Supplemental Information

Sleep disordered breathing is associated with brain vascular reactivity in spinal cord injury

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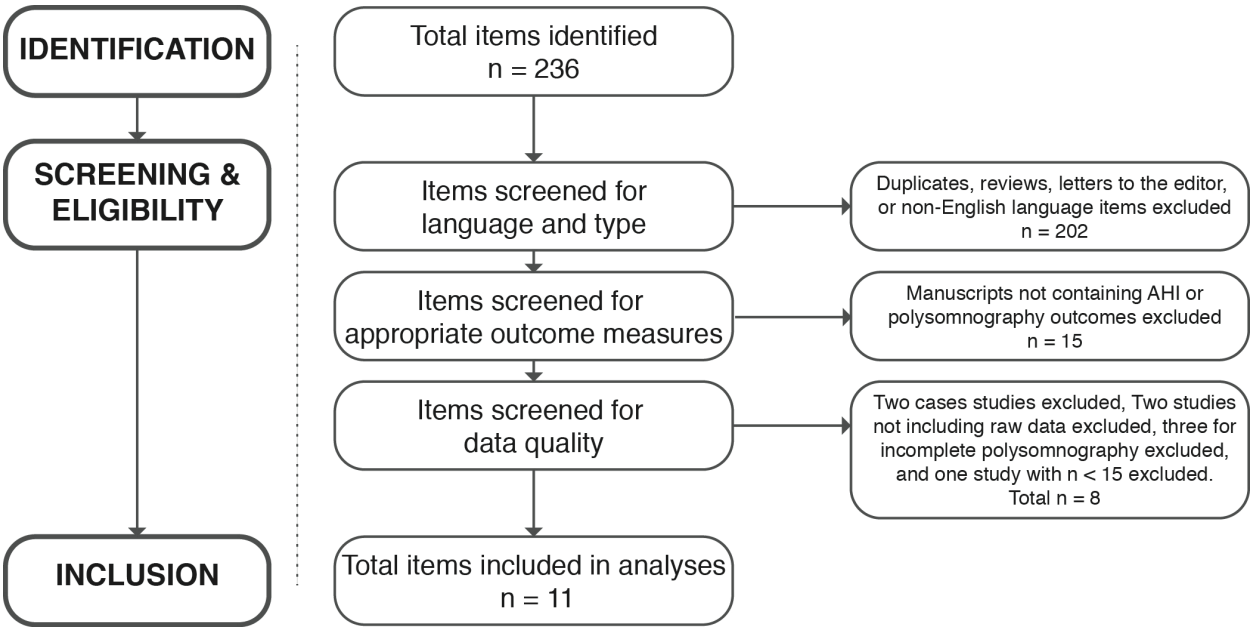

Figure e-1. Meta-analysis flow chart. Flow chart diagram describing meta-analysis methodology including the number of items identified, key screening and eligibility criteria, and final inclusion. Also see Table S3 for a final list of included studies. Abbreviations: AHI: Apnea-Hypopnea index.

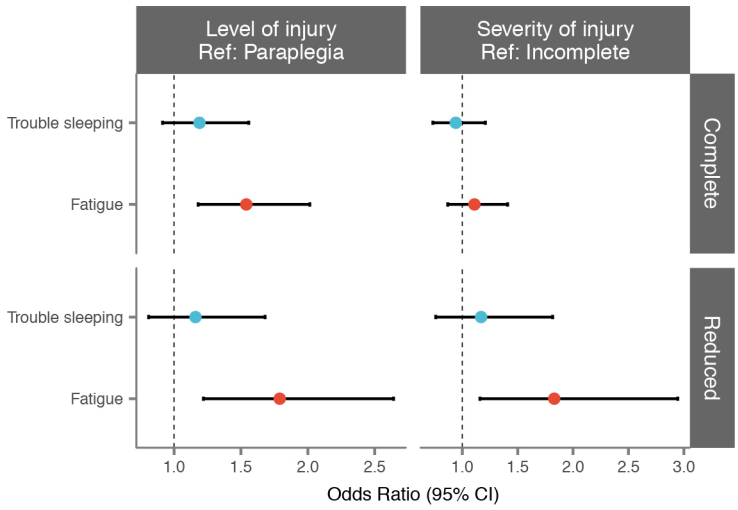

Figure e-2. Odds Ratio for Individuals with SCI from the SCI Community Health Survey. Odds ratios (OR) and 95% confidence intervals (CI; black lines) demonstrating severity and level dependence of trouble sleeping and fatigue in individuals with SCI. ORs are in relation to the relevant reference group. Dotted line represents equal odds between the experimental and reference group, for each comparison. Reduced datasets are subsets of the entire sample with only individuals with tetraplegia (for the severity of injury analysis) or complete injuries (for the level of injury analysis). Adjusted analyses accounted for age and sex.

