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EVIDENCE OF VAGUS NERVE SPROUTING TO INNERVATE THE URINARY BLADDER AND CLITORIS IN A CANINE MODEL OF LOWER MOTONEURON LESIONED BLADDER.

Hypothesis / aims of study

The vagus nerve is only thought to innervate the gastrointestinal tract as far caudally as the left colonic flexure in the dog and the transverse colon in the human whereas the descending colon, rectum and pelvic viscera receive their parasympathetic neuronal supply from the sacral cord via the pelvic splanchnic nerves. This is supported by the finding that electrical stimulation of the vagus nerve in the neurally intact dog has no effect on bladder pressure [1]. In humans, complete spinal cord injury does not block perceptual responses to genital self-stimulation [2] and functional magnetic resonance imaging (FMRI) shows activation of the inferior region of the solitary nucleus (medullary origin of the vagus nerve) induced by cervical self-stimulation in complete spinal cord injured women [3]. We tested the hypothesis that after bladder decentralization, the vagus nerve endings may sprout to innervate the pelvic viscera such as the urinary bladder, urethra, anal sphincter and clitoris.

Study design, materials and methods

A canine lower motoneuron lesioned bladder model was created by transecting all sacral nerve roots that induce increased detrusor pressure upon intraoperative electrical stimulation and all nerve roots caudal to S1. Four different types of bladder reinnervation surgeries were performed in a total of 27 female mongrel hounds: 1) bilateral genitofemoral nerve (GFN) to bilateral pelvic nerve (PN) transfer with vesicostomy (GFNT-V: n=12); 2) bilateral GFN to bilateral PN transfer without vesicostomy (GFNT: n=5); 3) left femoral nerve (FN) to bilateral PN transfer with vesicostomy (FNT-V: n=5); and 4) left FN to bilateral PN transfer without vesicostomy (FNT: n=5). Bladder emptying in animals without vesicostomies was accomplished by the Credé maneuver during the eight month recovery period (242±6.2days). Three weeks prior to euthanasia retrograde nerve labeling dyes were injected: fluorogold into the bladder wall lateral to the ureteral orifices, fast blue into the urethral sphincter, nuclear yellow into the anal sphincter, and fluoro ruby bilaterally into the clitoris. At euthanasia, functional reinnervation was evaluated by increased detrusor pressure induced by functional electrical stimulation (FES) of spinal cord segments, spinal roots or the transferred peripheral nerves. Spinal cord segments were examined for fluorescent labeled neuronal cell bodies. To determine whether the vagus nerve sprouted, the nodose ganglion and the solitary nucleus of the medulla were also examined for fluorescent dye labeled neuronal cell bodies.

Results

Return of bladder function was observed as follows: 1) in 8 of 12 GFNT-V dogs after direct stimulation of transferred GF nerve or lumbar spinal roots (mean detrusor pressure = 1.9±0.6 cm H2O); 2) in 4 of 5 GFNT dogs after direct stimulation of transferred GFN or FES of lumbar spinal cord segment contributing to GF nerve origin (L2-3; mean detrusor pressure = 4.7±1.7 cm H2O); 3) in all 5 FNT-V dogs after transcutaneous stimulation of transferred FN, or direct stimulation of lumbar cord segment or spinal roots contributing to FN origin (L2-5; mean detrusor pressure = 11.2±2.5 cm H2O); and 4) in 4 of 5 FNT dogs after direct stimulation of transferred FN or FES of lumbar cord segment contributing to FN origin (mean detrusor pressure = 4.8±1.3 cm H2O). In all animals with no FES induced increased detrusor pressure indicating no functional bladder reinnervation, no fluorogold labeled neuronal cell bodies were found in lamina IX of spinal ventral horns of spinal segments L2-5 (FN origin) or L3-4 (GFN origin) except for 1 of the 12 GFN-V animal in which spinal cord cell bodies were observed but FES did not induce increased detrusor pressure. In all other animals with FES induced increased detrusor pressure, abundant fluorogold labeled cell bodies were observed in the appropriate segments for the transferred GFN or FN in lamina IX of the spinal ventral horns.

Nodose ganglia were examined in 2 of the GFNT animals (one with and one without FES induced increase in detrusor pressure) and all 5 FNT-V animals. Solitary nuclei were examined in the same 2 GFNT animals and 3 of the 5 FNT-V animals. Nodose ganglia cell bodies retrogradely labeled with fluoro ruby from the clitoris were observed in both GFNT animals and 4 of the 5 FNT-V animals. Nodose ganglia cells labeled with fluorogold from the urinary bladder were not observed in the 2 GFNT animals but were seen in 3 of the 5 FNT-V animals. Solitary nucleus cell bodies labeled with fluoro ruby from the clitoris were seen in the GFNT animal with FES induced detrusor pressure and in 3 of the 3 FNT-V animals. Solitary nucleus cells labeled with fluorogold from the bladder was also observed in the same GFNT animals and in 2 of the 3 FNT-V animals. Fast blue labeled cell bodies from the urethra or fluoro ruby labeled cell bodies from the anal sphincter were observed in neither the nodose ganglia nor the solitary nuclei.

Interpretation of results

The FES results indicate that although the bladder can be reinnervated by nerve transfer using either the GFN or FN as donor nerve, the FN is more efficient likely due to its primarily motor function as opposed to the primarily sensory function of the GFN. This was confirmed by the observance of retrograde labeled neuronal cell bodies in the spinal segments of the transferred nerves. Evidence of vagal nerve sprouting was observed to innervate the bladder and, in a larger number of animals, the clitoris while no evidence of vagal innervation of the urethra or anal sphincters was seen.

Concluding message

These surgical approaches may be useful for patients with lower motor spinal cord injury to accomplish bladder emptying, improving their quality of life. The observed vagal nerve sprouting to innervate the clitoris 8 months after pelvic decentralization may offer an explanation for the previously reported genital self-stimulation induced perceptual responses and FMRI observed solitary nucleus activation in complete spinal cord injured women [2, 3].

References

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Disclosures

Funding: Funded by a PHS grant (1R01NS070267) from the National Institute of Neurological Disorders and Stroke, NIH, to Drs. Barbe and Ruggieri. **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Canine **Ethics Committee:** Temple University Institutional Animal Care and Use Committee in compliance with the United States Department of Agriculture and the Association for Assessment and Accreditation of Laboratory Animal Care International.