₂O), 1-wk-old (22 ± 3 cmH₂O), and 2-wk-old preparations (27 ± 4 cmH₂O), and gradually decreasing the temperature progressively reduced the responses (Fig. 4). At 19°C, the responses were 40–59% of the maximal amplitude. In bladders from older rats (5–6 wk and 6 mo), the inverse correlation was noted; i.e., the maximal contraction amplitude occurred at low temperatures (19–23°C), and the amplitude declined as the temperature was increased to 38°C (Fig. 4). In 3-wk-old preparations and, to a lesser extent, in 4-wk-old preparations, the variation in contraction amplitude was less obvious. The 3-wk preparations had a relatively flat temperature-response curve, whereas the 4-wk preparations had a biphasic curve in which the peak amplitudes occurred between 23°C and 29°C. Similar temperature-response curves were obtained when the temperatures were gradually increased (n = 2 for each age) or decreased (n = 2 for each age).

Baseline intravesical pressure (4–10 cmH₂O) in 2-day-to 6-wk-old rat bladders exhibited only a slight change (0–4 cmH₂O) at different temperature, and there was no consistent relationship between pressure and temperature. However, in adult rat bladders, baseline intravesical pressure was much higher (15–18 cmH₂O) at low temperatures (19–23°C) than at high temperature (3–6 cmH₂O, 34–38°C; Fig. 2). Therefore, all pressure measurements of spontaneous and evoked bladder activity in this paper include baseline and represent the difference between pressures detected when the cannula was positioned on the surface of the fluid in the recording chamber and when it was inserted into the bladder.

ES-evoked bladder contractions were of larger amplitude than spontaneous contractions at all temperatures and in all age preparations except in 2-day-old bladders at low temperatures below 23°C when ES did not evoke a contraction (Fig. 5). The ES-evoked contractions were blocked by concentrations of TTX (1 µM), which did not block spontaneous activity. The largest contraction pressures for the entire series of experi-
ments (63 ± 9 cmH₂O) were recorded at 27°C in 4-wk-old bladders (Fig. 5). The temperature-response curves for ES-evoked contractions showed the same trends as for spontaneous contractions. For example, in adult preparations, the peak contractions at 22–26°C were approximately twofold larger than at 37–38°C (Fig. 5).

The frequency of spontaneous bladder contractions increased with increasing temperatures in preparations of all ages (Figs. 2 and 6). Generally, the highest frequencies occurred at the highest temperature, although in 4-wk-old rat bladders, the maximal frequency occurred at 31°C. The rate of rise and duration of bladder contractions was also influenced by changes in temperature (Figs. 2 and 3). At higher temperatures, the spontaneous and ES-evoked contractions reached peak amplitude faster and returned to baseline more rapidly than at lower temperatures. However, in the 2-day- and 1-wk-old bladders even at 19°C, the contractions showed a rapid rise time (Fig. 2).

Movements of the anterior bladder wall in 1-, 3-, 5-wk-old, and adult bladder preparations (n = 4 for each age) were observed with a microscope at different temperatures (19°C, 28°C, and 37°C). The movements increased at higher temperatures. In 1-wk-old bladders, the frequency of movements correlated with the frequency of intravesical pressure waves at all temperatures. The movements either occurred simultaneously in all parts of the anterior surface of the bladder or began in one region and then spread to other regions. At 37°C, some additional movements were noted near the insertion site of the recording needle, but these movements did not correlate with pressure waves. In 3- and 5-wk-old neonatal bladders and adult bladders, the

Fig. 4. Relationship between temperature and intravesical pressure of spontaneous bladder contractions in isolated whole bladder of rats of different age. Each value is mean ± SE of 4 preparations. Linear regression is drawn in each figure. x, temperature; y, intravesical (bladder) pressure.

Fig. 5. Relationship between temperature and intravesical pressure of electrically induced bladder contractions in isolated whole bladder of rats of different age. Each value is mean ± SE of 4 preparations. Linear regression is drawn in each figure.
frequencies of wall movements and pressure waves were similar at 19°C, but at 28°C and 37°C, the frequency of wall movements exceeded the number of pressure waves. The ratio of movements to pressure waves was greater in bladders from older animals (Fig. 7). In adult preparations at 37°C, the frequency of movements was 32.3 ± 7.7/min, which was 7.9 times higher than the frequency of pressure waves (Fig. 7).

