

ARTICLE



Locomotor-respiratory coupling in ambulatory adults with incomplete spinal cord injury

Tommy W. Sutor¹, David D. Fuller² and Emily J. Fox^{2,3}✉

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STUDY DESIGN: Observational, analytical cohort study.

OBJECTIVES: After incomplete spinal cord injury (iSCI), propriospinal pathways may remain intact enabling coupling between respiration and locomotion. This locomotor-respiratory coupling (LRC) may enable coordination between these two important behaviors and have implications for rehabilitation after iSCI. However, coordination between these behaviors is not well understood and it is unknown if iSCI disrupts LRC. The objective of this study was to compare LRC in ambulatory adults with iSCI to able-bodied controls.

SETTING: Rehabilitation Research Center, Jacksonville, Florida, United States of America.

METHODS: Adults with iSCI (4 males, 1 female) and able-bodied controls (2 males, 3 females) walked at their fastest comfortable speed for 6 min over ground, and on a treadmill with bodyweight support (10–20%) and as-needed assistance at a standardized fast speed (controls) or their fastest speed (iSCI) for 6 min. LRC was quantified as the percent of breaths that were coupled with steps at a consistent ratio during the last 4 min of each walking condition.

RESULTS: Over ground, participants with iSCI demonstrated significantly more LRC than able-bodied controls ($72.4 \pm 6.4\%$ vs. $59.1\% \pm 7.5$, $p = 0.016$). During treadmill walking, LRC did not differ between groups (iSCI $67.5 \pm 15.8\%$ vs. controls $66.3 \pm 4.0\%$, $p > 0.05$).

CONCLUSIONS: Adults with iSCI demonstrated similar or greater LRC compared to able-bodied controls. This suggests that pathways subserving coordination between these behaviors remain intact in this group of individuals who walk independently after iSCI.

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INTRODUCTION

Incomplete spinal cord injury (iSCI) affects critical functions such as breathing and walking. Impaired breathing increases the risk of respiratory infections and hospitalization [1], and impaired walking negatively impacts mobility and daily activities [2]. In recent years, several studies have examined possible relationships between breathing and locomotion in the context of iSCI rehabilitation. For example, treadmill locomotor training can enhance accessory breathing muscle activation and improve breathing ability [3, 4], and over ground locomotor training can reduce variability in the ventilatory response to exercise [5]. However, temporal coordination between these two behaviors, known as locomotor-respiratory coupling (LRC), is largely unexplored in humans with iSCI. In quadrupeds, LRC is hypothesized to be driven by aspects of locomotion such as internal organ movements and by neural communication between spinal locomotor networks and brainstem respiratory control centers [6–9]. Similarly in humans, the basis of LRC is thought to depend on communication between locomotor and respiratory centers [10, 11]. Understanding how these functions are coordinated may ultimately influence rehabilitation decisions and development of strategies to improve breathing and walking outcomes.

One approach to quantify LRC in humans is examining “coupling frequency ratios”. This approach quantifies the frequency and consistency with which steps are coordinated with breathing (e.g., steps:breaths) and is based on extensive animal literature [12, 13]. For instance, in animal models, rhythmic limb afferent electric stimulation entrains phrenic nerve output frequency at various ratios – e.g., 2 limb stimulations: 1 phrenic burst, 3:1, 3:2, etc. [8, 14, 15]. Similar coupling frequency ratios have been observed during walking in able-bodied humans [12] and people with chronic obstructive pulmonary disease [13]. Importantly, when quantified using coupling frequency ratios, LRC is not significantly influenced by walking speed [12]. This is particularly important for the study of various populations who have walking impairments, such as those with iSCI.