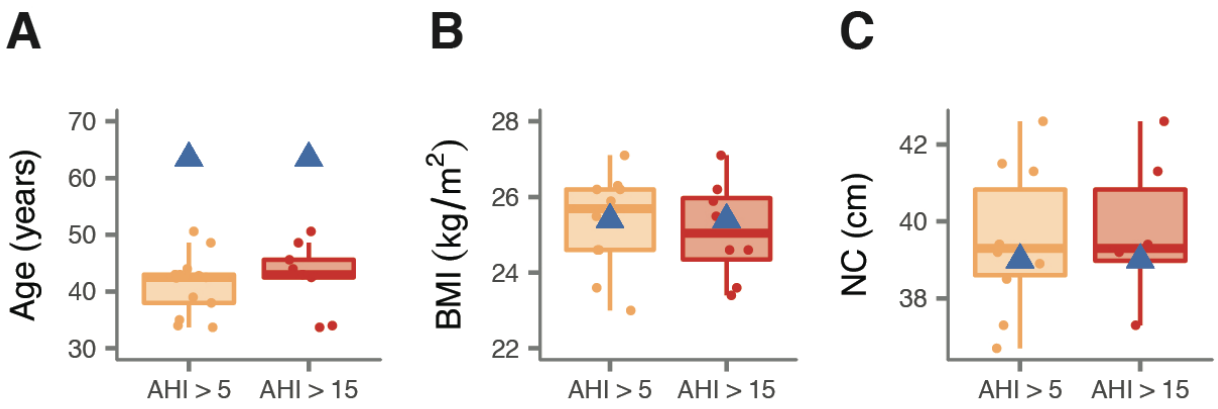

Figure e-3. Comparison of key factors between individuals with SCI and able-bodied reference data. Participant characteristics are similar for extracted data from the literature (points and box plots), compared to able-bodied data (blue triangles). This was true for studies examining Apnea-hypopnea index (AHI) > 5 and > 15. We examined age, body mass index (BMI) and neck circumference (NC). Of note is that the age of able-bodied individuals from the reference data was in fact higher, suggesting any observed increase in the prevalence of sleep apnea in individuals with spinal cord injury is not due to differences in this metric.

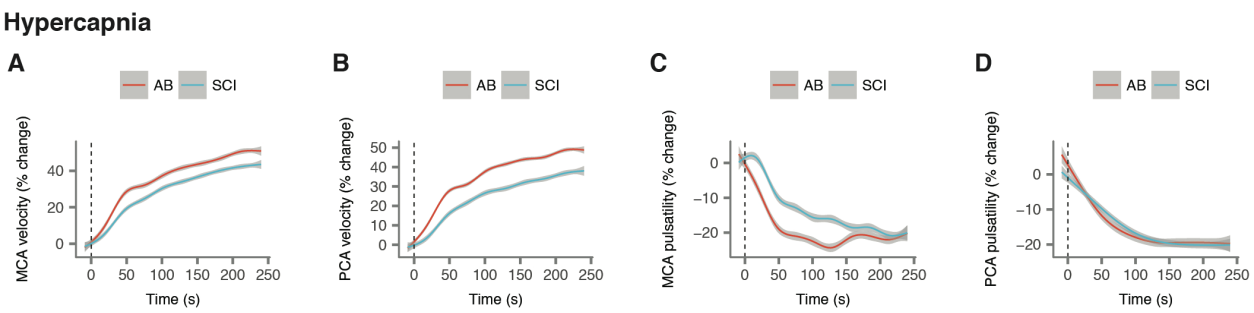

Figure e-4. Raw cerebrovascular responsiveness data during hypercapnia illustrates a differential response after spinal cord injury (SCI) compared to able-bodied (AB) individuals. Although no significant differences were observed in classical measures of amplitudinal responses, we found significant differences in various metrics of pulsatility between individuals with SCI versus AB individuals. Panels A-D represent the response to hypercapnia (4% CO_2) for middle cerebral artery (MCA) velocity (Panel A), posterior cerebral artery velocity (PCA), and the corresponding pulsatility metrics (Panels C and D). Quantifications of these metrics can be found in **Table S6**.