Effect of sympathectomy on the activity of whole bladder activity in 5-wk-old rats. The rats, which received 6-OHDA for 10 days (100 mg kg⁻¹ day⁻¹ ip) from birth to day 9 developed normally except for a 3- to 5-day delay in the opening of their eyelids. In addition, at 5 wk of age, the treated rats also exhibited ptosis, which is one of the characteristics of sympathectomy (2). The bladders from these animals exhibited spontaneous contractions that responded to temperature changes in a manner similar to those of untreated animals (Fig. 8). The amplitude of these spontaneous contractions was not significantly different from the responses of normal 5-wk bladders, although the frequency of these contractions was significantly lower (P < 0.0001, ANOVA).

Temperature characteristics of isolated whole bladder activity of adult rats with bladder outlet obstruction. Mean body weight (301 ± 16 g) of rats with outlet obstruction was not different from that of normal adult rats (284 ± 7 g) used in this study; whereas the bladder volume necessary to elicit spontaneous contractions was considerably larger in obstructed rats (3.83 ± 1.62 vs. 0.43 ± 0.07 ml). When the temperature of the perfusion fluid was increased in 1°C steps between 19°C and 38°C, the frequency of spontaneous activity increased at higher temperatures (Figs. 9 and 10), however, the increase was not as prominent as in normal adult bladders (Fig. 6). There was a significant difference (P < 0.0001, ANOVA) in the frequency of spontaneous contractions between obstructed bladders and normal adult bladders. The frequencies of bladder wall movements and intravesical pressure waves were similar at 19°C and 28°C, but, at 37°C, the frequency of wall movements exceeded the frequency of pressure waves (Fig. 7).

The amplitude of spontaneous activity in obstructed bladders showed a small variation with changes in

Fig. 7. Relationship between temperature and ratio of number of bladder wall movements (mov) and frequency (fre) of spontaneous bladder contractions in isolated whole bladders in 1-, 3-, and 5-wk-old and 6-mo-old rats. Each value is mean ± SE of 4 preparations. Significant difference: *P < 0.05 and **P < 0.01.
temperature, the amplitude being greater at lower temperatures (maximal pressure 22 ± 7 cmH₂O at 19°C) than at higher temperatures (14 ± 2 cmH₂O at 37°C; Fig. 10A). Interestingly, at low temperatures (19–23°C), the contractions were of larger amplitude in normal bladders (35 ± 5 cmH₂O at 23°C vs. 22 ± 7 cmH₂O at 19°C), whereas, at high temperatures (37°C), the contractions were larger in obstructed bladders (14 ± 2 cmH₂O vs. 9 ± 2 cmH₂O; Figs. 4 and 10A). There was a significant difference (P < 0.0001, ANOVA) in the amplitude of spontaneous contractions between obstructed bladders and normal adult bladders.

DISCUSSION

The present results indicate that the temperature response of the isolated whole urinary bladder preparation in vitro is a sensitive indicator of developmental and pathological changes in the smooth muscle. Comparisons of the amplitude of spontaneous as well as electrically evoked bladder contractions across a broad range of temperatures (19–38°C) revealed that in young neonatal rats (2 day-2 wk of age), high temperatures increased the amplitude of contractions, whereas in older neonates (4–6 wk of age) and adult rats, high temperatures decreased the amplitude of the contractions. Preparations from adult animals with chronically obstructed bladders or from 3-wk-old neonates that had enlarged and apparently obstructed bladders exhibited relatively small changes in contractile amplitude with changes in temperature. Because alterations in temperature are thought to change smooth muscle contractility by influencing voltage-gated Ca²⁺ channels and/or intracellular Ca²⁺ release (21, 28), the present findings indicate that Ca²⁺ signaling mechanisms in the neonatal and obstructed bladders are markedly different than in normal adult bladders.

Fig. 8. Effects of 6-hydroxydopamine (6-OHDA, 100 mg/kg ip everyday for 10 days after birth) on relationship between temperature and intravesical pressure (A) and frequency (B) of spontaneous bladder contractions in isolated whole bladder of 5-wk-old rat. Each value is mean ± SE of 4 preparations. Linear regression is drawn in each figure.

Shifts in temperature elicited two prominent effects in the whole bladder preparations: 1) a change in frequency of spontaneous contractions and 2) a change in amplitude of contractions. The change in frequency was similar in preparations of all ages, consisting of a marked increase in frequency with an increase in temperature. Although all preparations exhibited the temperature response, some differences were noted between preparations when the relationship between bladder wall movements and pressure waves was compared. At low temperatures, there was a one-to-one correlation, however, at high temperatures in older neonates and adult rat bladders, the ratio of the number of movements to pressure waves ranged from 2 to 8. This did not occur in young neonates (1–3 wk of age), which had a ratio between one and two. The increase in frequency at high temperatures could occur by several mechanisms: 1) an effect of temperature on the properties of stretch-activated channels that are thought to initiate spontaneous bladder contractions (28), 2) a depolarizing shift in the muscle resting membrane potential (10), or 3) desynchronization of muscle activity, leading to the initiation of spontaneous contractions at various sites in the bladder wall. The increased ratio of wall movements to pressure waves at high temperatures in older preparations supports the latter mechanism.