Human iSCI often results in damage to propriospinal pathways as well as connections between the spinal cord and brainstem nuclei [16]. Damage to these pathways has the potential to alter or abolish LRC after iSCI. Indeed, coupling is abolished in rats if afferent spinal pathways are transected [8]. Disruption of coordination between the locomotor and respiratory system may have important implications. For example, during endurance exercise in able-bodied individuals, decreased limb afferent

¹Research Service, North Florida/South Georgia Veterans Health System, Gainesville, FL, USA. ²Department of Physical Therapy, University of Florida, Gainesville, FL, USA. ³Brooks Rehabilitation, Jacksonville, FL, USA. ✉email: ejfox@php.ufl.edu

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feedback impairs breathing adaptations and decreases performance [17, 18]. Accordingly, reduced or impaired limb afferent feedback after human iSCI may impair breathing during walking, reducing endurance. Despite its potential importance for rehabilitation and SCI outcomes, little is known about the effects of iSCI on coordination between the locomotor and respiratory systems. A single case report in a person with iSCI demonstrated increased LRC during walking following 36 sessions of intense walking rehabilitation [19].

Understanding the effects of iSCI on LRC may provide insight about the neural connections enabling the coordination of breathing and walking after iSCI, and may inform future rehabilitation decisions for walking, breathing, or both. Therefore, the primary aim of this proof of concept pilot study was to compare LRC in adults with iSCI to able-bodied controls. We hypothesized that LRC would be reduced in people with iSCI.

METHODS

Participants

Adults with iSCI were recruited from a rehabilitation health system (Jacksonville, FL). Eligible participants were at least 6 weeks post iSCI C4-T12, with no concurrent neurological conditions such as traumatic brain injury or neurologic disease. Neurologic level and severity of injury was verified by a physical therapist expert in SCI and the International Standards for the Neurologic Classification of Spinal Cord Injury [20]. Non-injured, able-bodied adults were recruited from a convenience sample. Experimental protocols were approved by the University of Florida Institutional Review Board. All participants provided written informed consent prior to participation.

Breathing and walking characterization

Breathing ability was determined with maximal inspiratory and expiratory pressure tests using a handheld clinical manometer (MicroRPM, BD, Franklin Lakes, NJ, USA), and with a forced vital capacity test using a clinical spirometer (SpiroUSB, CareFusion, Yorba Linda, CA, USA). Testing procedures were standardized to adhere to American Thoracic Society guidelines [21]. A 10 m walk test assessed fastest comfortable walking speed, and a 6 min walk test assessed walking endurance [22]. Participants completed the tests using their typical assistive devices. For the 6 min walk test, participants were instructed to walk at their fastest comfortable pace around a 20 m circumference oval which minimized sharp turns requiring speed changes.

Locomotor-respiratory coupling data collection

During walking tests, stride cycles were recorded using electrogoniometers (Biometrics Ltd, Ladysmith, VA, USA) adhered to the lateral knee. Breath cycles were recorded with a temperature thermistor (Thought Technology Ltd, Montreal West, Quebec, Canada) secured under the participant's nostrils with medical tape. A mask over the participants' nose and mouth ensured that the thermistor detected temperature changes associated with inhalation and exhalation. The electrogoniometer and thermistor were connected to a wearable data encoder (FlexComp, Thought Technology Ltd, Montreal West, Quebec, Canada). Knee angle and breath timing were continuously recorded during walking at 500 Hz and transmitted via Bluetooth to Thought Technology's DcuDesigner software. Session data was converted into.txt files and stored for off-line analysis.

Previous reports have shown that voluntary attempts to synchronize breathing and locomotion rhythms substantially increases LRC relative to spontaneous coupling [23, 24]. Therefore, to ensure spontaneous LRC, all participants were provided general information and informed that the study was investigating breathing and walking after SCI. Participants were also asked to not talk and were not allowed to listen to music during bouts of walking, as sound can effect spontaneous LRC [25].