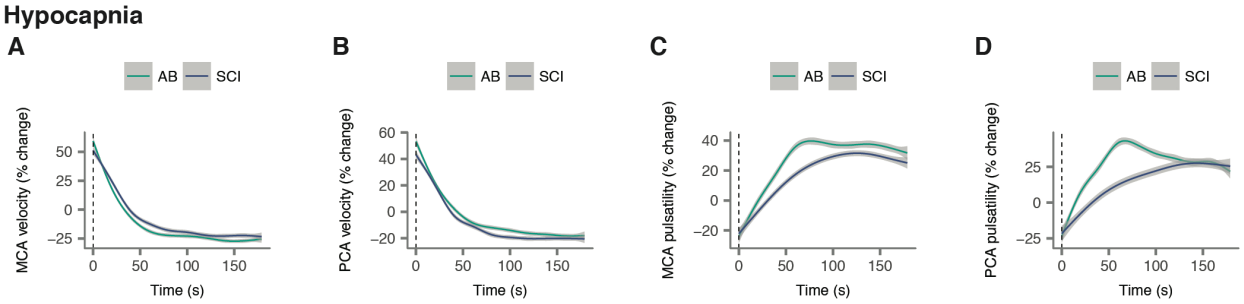

Figure e-5. Raw cerebrovascular responsiveness data during hypocapnia illustrates a differential response after spinal cord injury (SCI) compared to able-bodied (AB) individuals. Although no significant differences were observed in classical measures of amplitudinal responses, we found significant differences in various metrics of pulsatility between individuals with SCI versus AB individuals. Panels A-D represent the response to hypocapnia, where individuals were instructed to breathe deeply and rapidly to reduce end-tidal CO_2 to the equal and opposite degree as the hypercapnic response. Data are presented for middle cerebral artery (MCA) velocity (Panel A), posterior cerebral artery velocity (PCA), and the corresponding pulsatility metrics (Panels C and D). Quantifications of these metrics can be found in **Table S6**.

Table e-1. Characteristics of the 2 analytic samples from the SCI Community Health Survey

	Trouble sleeping			Fatigue		
Variable	**Total (n=1431)**	**With**	**Without**	**Total (n=1438)**	**With**	**Without**
Level of injury						
Tetraplegia	513 (43.6)	400 (78.0)	113 (22.0)	511 (43.5)	384 (75.2)	127 (24.9)
Paraplegia	665 (56.5)	463 (69.6)	202 (30.4)	664 (56.5)	476 (71.7)	188 (28.3)
Undefined	261	-	-	259	-	-
Injury severity						
Complete	560 (38.9)	414 (73.9)	146 (26.1)	560 (39.1)	417 (74.5)	143 (25.5)
Incomplete	879 (61.1)	630 (71.7)	249 (28.3)	874 (61.0)	658 (75.3)	216 (24.7)
Sex						
Male	970 (67.4)	694 (71.6)	276 (28.5)	967 (67.4)	697 (72.1)	270 (27.9)
Female	469 (32.6)	350 (74.6)	119 (25.4)	467 (32.6)	378 (80.9)	89 (19.1)
Median age, y	50	50	51	50	50	52

Table e-2. Likert scale responses for trouble sleeping and fatigue

Question	**Possible responses**
In the past 12 months, have you experienced this problem? Trouble Sleeping	0: Never 1: Once a year 2: A few times a year 3: A few times a month 4: A few times a week 5: Everyday
In the past 12 months, have you experienced this problem? Fatigue	0: Never 1: Once a year 2: A few times a year 3: A few times a month 4: A few times a week 5: Everyday

Table e-3. List of included studies in meta-analysis examining sleep apnea in spinal cord injury (n = 682 individuals with spinal cord injury).

