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Noninvasive Measurement of Sciatic Nerve Stiffness in Patients With Chronic Low Back Related Leg Pain Using Shear Wave Elastography

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Abbreviations

ANOVA, analysis of variance; EMG, electromyography; ICC, intraclass correlation coefficient; ROM, range of motion; SEM, standard error of measurement; SWE, shear wave elastography; SWV, shear wave velocity

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Objectives—The purpose of this study was to determine whether sciatic nerve stiffness is altered in people with chronic low back–related leg pain by using shear wave elastography.

Methods—In this cross-sectional study, the sciatic nerve shear wave velocity (ie, an index of stiffness) was measured in both legs of 16 participants (8 with unilateral low back–related leg pain and 8 healthy controls). Sciatic stiffness was measured during a passive ankle dorsiflexion motion performed at 2°/s in an isokinetic dynamometer. The ankle range of motion and passive torque, as well as muscle activity, were also measured.

Results—In people with low back–related leg pain, the affected limb showed higher sciatic nerve stiffness compared to the unaffected limb (+11.3%; $P = .05$). However, no differences were observed between the unaffected limb of people with low back–related leg pain and the healthy controls ($P = .34$).

Conclusions—People with chronic low back–related leg pain have interlimb differences in sciatic nerve stiffness, as measured by a safe and noninvasive method: shear wave elastography. The changes found may be related to alterations in nerve mechanical properties, which should be confirmed by future investigations.

Key Words—low back–related leg pain; musculoskeletal; nerve biomechanics; peripheral nerve; sciatica; shear wave velocity

Recent studies reported that people with chronic low back–related leg pain have changes in the sciatic nerve properties.^{1,2} Specifically, an increase in the cross-sectional area of the affected nerve was observed, in comparison to the unaffected nerve.^{1,2} Another study in this population revealed that the transverse displacement direction of the sciatic nerve was altered.³ However, these studies did not provide information about neural stiffness, which has been shown to be altered in other peripheral neuropathies.^{4,5} Neural stiffness measurement may represent a valuable tool for the diagnosis of peripheral neuropathies. However, there is currently no evidence of whether the sciatic stiffness is changed in people with low back–related leg pain.

Shear wave elastography (SWE) has recently been used to assess nerve mechanical properties in vivo,⁴ based on the relationship

between the shear wave velocity (SWV) and soft tissues stiffness ($R^2 = 0.94$).⁶ Briefly, SWE transmits ultrasonic waves to interact with tissues. In response, shear waves are produced, and their velocity can be measured and used to estimate the stiffness of tissues.⁷ Several studies reported good reliability for peripheral nerves stiffness measurements in healthy (intraclass correlation coefficient [ICC], 0.92)⁸ and clinical (ICC, 0.85) populations.⁴ In addition, tibial nerve stiffness was reported to be higher in people with diabetic neuropathy,⁵ as well as median nerve stiffness in people with carpal tunnel syndrome.⁴ Therefore, this study was designed to determine whether sciatic nerve stiffness is altered in people with chronic low back-related leg pain. We hypothesized that the sciatic nerve stiffness would be increased in the affected limb of people with low back-related leg pain compared to both the unaffected limb and healthy control participants.

Materials and Methods

Participants

Sixteen volunteers (8 people with chronic low back-related leg pain and 8 healthy control participants) were invited to participate in this study. Participants with chronic low back-related leg pain were included if the following criteria were present: (1) men and women between 18 and 45 years; (2) body mass index of less than 30 kg/m²; and (3) unilateral presence of pain, numbness, or both, originating in the lumbar spine or buttock region and traveling downward in the posterior area of the lower limb for longer than 6 months.⁹ Participants were excluded if they underwent spinal surgery or if they presented in an acute irritable state that prevented them to assume the test position (ie, prone). Healthy participants were matched to the participants with low back-related leg pain regarding age, sex, height, and weight and did not report any musculoskeletal problems or neurologic deficits.

All participants read and signed a written informed consent form according to the Declaration of Helsinki of 1975. This study was approved by the Ethics Committee of the Faculdade de Motricidade Humana, Universidade de Lisboa (approval No. 3/2015).