The 6 min walk test was used to assess LRC over ground (OG condition). Following this, participants performed a 6 min bout of treadmill walking (TM condition) with partial bodyweight support (Robomedica, Mission Viejo, CA, USA; or Woodway, Waukesha, WI, USA, Aretch, Ashburn, VA, USA) in a harness (Robertson Harness, Ft. Collins, CO, USA) at a predicted fast walking speed. A minimal amount of bodyweight support needed for each participant to voluntarily and

consistently step without upper extremity support was used. Our rationale was that the TM condition could enable a more rhythmic, consistent stepping pattern and therefore might influence the afferent input associated with locomotion and therefore influence LRC. The TM condition also enabled the use of an individualized target speed. The purpose of the target speed was to standardize speeds for each individual and facilitate comparisons. TM target speeds used the Froude number and were determined with the equation [26]:

$$V = \sqrt{l^*g^*Fr}$$

Where V = velocity (meters/second), l = participant leg length (meters), g = acceleration due to gravity (meters/second), and Fr = Froude number, a dimensionless value used to predict an individual's comfortable walking speed or the speed at which one transitions from walking to running [27]. In this study, a Froude number of 0.41 was used to predict a fast walking speed when accounting for leg length and bodyweight support provided as done previously [26].

If necessary, participants with iSCI were provided manual assistance at the legs and pelvis using standardized techniques [28] to achieve their predicted fast target speed. If the target speed was not accomplished, the percent of target walking speed achieved was noted.

Quantification of locomotor-respiratory coupling

Data were analyzed using Spike2 (CED, Cambridge, England). Peak knee flexions and initiation of each inhalation from the last 4 min of each walking bout were automatically detected and custom scripts were used to compute how many steps occurred per each consecutive breath.

For each participant coupling frequency ratios were calculated. Similar to previous methods [12, 24], a period of LRC was defined as at least four consecutive coupling frequency ratios with a consistent number of peak knee flexions per breath, if the ratio could be expressed as a whole integer. For example, four or more consecutive breath cycles in which three peak knee flexions occur is considered a period of coupling at a ratio of 3:1. If two different ratios occur in a consistent pattern for four or more breath cycles, this is also considered frequency coupling (Fig. 1). For each participant, the total percentage of breaths coupled at any ratio was determined, and the overall percent of coupled breaths (LRC) was compared between groups for each condition.

Statistics

Due to the small sample size, non-parametric Mann-Whitney U tests were used to compare 10 m walk times, 6 min walk distances, breathing ability, and overall LRC between groups for the OG and TM conditions. Statistical analyses were conducted with IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, N.Y., USA).

RESULTS

Participant characterization

Participant characteristics are reported in Tables 1 and 2. Participants with iSCI (four males, one female) and able-bodied controls (two males, three females) did not differ on age, maximal inspiratory and expiratory pressures, or forced vital capacity. Able-bodied controls walked significantly faster ($p = 0.008$) and farther ($p = 0.008$) on the 10MWT and 6MWT, respectively. Participants with iSCI received 20% bodyweight support during the TM condition, while able-bodied participants received 10% bodyweight support, mainly to stabilize the overhead support bar.

Locomotor-respiratory coupling

Participants with iSCI displayed more LRC ($72.4 \pm 6.4\%$) than able-bodied controls ($59.1\% \pm 7.5$) in the OG condition ($p = 0.016$). In the TM condition, participants with iSCI did not reach their target fast speed. Target speeds for fast walking on the treadmill for participants with iSCI ranged from 1.65–1.79 m/s. On average, they achieved 56.8% of their predicted fast speed (range: 0.58–1.2 m/s). Between-group comparisons of LRC indicated that participants with iSCI who walked at their fastest TM speed did not differ in LRC ($67.5 \pm 15.8\%$) compared to able-bodied controls walking at their predicted fast ($66.3 \pm 4.0\%$) speeds. Details are provided in Table 3.

