105

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RECOVERY OF BLADDER AND BOWEL FULLNESS SENSATION BY NERVE TRANSFER IN A CANINE DECENTRALIZED BLADDER MODEL

Hypothesis / aims of study

Motor reinnervation of the decentralized canine urinary bladder was previously confirmed by increased detrusor pressure induced by electrical stimulation of the transferred genitofemoral or femoral nerves in 21 of 28 animals.[1] Evidence of bladder and bowel fullness sensation in these new neuronal pathways was also reported based on observation, using video surveillance cameras over the housing cages, of micturition and defecation postures in the reinnervated animals.[2] These behavior observations provide the most global assessment of whether or not the animals have been able to recover bladder and bowel function. In order to completely prove that the reinnervation surgeries are responsible for restoring these functions, it is necessary to demonstrate that these behaviors are not observed in decentralized animals that have not undergone nerve transfer surgeries. Our focus here was to determine whether these postures are eliminated in decentralized animals and assess sensory nerve reinnervation with retrograde neurotracing techniques.

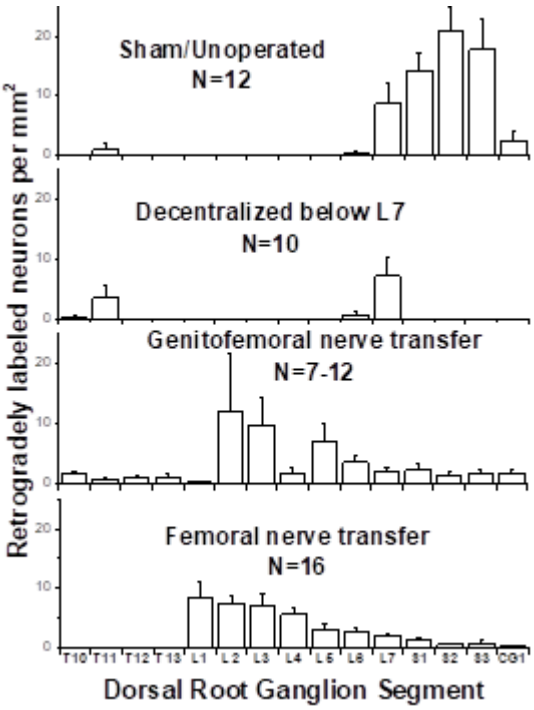
Study design, materials and methods

The pelvis was decentralized by bilateral transection of hypogastric nerves and all spinal nerve roots caudal to L7 in 6 female canines. A separate group of 8 animals was decentralized identically with the additional bilateral transection of L7 dorsal roots. Video surveillance allowed measurement of the frequency and duration of urination and defecation postures over 24 hours at monthly intervals post operatively (PO) by observers blinded to the surgical interventions. In the 8 animals with the additional L7 dorsal root transections and in 3 unoperated controls, conscious filling cystometrogram recordings were done and then the bladder was filled to this cystometric capacity, the Foley catheter was removed, the animals were placed in a transport cage and observed for micturition behavior over the following 10 minutes. Any bladder contents expelled during this period was collected, measured and compared to the cystometric capacity volume that was perviously infused into the bladder. Retrograde neurotracing from the bladder to dorsal root ganglia (DRG) was done by cystoscopic injection of Fluoro-Gold at 4 sites around each ureterovesical junction 3 weeks prior to euthanasia and quantitating Fluoro-Gold labeled neuronal cell bodies in the DRG at spinal segments from the 10th thoracic through the 1st coccygeal level. DRG retrograde tracing results are also presented for the 28 animals from the previous investigation in which the genitofemoral nerve or branches of the femoral nerve were transferred to anterior vesical branches of the pelvic nerve in which motor reinnervation of the bladder was confirmed by functional electrical stimulation of the transferred nerves.[1]