Equipment and Variables

Dynamometry

Passive ankle motion was executed by an isokinetic dynamometer (System 3; Biodex Medical Systems, Inc,

Shirley, NY) at 2°/s. The ankle angle and torque were sampled at 1000 Hz (MP100 acquisition system; Biopac Systems, Inc, Santa Barbara, CA). Participants rested prone with the knee fully extended and the lateral malleolus aligned to the dynamometer axis (Figure 1A). The neutral position of the ankle (0°) was defined as the perpendicular position between the foot and leg and determined by using an inclinometer.

Shear Wave Elastography

The procedures for the sciatic nerve stiffness measurement were similar to those in previous studies from our group.⁸ Briefly, an ultrasound scanner (Aixplorer version 10.0; SuperSonic Imagine, Aix-en-Provence, France) was used to assess (1 Hz) the sciatic SWV with a linear array transducer (SL 10-2 MHz, Super Linear 15-4; Vermon, Tours, France) in the musculoskeletal preset (penetrate mode, smoothing level 9, and the persistence off). The maximal SWV scale value was set at 17.0 m/s. The sciatic nerve was first identified transversely (Figure 1B) by scanning the posterior thigh in B-mode, 10 cm below the gluteal fold. Then the transducer was orientated longitudinally until both the superficial and deep epineuria of the nerve could be observed (Figure 1, C and D). A waterproof marker was used to indicate the transducer location on the skin, to ensure that preprocedural and postprocedural measurements were performed in the same location. Video clips with both B-mode and SWE mode displayed were recorded during passive ankle dorsiflexion.

Electromyography

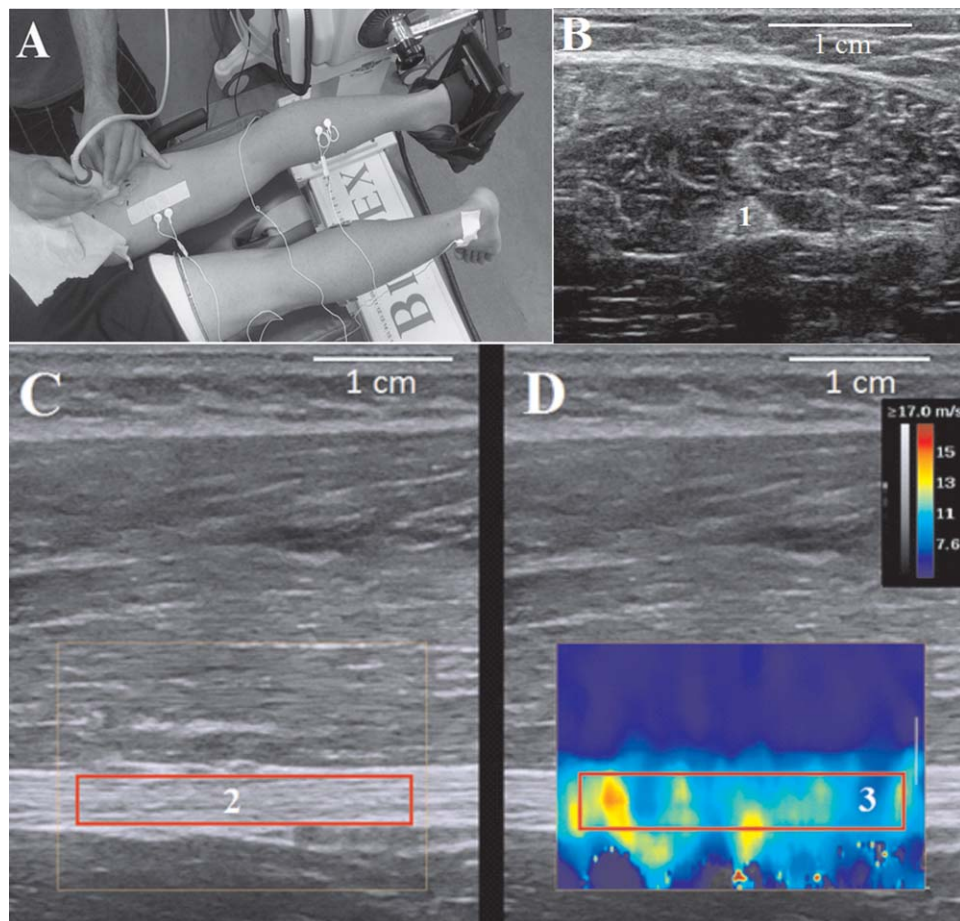
Surface electromyography (EMG) was used to record muscle activity with a telemetric system (Plux, Lisbon, Portugal). We used EMG as a control variable to monitor muscle activity during the SWV assessments, thus ensuring a passive nature to the motion. Surface electrodes (BlueSensor N; Ambu, Copenhagen, Denmark) were placed over the semitendinosus, medial gastrocnemius, and tibialis anterior muscles of both lower limbs. Signals were sampled at 1 kHz, amplified ($\times 1000$), digitally filtered (20–500 Hz), and full-wave rectified. Smoothing with a low-pass filter (10 Hz, Butterworth fourth order) was applied. The smoothed EMG signals were then amplitude normalized to the maximal isometric voluntary contraction.

