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NEUROMUSCULAR NICOTINIC RECEPTORS MEDIATE BLADDER CONTRACTIONS FOLLOWING REINNERVATION WITH GENIOTOFEMORAL TO PELVIC NERVE TRANSFER

Hypothesis / aims of study

Following bladder denervation by transection of sacral spinal cord roots, genitofemoral nerve (GFN) transfer to vesical branches of the pelvic nerve (GFNT) reinnervates the canine bladder as demonstrated by bladder contraction during functional electrical stimulation of the transferred GFN. Anterograde lipophilic dye tracing studies showed that new neuronal pathways established by root transection and immediate repair, or by either genitofemoral or coccygeal nerve transfer, reinnervate both intramural bladder ganglia and detrusor smooth muscle cells directly. It is not known whether the new pathway induces bladder contraction normally with neuronally released acetylcholine activating bladder smooth muscle muscarinic receptors or whether the direct innervation of detrusor smooth muscle involves other neurotransmitters and receptors. This study investigates whether the reinnervated neuronal pathway mediates contraction via the same neurotransmitter and receptor mechanisms as the original pathway.

Study design, materials and methods

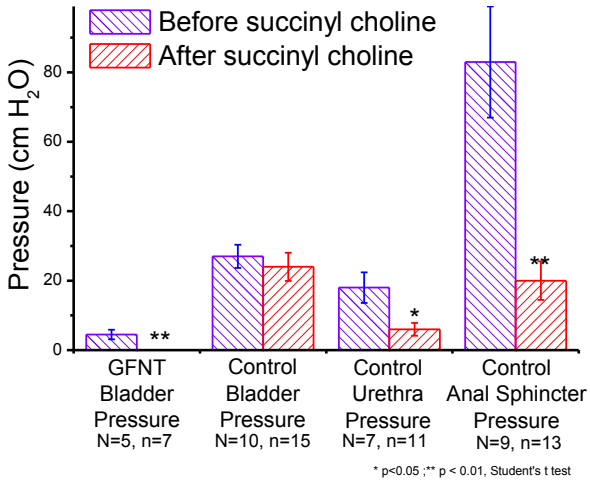
Bladder, urethra and anal sphincter denervation: With the animal in the prone position, a 30° V laminectomy of the T7 vertebral body and partial laminectomies of the T6 and S1 vertebral bodies were done so that the sacral ventral roots innervating the bladder could be stimulated with a unipolar probe electrode. The two bilateral ventral roots that induced increased bladder pressure upon intraoperative electrical stimulation were transected. In the initial animals, completeness of bladder denervation was confirmed by an absence of bladder contractions upon stimulation of the entire conus medullaris using an epidural electrode placed in the midline under the T5 vertebral body.

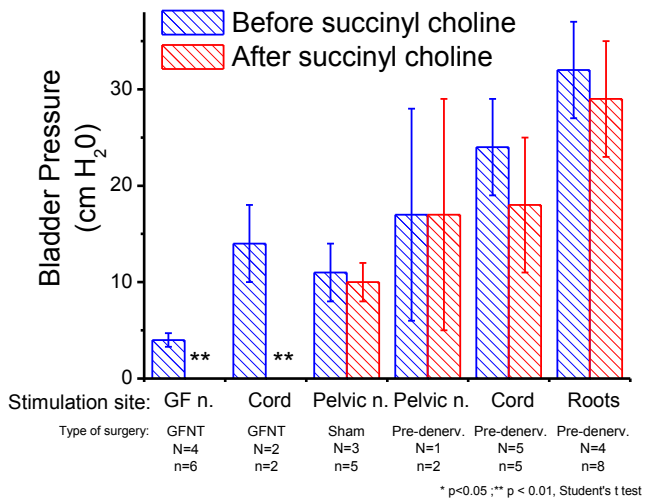
Nerve transfer: After denervation, GFN were transferred bilaterally to vesical branches of the pelvic nerve and implanted with nerve cuff electrodes interfaced with Bion radiofrequency micro-stimulators (RFMS). RFMS are completely implanted and can be activated with an induced current produced by an external coil. Emptying of the denervated neurogenic bladder was accomplished with an abdominal vesicostomy. Once bladder reinnervation occurred (25±4 weeks post operatively), the effect of GFN stimulation on bladder pressure was determined before and 10 minutes after neuromuscular blockade with 1.5 mg/kg succinyl choline in 5 GFNT animals. For controls, the effects of succinyl choline on bladder contractions was determined by intraoperative electrical stimulation of the entire lumbosacral spinal cord in 2 dogs, by stimulation of sacral spinal nerve roots in 4 dogs, and by stimulation of vesical branches of the pelvic nerve in 4 dogs.

Results

Functional electrical stimulation (FES) results: Of the 12 animals with GFNT, 10 (83%) demonstrated functional bladder reinnervation as evidenced by increased bladder pressure during stimulation of the transferred GFN in isoflurane anesthetized dogs. This was observed bilaterally in 3 dogs, and unilaterally in 7. Activation of the RF micro-stimulators interfaced with nerve cuff electrodes surrounding the transferred GFN resulted in increased bladder pressure in 7 animals (58%), bilaterally in 2 and unilaterally in 5.

Effects of neuromuscular blockade with succinyl choline: In normal control animals (either non-operated or sham operated) succinyl choline had no effect on bladder pressure induced by stimulation of either the lumbosacral spinal cord or the S2-3 spinal roots. Succinyl choline substantially reduced urethra and anal sphincter pressure induced by spinal cord or nerve root stimulation. In animals with bladder reinnervation by genitofemoral nerve transfer, bladder pressure increases induced by stimulation of either the transferred genitofemoral nerves or the L2-3 spinal cord (genitofemoral nerve origin), were completely blocked by succinyl choline.





Interpretation of results

Although the GFN transfers were performed bilaterally, physiological evidence of bilateral functional reinnervation was observed in only 3 of the 10 animals with return of bladder function. Based on these results it must be concluded that unilateral reinnervation surgery cannot be recommended.

In the normal bladder, all axons in the pelvic nerve innervate intramural postganglionic (parasympathetic) ganglia cells; this pathway is not blocked by succinyl choline. Anterograde labeling methods showed that root repair (repair of the transected nerves using the same nerve root that normally innervates the bladder) or nerve transfer using different nerves, lead to reinnervation of intramural ganglia as well as direct regrowth of axons to the bladder detrusor muscle. The new neuronal pathway, achieved by GFNT, was blocked by succinyl choline.

Concluding message

These data suggest that succinyl choline sensitive nicotinic receptors that normally mediate only skeletal muscle neuromuscular junction neurotransmission, appear in the new neuronal pathway to the detrusor muscle after GFNT. This suggests neuroplasticity in the end organ after reinnervation by somatic motor axons.

References

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Disclosures

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