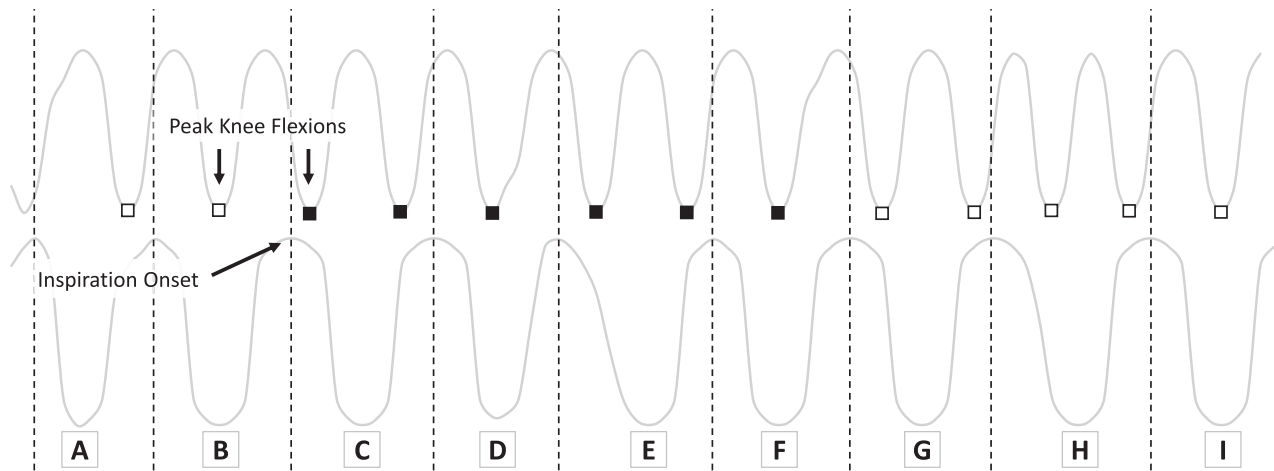


Fig. 1 Example data demonstrating coupling between walking and breathing. Traces represent knee angle (top trace), peak knee flexions (squares) and breathing (bottom trace) with onset of inspiration (dotted lines). Panels C–F show four consecutive breaths that consistently alternate between a 2:1 and 1:1 coupling frequency ratios (consistent alternating number of knee flexions highlighted as black squares). Breaths C–F are coupled at a 3:2 coupling frequency ratio.

Table 1. Participant characteristics.

	Age	Gender	10MWT (m/s)	6MWT (m)	MIP (cmH ₂ O)	MEP (cmH ₂ O)	FVC (% APM)
AB participants							
AB1	23	F	1.98	468.6	135	126	101
AB2	21	F	2.02	672	78	83	79
AB3	31	M	1.89	611.5	78	80	90
AB4	23	F	2.39	669.6	85	120	94
AB5	29	M	2.15	606.2	106	103	99
Average	25.4	N/A	2.09	605.6	96.4	102.4	93
SD	4.3	N/A	0.2	82.6	24.4	20.9	8.7
iSCI participants							
iSCI1	43	F	1.14	370	74	101	94
iSCI2	33	M	1.67	395.3	108	117	75
iSCI3	64	M	1.69	362.4	87	90	88
iSCI4	41	M	1.25	324.5	76	59	74
iSCI5	21	M	2.30	469.7	49	83	85
Average	40.40	N/A	1.61	384.38	78.80	90.00	83
SD	15.8	N/A	0.5	54.0	21.4	21.6	8.6
Between-group significance	$p > 0.05$		$p = 0.008$	$p = 0.008$	$p > 0.05$	$p > 0.05$	$p > 0.05$

AB Able-bodied controls, 10MWT 10 m walk test, 6MWT 6 min walk test, MIP Maximal inspiratory pressure, MEP Maximal expiratory pressure, FVC Forced vital capacity, %APM Percent of age-predicted maximum, SD Standard deviation.

Table 2. Injury characteristics of iSCI participants.

Participant ID	Injury level	Time since injury (months)	Lower extremity motor score (out of 50)	Assistive device
iSCI1	T12	5	28	rolling walker
iSCI2	C5	25	47	none
iSCI3	T6	3	50	cane
iSCI4	C5	52	49	none
iSCI5	C3	36	48	none

DISCUSSION

Contrary to our hypothesis, the five participants with iSCI demonstrated greater LRC during OG walking, and no differences in overall LRC during TM walking, compared to able-bodied controls. Study outcomes reflect a small sample of individuals with

differing walking abilities and characteristics – these and other factors are discussed in subsequent sections.