Protocol

Participants visited the laboratory in a single session. Initially, demographic and clinical information were collected. Disability levels were determined by using the Roland-Morris Disability Questionnaire (ie, scores ranging from 0 to 24, where 0 corresponds to no disability and 24 to maximal disability)¹⁰ and the Oswestry Disability Index 2.0 (ie, scores in percentages, where 0% corresponds to no disability and 100% to maximal disability)¹¹; the intensity of pain was measured by using a 10-point numeric rating scale. Patients were also asked about the primary anatomic location of their pain and its behavior (eg, whether it was constant or intermittent, what the aggravating factors were, and how it changed throughout the day). In addition, the duration of the symptoms was also registered. Afterward, participants

were positioned prone on the dynamometer table for the sciatic stiffness assessment. The participants' maximal passive ankle dorsiflexion range of motion (ROM) was determined by using a handheld stop button. The ankle movement was performed at $2^\circ/\text{s}$, and the participant voluntarily stopped the dynamometer when the point of stretching discomfort was reached, and then the footplate immediately returned to a plantar flexion position. After this procedure, 4 plantar flexion–dorsiflexion cycles, starting from 40° of plantar flexion to the maximal dorsiflexion angle, were performed at $5^\circ/\text{s}$ for conditioning purposes.¹² Thereafter, the sciatic nerve stiffness and ankle torque and angle were assessed in 2 maximal dorsiflexion ROM repetitions ($2^\circ/\text{s}$). Between both repetitions there was a 1-minute rest, while the transducer was

Figure 1. **A**, Experimental setup. **B**, Cross-sectional view of the sciatic nerve (1) in B-mode. **C**, Longitudinal view of the sciatic nerve in B-mode. **D**, The elastographic window was defined above the nerve section, and the largest area within the epineurium was considered the region of interest (2 and 3).



removed from the site of measurement and repositioned in the exact same location for a reliability analysis. These procedures were reproduced for both lower limbs. After the sciatic stiffness measurements, patients were seated in the dynamometer to perform 2 maximal isometric voluntary contractions (1-minute rest between repetitions) for plantar flexor, dorsiflexor, and knee flexor muscles of both limbs for EMG normalization.

Data Processing

Data acquisition was synchronized by using an external trigger recorded with the Biopac MP100 acquisition system and processed by using customized MATLAB routines (The MathWorks, Natick, MA). Briefly, in the ultrasound clips, the sciatic region of interest was determined by selecting the largest area within the epineurium boundaries in the elastographic window (Figure 1, C and D). This procedure was repeated for each frame (ie, every second for the total video recording) to ensure that the region of interest would not be affected by nerve motion during the maneuvers. When selecting the region of interest, care was taken to avoid artifacts (regions with saturation). Color pixels were converted to SWV values according to the scale used, and their average was used for the statistical analysis.

