Background: Incomplete bladder emptying due to detrusor underactivity (DU) is a significant problem underlying underactive bladder (UAB). Also, TRPV4 has been reported to be one of the mechanosensitive channels expressed in the bladder. In this study, we sought to produce a consistent rat model of UAB with pelvic nerve crush (PNC) and evaluated the therapeutic effect of intravesical application of a TRPV4 agonist (GSK 1016790A) on the UAB condition.

Materials and Methods: [Animal model] In Female Sprague-Dawley rats, the visceral branches of bilateral pelvic nerves were identified near the internal iliac vessels, and bilateral PNC was made by two times of nerve compression of either side with each 20–second duration using sharp forceps.

Results:
1. Morphology: Bladder weight was significantly increased in PNC rats (Normal=0.078±0.012, PNC=0.22±0.012, p<0.0001).
2. Awake CMG (Fig.1): PNC rats showed significant increases in voided volume, post-void residual urine volume, and residual urine rate compared to control rats. PNC rats also revealed the significant increases in inter contraction intervals (ICI), a number of non-voiding contractions, and threshold pressure while the amplitude of bladder contraction during voiding was significantly decreased.
3. Intravesical TRPV4 administration to normal rats (Fig.2): Intravesical 1.5μM of GSK 1016790A application did not significantly affect any CMG parameters.
4. Intravesical TRPV4 administration to PNC rats (Fig.3): Intravesical 1.5μM of GSK 1016790A significantly decreased ICI, voided volume, and post-void residual urine volume in PNC rats.
5. mRNA expression of TRPV4 in the bladder mucosa was significantly increased in PNC rats compared to the normal rats (p=0.0013)(Fig.4).
6. PNC rats exhibited impaired urethral relaxation during isovolumetric (ISO) bladder contraction (Fig.5).

Conclusions:
1. Rats with pelvic nerve injury induced by a PNC method, which showed the characteristics of DU, seem to be an appropriate model for evaluation of peripheral neurogenic mechanisms of UAB.
2. TRPV4 that reduced the bladder capacity and residual urine volume in PNC rats could be a potential target for the treatment of UAB.
3. PNC rats had impaired urethral relaxation. The therapy to enhance urethral relaxation may be effective for UAB treatment.