Results

In the 6 animals with intact L7 dorsal roots, all 6 showed micturition postures but only 2 of these 6 showed defecation postures at each monthly 24 hour observation period from the first through the 12th postoperative month. In the 8 animals with the additional L7 dorsal root transection, none showed defecation postures up to 12 months PO. One has shown no micturition postures over 12 months PO and one has shown 2 single incidences of micturition postures at 5 and 10 months PO. Three of the 6 that did show consistent micturition postures at monthly observation periods were euthanized at 8-9 months PO. Urinalysis and cultures were performed in the remaining 5 animals. Four of the 5 showed microhematuria. Triple phosphate struvite crystalluria was found in 2, both of which were culture positive (Proteus mirabilis in one and both Proteus and Enterococcus species in the other). Two of the other animals were culture positive for Enterococcus species and, as of this submission, these urinary tract infections have resolved in 3 of these 4 following Enrofloxacin treatment. Filling cystometrograms were not performed in animals with active urinary tract infections but 4 of the 5 have been tested 3 times at weekly intervals and only 1 of these 4 showed micturition postures on one single occasion at the end of the 10 minute observation period with the bladder filled to cystometric capacity. All of the 3 unoperated control animals showed micturition postures within 3 minutes after removal of the Foley catheter and recovered voided volume was 75-79% of their cystometric bladder capacity.

Retrograde neurotracing results in these animals and cohorts of animals from previous investigations are shown in the figure at the right. A substantial number of bladder sensory neuronal cell bodies in the L7 DRG are observed in both the sham/unoperated normal controls as well as the decentralized group without L7 dorsal root transection. DRG labeling results from the bladder has not yet been done in the animals decentralized with the additional L7 dorsal root transections. Of interest, this L7 DRG labeling was much less in the genitofemoral and femoral nerve to anterior vesical branch of the pelvic nerve transfer groups. Substantial DRG labeling was observed in the L2-L5 level in the genitofemoral nerve transfer group and in the L1-L4 level in the femoral nerve transfer groups reflecting the spinal origin of these transferred nerves.



Interpretation of results

Although the L7 DRG labeling in the decentralized group may explain the micturition postures observed in these animals, because there was much more labeling in the DRG segments from the donor nerves in the nerve transfer groups (both genitofemoral and femoral nerve transfer), there is a high possibility that bladder sensation is being transmitted through the new neuronal pathways in these nerve transfer animals.

Concluding message

In the L7 dorsal root intact decentralized group, all were able to sense bladder fullness and 2 of 6 could detect bowel fullness suggesting residual sensory bladder innervation likely from the remaining lower lumbar dorsal root fibers. Fewer dogs with the additional L7 dorsal root transection were able to detect bladder fullness. The ability of 6 of 8 animals in the L7 dorsal root transected decentralized group to sense bladder fullness may be from sensory nerve sprouting or variations in the bladder sensory innervation, as described previously.[3] Bowel fullness sensation appears to be primarily mediated by sacral sensory innervation. The substantial L1-L5 DRG labeling in the nerve transfer groups strongly supports the hypothesis that both bladder and bowel fullness sensation are transmitted through these new neuronal pathways established by the nerve transfer surgery. These conclusions will be further tested by observation of whether or not micturition and defecation postures and bladder emptying behavior returns with nerve transfer surgery to be performed in these animals one year after the decentralization surgery.

References

1. Gomez-Amaya SM, et al Bladder reinnervation using a primarily motor donor nerve (femoral nerve branches) is functionally superior to using a primarily sensory donor nerve (genitofemoral nerve). Journal of Urology. 2015; 193(3):1042-51. PMC4305355.
2. Ruggieri MR, Sr., et al Sensation of bladder fullness by a new neuronal pathway established by genitofemoral or femoral nerve transfer to an anterior vesical pelvic nerve branch in a canine decentralized bladder model. Journal of Urology. 2016;195(4):e373.
3. Gomez-Amaya SM, et al. Gross anatomical study of the nerve supply of genitourinary structures in female mongrel hound dogs. Anatomia, Histologia, Embryologia: Veterinary Medicine Series C. 2015;44(2):118-27. PMC4198519

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