

THE DEVELOPMENT OF ABERRANT BLADDER REFLEXES THAT DRIVE HIND LIMB LOCOMOTOR ACTIVITY FOLLOWING COMPLETE SUPRASACRAL SPINAL CORD INJURY

Hypothesis / aims of study

Many rats with chronic suprasacral spinal cord injury (SCI) demonstrate hind limb locomotor activity in response to external crede or high pressure non-voiding and voiding contractions during cystometry. We propose that this aberrant, pressure-driven bladder reflex pathway might be utilized to facilitate walking in SCI patients. As a first step in exploring this possibility, we examined the relationship between intravesical pressure (IVP) and hind limb locomotor activity in chronic, complete suprasacral SCI rats.

Study design, materials and methods

Female rats (4 weeks post-SCI at T9-10, n=16) were anesthetized with isoflurane and fitted with suprapubic bladder catheters and right quadriceps EMG electrodes to monitor bladder and hind limb locomotor activities, respectively. The animals were mounted in Ballman restraint cages to which they had been previously acclimated. The catheter was connected to a pressure transducer, an infusion pump, and a saline-filled reservoir mounted on a metered vertical pole (pressure clamp). After 30 min of recovery from anaesthesia, the bladder was filled at 0.1 ml/min with saline to verify bladder-to-bladder reflex activity. Next, after a total of 1 hr since anaesthesia, IVP was increased in an interrupted stepwise fashion from 0-120 cmH₂O at 10 cmH₂O increments. Each step consisted of five minutes: 3 minutes at the new pressure followed by 2 minutes at 0 cmH₂O. Bladder pressures and the number of locomotor events (as defined by rhythmic EMG discharges of 3-10 cycles/event) were recorded for each pressure step. This process was repeated for two more trials for each rat to assess the durability of the reflex. Data were analysed using ANOVA with repeated measures both within and across pressure escalation trials. P<0.05 was considered significant.

Results

ANOVA revealed that locomotor events increased with increasing IVP and decreased with the number of escalation trials (P<0.0001 for both effects). The increase in the number of locomotor events with increasing IVP appeared to plateau at ~50-60 cmH₂O (P<0.05 for all). The average of the maximal number of locomotor events for each animal decreased steadily from ~3.0, 2.5 and 1.75 over the three trials.

A similar pattern in the relationship between IVP and bladder contraction frequency during clamped baseline pressures was also observed, with plateau of bladder contraction frequency also at ~50-60 cmH₂O. This may be expected by an interaction of the filling rate to volume threshold as IVP is increased and the limits of the bladder smooth muscle to contract and relax maximally (i.e. during high pressure non-voiding or voiding contractions).

Interpretation of results

While these results indicate that there is a relationship between IVP and hind limb locomotor activity, this relationship is not linear with throughout the range of IVP utilized in this study. This latter observation suggests either that a limiting factor exists or that baseline IVP is not the main driver for hind limb locomotor activity. That the frequency of high pressure bladder contractions is both similarly related to IVP and is associated with hind limb locomotor activity suggests that it is the high pressure contraction event itself that is driving hind limb locomotor activity, rather than baseline or even peak contraction IVP. Previous studies of vagal tension-related afferents in the gastrointestinal system have suggested the existence of afferents in parallel and in series with smooth muscle bundles that behave differently depending on state of distension and contraction [1]. Thus, our new hypothesis is that it is the mismatch between the partial reduction of tension on afferents in parallel and the increase of tension on afferents in series during a bladder contraction at full bladder distension (i.e. during clamped IVP) that is responsible for triggering the hind limb locomotor central pattern generator in the spinal cord. To our knowledge, this is the first report of such an afferent signalling pathway from the urinary bladder, a visceral organ innervated by the sacral parasympathetic nucleus. Thus, it is the relationship between IVP and bladder contraction frequency that indirectly drives hind limb locomotor activity, rather than baseline IVP as originally hypothesized. That such an afferent drive from the urinary bladder to the hind limb locomotion central pattern generator does not exist normally suggests the development of novel connections to the higher level thoraco-lumbar central pattern generator [2] by lumbo-sacral bladder afferents as part of the development of mass reflexes distal to the SCI.

Concluding message

There is a positive relationship between high pressure bladder contractions and hind limb locomotor activity during increases in baseline IVP that suggests the emergence of an aberrant bladder-to-hind limb locomotor reflex pathway following SCI. This reflex pathway may be driven by a mismatch between tension afferents in parallel and in series with bladder smooth muscle bundles during high pressure bladder contractions under conditions of full bladder distension by IVP clamped pressures. Interactions of signals from both in series and in parallel afferents have been suggested [3], but have not been described previously as far as we have been able to ascertain. Finally, it may be possible to harness this reflex pathway independently of the state of the bladder.

References

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2. Harris-Warrick R, 2013, Encyclopedia of Computational Neuroscience, Springer Science + Business Media, New York
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