

BLADDER REDUCTION SURGERY ACCELERATES THE APPEARANCE OF SPONTANEOUS VOIDING IN NEONATAL RATS

Hypothesis / aims of study: Patients with nocturnal enuresis may have a small functional bladder capacity or altered sensation of bladder fullness. Could abnormal bladder capacity affect how the brain senses bladder fullness? The perigenital-bladder reflex, which requires the mother rat to lick the perigenital area of rat pups to empty the bladder, is present between birth and 2 weeks of life, until it is replaced by the supraspinal bladder-bladder reflex at 3 weeks of life. Neonatal rats do not show voiding contractions under urethane anesthesia until they are 3 weeks old. At the same time, in-vitro myogenic spontaneous bladder contractions peak at 2 weeks of life and start to decrease at 3 weeks of life. We wished to determine if experimental reduction of bladder volume could affect the maturation of voiding reflexes or bladder smooth muscle.

Study design, materials and methods: Pilot studies on 32 animals comparing 3 different methods of bladder reduction were carried out. Subsequently, 1 and 3 week old Sprague-Dawley rats underwent 50% reduction of bladder volume using the optimal method (n=33) or sham surgery (n=31). T₈-T₁₀ spinalization was performed in another 12 animals. The latency of the perigenital-bladder reflex, onset of spontaneous voiding, and body weight were measured. Cystometry under urethane anesthesia, and measurements of in-vitro spontaneous and KCl-evoked contractions were performed.

Results: Bladder reduction by suturing the anterior and posterior dome together, combined with an external ligature, most consistently produced a 50% reduction in urine volume emptied by perigenital stimulation. Bladder reduction by this method led to the immediate appearance of spontaneous voiding in 1 week old rats. Cystometry at 2 weeks showed voiding contractions in rats that had undergone bladder reduction (n=8), which could be abolished by acute T₈-T₁₀ spinalization (n=4). Voiding contractions were not seen in animals that underwent sham surgery (n=4) or concurrent T₈-T₁₀ spinalization and bladder reduction (n=3). The perigenital-bladder reflex, somatic growth, spontaneous bladder contractions, and bladder contractility were not affected by bladder reduction. Bladder capacity at 9 weeks was significantly larger in animals undergoing bladder reduction at 1 week (n=5) compared to sham animals (n=4), 540 vs 256 μ l (p=0.04), and maximum voiding pressure was also lower, 32.1 vs. 50.8 cm H₂O (p=0.04), but not in animals undergoing bladder reduction at 3 weeks.

Interpretation of results: Bladder reduction surgery allows for the early appearance of the supraspinal bladder-bladder reflex in 1 week old rats. This change may be due to lowering of external urethral sphincter pressure. The early emergence of the bladder-bladder reflex does not cause regression of the perigenital-bladder reflex, nor does it cause a more rapid down-regulation of in-vitro spontaneous bladder contractions. Bladder reduction at 1 week of life stimulates remodelling of the bladder into a larger organ, but this regenerative ability is lost if bladder reduction is carried out at 3 weeks of life. It appears that while maturation of bladder / sphincter coordination and bladder smooth muscle occur at the same time, the neural mechanism underlying the switch from the perigenital-bladder to bladder-bladder reflex is not responsible for stabilizing the bladder smooth muscle.

Concluding message: Bladder reduction surgery removes the central inhibition of spontaneous voiding in the neonatal rat. This suggests that changes in neonatal bladder capacity can alter how the central nervous system regulates the bladder.

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Is this a clinical trial?	No
What were the subjects in the study?	ANIMAL
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	Yes
Name of ethics committee	Animal Experimentation Ethics Committee, Chinese University of Hong Kong