A possible explanation of study outcomes may be that in this group of ambulatory individuals with iSCI, spared pathways were sufficient to enable coupling between walking and breathing.

Table 3. Results.

	OG LRC	TM LRC	Predicted fast TM speed (m/s)	
AB participants				
AB1	63.8%	62.6%	1.8	
AB2	66.7%	66.4%	1.8	
AB3	55.4%	72.7%	1.7	
AB4	61.7%	63.3%	1.9	
AB5	47.9%	66.7%	1.8	
Average	59.1%	66.3%	1.8	
SD	7.5%	4.0%	0.1	
iSCI participants			Obtained speed (m/s)	
iSCI1	77.5%	82.8%	1.7	0.6
iSCI2	64.7%	65.4%	1.8	1.2
iSCI3	69.3%	42.0%	1.7	1.0
iSCI4	80.4%	70.2%	1.7	1.0
iSCI5	70.3%	77.3%	1.8	1.1
Average	72.4%	67.5%	1.7	1.0
SD	6.4%	15.8%	0.1	0.2
Between-group significance	$p = 0.016$	$p > 0.05$		

The bold values are meant to emphasize the group averages and standard deviations.

AB Able-bodied controls, OB Over ground, TM Treadmill, LRC Locomotor-respiratory coupling, SD Standard deviation.

More specifically, our hypothesis was based on animal literature demonstrating that spinal cord injury abolishes the influence of lumbar afferents on phrenic motor output [8, 29]. Thus, we theorized that an incomplete injury to the spinal cord would partially disrupt the ascending influence of lumbar afferents, reducing but not abolishing LRC. However, a surgical transection of dorsal spinal cord tissue (i.e., in a rodent model) is not necessarily analogous to injuries sustained by people with iSCI. Human iSCI can involve substantial motor and sensory sparing [30] such as evident in study participants. Incomplete injuries often spare considerable spinal cord tissue which serves as a substrate for functional recovery of neural networks and associated interactions [30–32].

Spinal locomotor networks can remodel after iSCI, including the formation of “detour circuits” formed between surviving propriospinal neurons and other spinal cord tracts [30, 31]. Propriospinal neurons play a critical role in processing sensory and motor information, and often increase sprouting after injury to establish these detour circuits [31, 32]. Participants with iSCI in this study had substantial sensory and motor sparing, possibly due to both uninjured spinal tissue as well as via propriospinal neuron-derived detour circuits. Additionally, since these individuals walked at home and in the community full time, ongoing use of these pathways may have strengthened connections between the respiratory and locomotor centers. Theoretically, residual pathways, sprouting or use-dependent plasticity could promote connections between lumbar afferents and supraspinal respiratory centers, enabling preservation of LRC after iSCI.

Although LRC has been investigated across species, in varying forms of locomotion, and using varied methodologies (for a comprehensive review, see Stickford and Stickford [10]), the results of this pilot study are most comparable to investigations of LRC using coupling frequency ratios in populations with breathing or walking impairments [12, 13]. In particular, individuals with chronic obstructive pulmonary disease, which impairs both breathing and walking [33], demonstrate greater LRC than those without chronic obstructive pulmonary disease during treadmill walking (over ground walking was not assessed) [13]. In this study, LRC differences were not evident during TM walking, but all participants received bodyweight support and participants with

iSCI received more support than controls. This is a difference between the TM and OG conditions where all participants walked without bodyweight support (similar to previous reports) and participants with iSCI had higher LRC. It is possible that full weight bearing during walking influences LRC. Furthermore, people with iSCI often have elevated responses to afferent input, i.e., that manifest as hyperactive reflexes [34]. An increased response to afferent input may exert a greater influence on breathing, explaining higher LRC in participants with iSCI over ground when both groups bore full bodyweight. This is speculative, as responses to afferent input were not tested in this study; determining responses to afferent input, influences on LRC, and the role of partial or full bodyweight bearing requires further experimentation.

