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EFFECTS OF PHYSICAL ACTIVITY ON URINARY TRACT FUNCTION AFTER SPINAL CORD INJURY

Hypothesis / aims of study

Bladder management following spinal cord injury (SCI) has an enormous impact on quality of life as it requires intermittent catheterization throughout the day/night to control and avoid incontinence, bladder overdistention (which can create high pressure and reflux to the kidneys), inflammation, infections, and autonomic dysreflexia. Restoring bladder function is ranked as a top priority of the SCI population. Locomotor training (LT) has emerged as a safe and effective therapy for post-SCI motor deficits with many benefits (cardiovascular function, strength, mobility). Several human case studies and anecdotal reports have documented improvements in bladder function due to LT strategies. In addition, it is also known that exercise and activity dependent tasks are highly influential on a family of molecules called neurotrophic factors which are involved in neuronal maintenance, plasticity, growth, and repair. Nerve growth factor, one member of the neurotrophin family, is particularly indicative of bladder dysfunction after SCI and in other models has recently been suggested to be a potential biomarker of bladder dysfunction and recovery. Thus, our goal was to determine in a clinically relevant rat SCI model if LT could improve bladder function and to examine the effects of exercise on neurotrophic levels in bladder.

Study design, materials and methods

The Infinite Horizon impactor device (Precision Systems and Instrumentation, LLC; Fairfax Station, VA) was used to make a clinically relevant contusion injury (225 kilodyne; under ketamine/xylazine anesthesia) at the T9 spinal level. SCI male Wistar rats were randomly divided into 3 groups two weeks post-injury: quadrupedal-trained (n=16), forelimb-trained (n=16; exercise controls), and non-trained controls (n=14). Seven rats were used as non-injured controls (surgical shams). The quadrupedal-trained group of rats followed a step-training regimen over a treadmill belt assisted by a body weight support system (Exer-3R treadmill from Columbus Instruments). The forelimb only group was treated the same way, except the hind limbs were slightly elevated so they did not come in contact with the treadmill. Training was initiated 14 days after injury for one hour a day seven days a week for ten weeks. Metabolic cages (a six station CLAMS unit) was used once a week for all SCI rats throughout the course of the 10 week period of training to measure the rats' fluid intake and urine output. Filling cystometry (non-stop transvesical) experiments were conducted at the end of training for all groups of rats (done while awake, two hours after catheter implantation under brief gas anesthesia). Following the recordings, rats were immediately perfused for tissue retrieval (spinal cord lesion site, kidney and bladder tissue). Western blots were done to assess the expression of two proteins in the kidneys whose presence are indicative of tissue stress or damage (TGFβ and CD11b). Bladder tissue was divided into two; half was used for measuring connective tissue proteins that provide tensile strength and elasticity (elastin and collagen – using ELISA kits), and half was used for assessing neurotrophic factor content (NGF, BDNF and NT-3) with RNA extraction and real-time reverse transcription polymerase chain reaction (qRT-PCR).

Results

Both quadrupedal and forelimb training for 60 minutes per day returned mean urine volume (24-hour production) toward pre-injury levels with a significant reduction in the average volume per void relative to the non-trained SCI controls. There were no differences in the total number of urine events and total amount of water intake between groups. Cystometry data indicate a significant increase in maximal amplitude of contraction for only the non-trained SCI group relative to sham controls. Contraction time, intercontraction interval and peak pressure did not differ between groups. Analysis of the various markers in kidney and bladder tissue related to urinary tract function also indicate a benefit of exercise training post-injury (only the SCI non-trained control group differed from non-injured sham controls – TGFβ and NGF/NT-3, respectively). There were however, no differences in bladder weight and the ratio of elastin-to-collagen between SCI groups and no differences in extent of spinal cord damage (epicenter lesion area and total lesion volume).

Interpretation of results

The metabolic and cystometry data indicate larger amplitudes of contraction and volumes per void post-SCI relative to SCI groups receiving daily physical activity, suggesting that exercise including LT reduces SCI-induced persistent polyuria (increased urine production). The return of select biomarkers in kidney and bladder tissue toward more normal levels indicates a further benefit of exercise training post-injury. In addition, preliminary experimental data obtained from human SCI subjects (part of a different study being done in parallel) indicate a benefit of exercise on bladder function post-SCI, both alone as well as in combination with epidural stimulation.

Concluding message

Our studies to date indicate that activity based training can influence urologic outcomes which is of great important to persons with SCI. These novel findings suggest that physical activity after SCI could translate to significant quality of life gains.

Disclosures

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