The change in the amplitude of the contractions at different temperatures is more complicated, because the changes were age and pathology dependent. Although the temperature effects were more obvious on spontaneous contractions, they also occurred with electrically evoked contractions that were blocked by TTX and, therefore, mediated by neurotransmitters released by intramural nerves. The effect of cold temperatures to enhance the contractility of bladders from older animals was not surprising, because cooling is known to increase the contractility of smooth muscle from various organs including the bladder (10, 19, 21). Cold temperatures can also increase the contractile responses to excitatory agents such as cholinergic and adrenergic agonists (8, 20). It has been proposed that cooling can act by several mechanisms. For example, the extent of myosin light chain phosphorylation is higher at lower temperature than at higher temperature (16). Cooling could suppress the activity of an electrogenic Na⁺-K⁺ pump and, thereby, depolarize the...
smooth muscle cells (19). The ability of quabain to enhance smooth muscle contractility has been attributed in part to this mechanism. An effect of cold on intracellular Ca$^{2+}$ mechanisms may also play a role (8, 21). Inhibition of Ca$^{2+}$ ATPase, which is known to participate in the extrusion and sequestration of Ca$^{2+}$, could lead to an increase in intracellular Ca$^{2+}$ and, thereby, enhance contractile activity (21). An increase in baseline tone at low temperatures in older bladders would be consistent with this mechanism.

The opposite effect of temperature changes on the contractility of bladders from young neonates suggests that contractile and/or Ca$^{2+}$ mechanisms are very different in immature and mature bladder muscle. This difference was also obvious in the rise time of the contractions; the rise time in younger bladders being faster than in older bladders, especially at lower temperatures (Figs. 2 and 3). The electrical coupling between muscle cells and, therefore, the spread of excitatory activity through the bladder could be correlated with the rise time of the contractions, because these contractions presumably start at a particular site and then extend to the entire bladder. The presence at high temperatures of synchronous activity in young bladders but desynchronized activity in older bladders (12) is consistent with the concept of better coupling in the young bladders. This might reflect the smaller size of the muscle cells in the neonate or the presence of more efficient electrical coupling between cells.

Bladders removed from adult rats with chronic partial urethral obstruction or from neonatal rats at 3 wk of age did not exhibit a prominent change in contraction amplitude at different temperatures, although the frequency of contractions did increase at high temperatures. Why might obstructed adult and 3-wk-old bladders exhibit similar properties? Both types of bladders had an increased volume threshold for inducing spontaneous activity, suggesting that both bladders were enlarged and obstructed. At 3 wk of age in the neonatal rat, voiding function changes dramatically. The bladder-to-bladder reflex emerges, and the perigenital-to-bladder reflex activated by the mother licking the perineum is less likely to be triggered because the pups start to eat solid food, are more active, and spend less time nursing from their mother. It seems reasonable to assume that if the supraspinal bladder-to-bladder reflex is not fully developed during this transition period and if, at the time, perigenital stimulation is performed less frequently, the pups will exhibit urinary retention similar to adult animals with urethral obstruction. At 4 wk of age, the volume threshold returned to a lower level, possibly reflecting maturation of the bladder-to-bladder reflex pathway and the emergence of efficient voiding in the older animal.

The reason for the flat temperature response curve in obstructed and 3-wk-old neonatal rats is uncertain. It is known that chronic obstruction can elicit several changes in bladder smooth muscle, including 1) a decrease in the rate of rise and increase in the duration of the action potential, 2) a reduction in the time and space constant of the muscle, 3) a reduction in spontaneous activity, 4) an increase in Na$^{+}$-K$^{+}$ pump activity, and 5) decreased contraction velocity (17, 18). Obstruction also reduced the temperature-frequency response curve in the present experiments and significantly reduced the ratio between bladder wall movements and pressure waves at normal body temperature. Thus the obstructed bladder in comparison to the normal bladder appears to have more synchronized spontaneous activity at higher temperatures. This might account for the observation in vivo that obstructed bladders exhibit relatively large-amplitude spontaneous ("unstable") contractions in the absence of neural input. In normal adult bladders, spontaneous activity increases at higher temperatures but also becomes desynchronized so that the amplitude of the contractions decreases. This does not occur in obstructed adult or neonatal bladders. Desynchronization may be induced by a high level of spontaneous activity of individual muscle cells that renders them less susceptible to the spread of electrical activity from adjacent cells and, thereby, prevents coordinated contractions of the entire bladder. A reduction in the spontaneous activity of individual bladder muscle cells that is known to occur in obstructed bladders (17) can paradoxically facilitate spread of excitation throughout the bladder and, thereby, induce large amplitude intrinsic pressure waves.