Limitations

Methodological limitations may have influenced the outcomes of this study. In particular, the iSCI group characteristics were not fully matched to those in the control group. The individuals with iSCI were older (mean age of 40 years) than the individuals in the control group, and 4 of 5 individuals with iSCI were male. These characteristics, however, align closely with characteristics of the SCI population. Additionally, greater variability is evident in the age and 10MWT times in the iSCI group. Although participants with iSCI walked slower than able-bodied controls, participants with iSCI were relatively high functioning; 4 out of 5 participants had lower extremity motor scores approximating normal, and all were full time community ambulators. Thus, the results of this study may not generalize to other individuals with iSCI, such as those with more severe injuries and greater impairments. Lastly, while analyses of factors like injury level, severity, or chronicity on LRC were beyond the scope of this pilot study, future investigations should consider these influences.

Future directions and implications

This pilot study contributes to the evidence of preserved LRC in adults with walking and breathing impairments. Collectively, outcomes across studies and in individuals with varying diagnoses (i.e., iSCI and COPD) suggest that LRC may be a fundamental characteristic of walking (i.e., since breathing always occurs with

walking, but walking isn't always performed during breathing), similar to other coordination features such as arm swing or trunk rotation [35]. These coordination aspects also are thought to be mediated by propriospinal pathways and interactions between rhythmic networks.

Understanding of LRC may be useful for development of comprehensive rehabilitation strategies and understanding of outcomes based on current approaches. For instance, if residual pathways enabling interactions between walking and breathing are preserved after iSCI, then examining the effects of walking characteristics and impairment on breathing would be warranted. Investigating LRC in a feed-forward context, i.e., altering breathing rhythm or ventilatory resistance, to determine the effects on LRC or walking control may be valuable. Such investigations are warranted given that brainstem breathing control centers can influence lumbar locomotor centers [36, 37], and voluntary breathing maneuvers can influence the excitability of non-breathing limb muscles [38]. Additionally, it would be valuable to investigate LRC during other locomotor behaviors such as during use of cycle ergometers and electrical stimulation enabled cycling or other rhythmic reciprocal activities. This could allow exploration of LRC in people with more severe iSCI, particularly since breathing deficits can be more severe in people with higher injury levels or motor complete SCIs [39–41].

CONCLUSION

Outcomes from five ambulatory individuals with iSCI suggest LRC remains intact after injury and may occur at increased rates relative to able-bodied controls. The walking and breathing abilities demonstrated by these individuals suggest that pathways subserving coordination of these behaviors were preserved in these individuals.

DATA AVAILABILITY

The datasets generated and/or analyzed are available upon reasonable request.