Study	Date	PMID	n
Peters et al.	2017	28464758	273
Schembri et al.	2017	28364492	173
Bascom et al.	2015	26290534	18
Sankari et al.	2015	25510191	28
Proserpio et al.	2015	25454844	35
Sankari et al.	2014	24426822	26
Sankari et al.	2014	24114704	16
Sankari et al.	2014	24744387	16
Tran et al.	2010	19947995	16
Leduc et al.	2007	17321826	41
McEvoy et al.	1995	7638801	40
Normative data			
Young et al.	2002	11966340	2648

For Tables e-4 and e-5 please see the attached datasets.

Table e-6. ORs (95% CIs) for Trouble sleeping.

	Complete		Reduced	
Variable	**Raw OR Trouble sleeping (95% CI)**	**AOR Trouble sleeping (95% CI)**	**Raw OR Trouble sleeping (95% CI)**	**AOR Trouble sleeping (95% CI)**
Level of injury				
Tetraplegia	1.5 (1.2, 2.0)	1.5 (1.2, 2.0)	1.8 (1.2, 2.6)	1.8 (1.2, 2.6)
Paraplegia[a]	1	1	1	1
Sex				
Male	1.2 (0.92, 1.6)	1.2 (0.93, 1.7)	1.0 (0.71, 1.5)	1.1 (0.74, 1.6)
Female[a]	1	1	1	1
Age	0.99 (0.98, 1.0)	0.99 (0.98, 1.0)	1 (0.99, 1.0)	1.0 (0.99, 1.0)
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Severity of injury				
Complete	1.1 (0.88, 1.4)	1.1 (0.87, 1.4)	1.8 (1.2, 2.9)	1.8 (1.2, 3.0)
Incomplete[a]	1	1	1	1
Sex				
Male	1.2 (0.91, 1.5)	1.2 (0.90, 1.5)	1.0 (0.64, 1.7)	1.1 (0.66, 1.7)
Female[a]	1	1	1	1
Age	0.99 (0.98, 1.0)	0.99 (0.99, 1.0)	1.0 (0.99, 1.0)	1.0 (0.99, 1.0)

Abbreviations: CI = confidence interval; OR = odds ratio. ORs derived from logistic regression models. Both unadjusted and adjusted ORs are reported: AOR is adjusted for age and sex. Reduced model indicates either tetraplegia only (with severity of injury as the predictor) or complete injuries only (with tetraplegia as the predictor). a = Reference category.

Table e-7. ORs (95% CIs) for Fatigue.

	Complete		Reduced	
Variable	**Raw OR Fatigue (95% CI)**	**AOR Fatigue (95% CI)**	**Raw OR Fatigue (95% CI)**	**AOR Fatigue (95% CI)**
Level of injury				
Tetraplegia	1.2 (0.92, 1.6)	1.2 (0.91, 1.6)	1.2 (0.83, 1.7)	1.2 (0.81, 1.7)
Paraplegia[a]	1	1	1	1
Sex				
Male	1.6 (1.2, 2.2)	1.6 (1.2, 2.2)	1.3 (0.87, 1.9)	1.3 (0.85, 1.9)
Female[a]	1	1	1	1
Age	0.99 (0.98, 1.0)	0.99 (0.99, 1.0)	0.99 (0.98, 1.0)	0.99 (0.98, 1.0)
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Severity of injury				
Complete	0.96 (0.75, 1.2)	0.94 (0.73, 1.2)	1.2 (0.77, 1.8)	1.2 (0.76, 1.8)
Incomplete[a]	1	1	1	1
Sex				
Male	1.7 (1.3, 2.2)	1.6 (1.2, 2.1)	1.4 (0.85, 2.3)	1.3 (0.83, 2.2)
Female[a]	1	1	1	1
Age	0.99 (0.98, 1.0)	0.99 (0.98, 1.0)	0.99 (0.97, 1.0)	0.99 (0.97, 1.0)

Abbreviations: CI = confidence interval; OR = odds ratio. ORs derived from logistic regression models. Both unadjusted and adjusted ORs are reported: AOR is adjusted for age and sex. Reduced model indicates either tetraplegia only (with severity of injury as the predictor) or complete injuries only (with tetraplegia as the predictor). a = Reference category.