The role of the sympathetic nervous system in the maturation of bladder function is of interest because it has been reported that the sympathetic innervation of the rabbit bladder and the responsiveness to catecholamines develops postnatally (11). In addition, in the hypogastric ganglion, which provides an innervation to the urogenital organs, tyrosine hydroxylase activity is low during the first postnatal week in the rat and increases markedly during the third to seventh postna-
nal week (7). However, chemical sympathectomy with 6-OHDA during the first postnatal week had a small influence on the temperature characteristics of the bladder removed from 5-wk-old rats, indicating that sympathetic nerves are not essential for the developmental changes. Because the parasympathetic innervation is functional at birth and the afferent pathways are also present during the first postnatal week (25), it would appear that innervation is not a critical factor in the maturation of the temperature response of the bladder.

In summary, the isolated whole bladder of neonatal and adult rats exhibits intrinsic activity that varies in amplitude and frequency depending on the temperature of the superfusion solution. In preparations of all ages, the frequency of spontaneous bladder activity increased with increasing temperature; however, age and pathology influenced the effect of temperature on the amplitude of spontaneous activity. At higher temperatures, contractions increased in amplitude in bladders from 1- to 2-wk-old rats but decreased in bladders from older neonates and adult rats. The transition from the immature to mature pattern occurred in 3-wk-old bladders that had a relatively flat temperature-amplitude curve. It is speculated that the decrease in amplitude at higher temperatures is caused by desynchronization of bladder activity and initiation of contractile responses at many loci in the bladder wall. At lower temperatures, activity is more coordinated, originating at one site from which it spreads throughout the bladder. Desynchronization may function to maintain low intravesical pressures during bladder filling and, thereby, contribute to continence; whereas synchronization can lead to large amplitude intrinsic bladder contractions and may create bladder instability and hyperactivity. In this regard, it is noteworthy that the chronically obstructed bladder of the adult rat, which is known to be hyperactive (15), exhibited a temperature-response pattern similar to that of a 3-wk-old neonatal rat. This suggests that neonatal bladder like the adult obstructed bladder is intrinsically hyperactive. This feature may be useful to promote voiding during the developmental period when the central nervous control is immature and inefficient. On the other hand, the normal adult bladder exhibits intrinsic properties that promote storage function and continence. In the adult, coordinated smooth muscle activity necessary for voiding is generated by central reflex mechanisms. The intrinsic hyperactivity of the neonatal bladder may be regulated in vivo by a tonically active inhibitory neural pathway that is driven by inputs from the spinal cord (25).

Perspectives

Intercellular communication in bladder smooth muscle appears to change during postnatal development. Isolated whole bladders from neonatal rats maintained at body temperature exhibited large amplitude rhythmic contractions, indicating synchronous activation of muscle cells. However, bladders from adult rats exhibited small amplitude contractions, indicating poor intercellular communication and asynchronous activity. These data suggest that the neonatal bladders are less efficient than adult bladders in storing urine. This may reflect the persistence in the postnatal period of properties of the fetal bladder, which functions more as a conduit for urine drainage than as a reservoir for urine storage. Large-amplitude rhythmic bladder contractions in the fetus could function as peristaltic waves to continually empty the bladder. The existence in neonatal rats of tonic neural inhibitory input from the spinal cord to the bladder (25) may act to suppress this intrinsic bladder activity. Bladders from neonatal and mature rats also responded differently to stepwise reductions in temperature. Rhythmic contractions increased in amplitude in bladders from mature rats and decreased in bladders from neonatal rats. This might be related to alterations in intracellular release and/or reuptake of Ca2++. This change occurred at ~3 wk of age when rat pups began to void reflexly in response to bladder distension. Because maturation of neural voiding mechanisms occurs in concert with changes in smooth muscle activity, it is tempting to speculate that neural activity may contribute to the emergence of the storage functions of the mature bladder smooth muscle.

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