REFERENCES

- Krause JS, Cao Y, DeVivo MJ, DiPiro ND. Risk and protective factors for cause-specific mortality after spinal cord injury. *Arch Phys Med Rehabil*. 2016;97:1669–78.
- Riggins MS, Kankipati P, Oyster ML, Cooper RA, Boninger ML. The relationship between quality of life and change in mobility 1 year postinjury in individuals with spinal cord injury. *Arch Phys Med Rehabil*. 2011;92:1027–33.
- Terson de Paleville D, McKay W, Aslan S, Folz R, Sayenko D, Ovechkin A, et al. Locomotor step training with body weight support improves respiratory motor function in individuals with chronic spinal cord injury. *Respir Physiol Neurobiol*. 2013;189:491–7.
- Tiftik T, Gokkaya NK, Malas FU, Tunc H, Yalcin S, Ekiz T, et al. Does locomotor training improve pulmonary function in patients with spinal cord injury? *Spinal cord*. 2015;53:467–70.
- Panza GS, Guccione AA, Chin LM, Gollie JM, Herrick JE, Collins JP, et al. Effects of overground locomotor training on the ventilatory response to volitional treadmill walking in individuals with incomplete spinal cord injury: a pilot study. *Spinal Cord Ser Cases*. 2017;3:17011.
- Boggs DF. Interactions between locomotion and ventilation in tetrapods. *Comp Biochem Physiol A Mol Integr Physiol*. 2002;133:269–88.
- Bramble DM, Carrier DR. Running and breathing in mammals. *Science*. 1983;219:251–6.
- Morin D, Viala D. Coordinations of locomotor and respiratory rhythms in vitro are critically dependent on hindlimb sensory inputs. *J Neurosci*. 2002;22:4756–65.
- Le Gal J-P, Juvin L, Cardoit L, Morin D. Bimodal respiratory-locomotor neurons in the neonatal rat spinal cord. *J Neurosci*. 2016;36:926–37.
- Stickford ASL, Stickford JL. Ventilation and locomotion in humans: mechanisms, implications, and perturbations to the coupling of these two rhythms. *Springer Sci Rev*. 2014;2:95–118.
- Banzett RB, Mead J, Reid MB, Topulos GP. Locomotion in men has no appreciable mechanical effect on breathing. *J Appl Physiol* (1985). 1992;72:1922–6.
- O'Halloran J, Hamill J, McDermott WJ, Remelius JG, Van Emmerik RE. Locomotor-respiratory coupling patterns and oxygen consumption during walking above and below preferred stride frequency. *Eur J Appl Physiol*. 2012;112:929–40.
- Yentes JM, Denton W, Samson K, Schmid KK, Wiens C, Rennard SI, et al. Energy efficient physiologic coupling of gait and respiration is altered in chronic obstructive pulmonary disease. *Acta Physiol (Oxf)*. 2019;225:e13217.
- Iscoe S, Polosa C. Synchronization of respiratory frequency by somatic afferent stimulation. *J Appl Physiol*. 1976;40:138–48.
- Hormigo KM, Zholudeva LV, Spruance VM, Marchenko V, Cote M-P, Vinit S, et al. Enhancing neural activity to drive respiratory plasticity following cervical spinal cord injury. *Exp Neurol*. 2017;287:276–87.
- Laliberte AM, Goltash S, Lalonde NR, Bui TV. Propriospinal neurons: essential elements of locomotor control in the intact and possibly the injured spinal cord. *Front Cell Neurosci*. 2019;13:512. <https://doi.org/10.3389/fncel.2019.00512>.
- Amann M, Blain GM, Proctor LT, Sebranek JJ, Pegelow DF, Dempsey JA, et al. Group III and IV muscle afferents contribute to ventilatory and cardiovascular response to rhythmic exercise in humans. *J Appl Physiol* (1985). 2010;109:966–76.
- Amann M, Blain GM, Proctor LT, Sebranek JJ, Pegelow DF, Dempsey JA, et al. Implications of group III and IV muscle afferents for high-intensity endurance exercise performance in humans. *J Appl Physiol* (1985). 2011;589:5299–309.
- Sherman MF, Lam T, Sheel AW. Locomotor-respiratory synchronization after body weight supported treadmill training in incomplete tetraplegia: a case report. *Spinal Cord*. 2009;47:896–8.
- Kirshblum SC, Burns SP, Biering-Sorensen F, Donovan W, Graves DE, Jha A, et al. International standards for neurological classification of spinal cord injury (revised 2011). *J Spinal Cord Med*. 2011;34:535–46.
- American Thoracic Society/European Respiratory Society. ATS/ERS Statement on respiratory muscle testing. *Am J Respir Crit Care Med*. 2002;166:518–624.
- van Hedel HJ, Wirz M, Dietz V. Assessing walking ability in subjects with spinal cord injury: validity and reliability of 3 walking tests. *Arch Phys Med Rehabil*. 2005;86:190–6.
- Rassler B, Kohl J. Analysis of coordination between breathing and walking rhythms in humans. *Respir Physiol*. 1996;106:317–27.
- Hill AR, Adams JM, Parker BE, Rochester DF. Short-term entrainment of ventilation to the walking cycle in humans. *J Appl Physiol* (1985). 1988;65:570–8.
- Hoffmann CP, Torregrosa G, Bardy BG. Sound stabilizes locomotor-respiratory coupling and reduces energy cost. *PLoS One*. 2012;7:e45206.
- Ruckstuhl H, Kho J, Weed M, Wilkinson MW, Hargens AR. Comparing two devices of suspended treadmill walking by varying body unloading and Froude number. *Gait Posture*. 2009;30:446–51.
- Kram R, Domingo A, Ferris DP. Effect of reduced gravity on the preferred walk-run transition speed. *J Exp Biol*. 1997;200:821–6.
- Behrman AL, Harkema SJ. Physical rehabilitation as an agent for recovery after spinal cord injury. *Phys Med Rehabil Clin N Am*. 2007;18:183–202.
- Le Gal J, Juvin L, Cardoit L, Thoby-Brisson M, Morin D. Remote control of respiratory neural network by spinal locomotor generators. *PLoS One*. 2014;9:e89670.
- Friedli L, Rosenzweig ES, Barraud Q, Schubert M, Dominici N, Awai L, et al. Pronounced species divergence in corticospinal tract reorganization and functional recovery after lateralized spinal cord injury favors primates. *Sci Transl Med*. 2015;7:302ra134.
- Bareyre FM, Kerschensteiner M, Raineteau O, Mettenleiter TC, Weinmann O, Schwab ME. The injured spinal cord spontaneously forms a new intraspinal circuit in adult rats. *Nat Neurosci*. 2004;7:269–77.
- Flynn JR, Graham BA, Galea MP, Callister RJ. The role of propriospinal interneurons in recovery from spinal cord injury. *Neuropharmacology*. 2011;60:809–22.
- Yentes JM, Rennard SI, Schmid KK, Blanke D, Stergiou N. Patients with chronic obstructive pulmonary disease walk with altered step time and step width variability as compared with healthy control subjects. *Ann Am Thorac Soc*. 2017;14:858–66.
- Thompson AK, Wolpaw JR. Restoring walking after spinal cord injury: operant conditioning of spinal reflexes can help. *Neuroscientist*. 2015;21:203–15.
- Klimstra MD, Thomas E, Stoloff RH, Ferris DP, Zehr EP. Neuromechanical considerations for incorporating rhythmic arm movement in the rehabilitation of walking. *Chaos*. 2009;19:026102.
- Boers J, Kirkwood PA, de Weerd H, Holstege G. Ultrastructural evidence for direct excitatory retroambiguus projections to cutaneous trunci and abdominal external oblique muscle motoneurons in the cat. *Brain Res Bull*. 2006;68:249–56.
- Ford TW, Kirkwood PA. Respiratory drive in hindlimb motoneurons of the anaesthetized female cat. *Brain Res Bull*. 2006;70:450–6.
- Li S, Rymer WZ. Voluntary breathing influences corticospinal excitability of nonrespiratory finger muscles. *J Neurophysiol*. 2011;105:512–21.

39. Linn WS, Spungen AM, Gong H, Adkins RH, Bauman WA, Waters RL. Forced vital capacity in two large outpatient populations with chronic spinal cord injury. *Spinal Cord*. 2001;39:263–8.
40. Mateus SR, Beraldo PS, Horan TA. Maximal static mouth respiratory pressure in spinal cord injured patients: correlation with motor level. *Spinal Cord*. 2007;45:569–75.
41. Raab AM, Krebs J, Perret C, Michel F, Hopman MT, Mueller G. Maximum inspiratory pressure is a discriminator of pneumonia in individuals with spinal-cord injury. *Respir Care*. 2016;61:1636–43.

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AUTHOR CONTRIBUTIONS

TWS, DDF, and EJF conceived and design the study protocol. TWS and EJF carried out study procedures and acquired data. TWS performed data analyses and designed the figure. TWS and EJF interpreted results. TWS drafted the initial manuscript and DDF and EJF contributed, provided edits and reviewed the final manuscript.

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

Correspondence and requests for materials should be addressed to Emily J. Fox.

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