As the maximal ankle ROM was different between participants, the ankle angles were normalized to the maximal ROM. The ankle range until 80% of the maximal ROM was considered for the analysis. This ROM cutoff was also used in a previous study,⁸ since the elastogram in some participants reached the maximal value of the scale (ie, 17 m/s), and considerable artifacts occur above this ankle ROM.

Statistical Analyses

The number of participants for this study was determined by using G*Power 3.0.10 software.¹³ With the use of an α of .05, a power of 0.9, a correlation among repetitions of 0.85, and an estimated effect size of 0.3 (correlation and effect size were determined with data from a previous pilot study), a total sample of 12 participants (ie, 6 per group) was determined. This number was increased to 16 (ie, 8 per group) in anticipation of dropouts or missing data.

Descriptive statistics (eg, mean and standard deviation) were used for sample characterization. A *t* test for independent samples was used to assess the differences

between groups regarding demographic variables (eg, age, weight, height, and body mass index).

Reliability measures for the SWV assessment included the ICC_{3,1}, the standard error of measurement (SEM), and the minimal detectable difference. The SEM was calculated as follows: $SEM = \sqrt{MS_{Error}}$, where MS_{Error} represents the mean square error obtained from a 2-way random effects analysis of variance (ANOVA). The minimal detectable difference was determined by the formula: minimal detectable difference = $SEM \times 1.96 \times \sqrt{2}$. Effect sizes were determined by calculating the Cohen *d*, as follows: $(\bar{X}_2 - \bar{X}_1) / SD$ pooled.

Data were tested for normality by the Shapiro-Wilk test. A 2-way repeated measures ANOVA [limb (affected or unaffected) \times ankle ROM (0%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, or 80 % of maximal ROM)] was conducted for each group to compare sciatic stiffness between limbs throughout the ankle ROM. A 2-way mixed ANOVA [group (low back-related leg pain or healthy control) \times ankle ROM (0%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, or 80% of maximal ROM)] was performed to assess the difference between the groups in sciatic stiffness throughout the ankle ROM for each limb. In all ANOVAs, the additional assumption of sphericity was assessed by the Mauchly test, and when it was violated, the degrees of freedom were corrected by Greenhouse-Geisser estimates. Statistical significance was set at $P < .05$. SPSS version 21.0 software (IBM Corporation, Armonk, NY) was used for the statistical analyses.

Results

Demographic variables are reported in Table 1. No significant differences were found between the participants with low back-related leg pain and the healthy

Table 1. Demographic Variables for the Low Back-Related Leg Pain and Healthy Groups

Variable	Leg Pain (n = 8)	Healthy (n = 8)	P
Male/female	6/2	5/3	
Age, y	30.8 (7.4)	28.1 (8.3)	.517
Weight, kg	74.7 (8.2)	68.1 (11.3)	.204
Height, m	1.77 (0.08)	1.73 (0.11)	.386
Body mass index, kg/m ²	23.7 (1.5)	22.6 (1.6)	.182
Dorsiflexion ROM, °	33.5 (7.1)	34.4 (7.5)	.814

Values are presented as mean (SD) where applicable.

participants. The clinical characteristics of the participants with low back-related leg pain are presented in Table 2.

The stiffness measurements revealed good intrarater reliability, with ICC values ranging from 0.87 (confidence interval, 0.50-0.97) at a 60% of maximal ROM and 0.99 (confidence interval, 0.94–0.99) at a 20% of maximal ROM. The mean (SD) SEM across the ankle percentiles was 0.56 (0.24) m/s, and the mean (SD) minimal detectable difference was 1.54 (0.67) m/s.

During all measurements, the mean (SD) EMG values for semitendinosus, medial gastrocnemius, and tibialis anterior muscles were, respectively, 1.6% (0.8%), 1.9% (0.9%), and 2.8% (2.1%) for the low back-related

leg pain group and 1.5% (1.1%), 2.0% (0.9%), and 2.8% (1.3%) for the control group.

An example of SWV-versus-ankle ROM curves for both the affected and unaffected limbs of a participant with low back-related leg pain is shown in Figure 2. Detailed information about the sciatic SWV throughout the ankle ROM percentiles in both groups is shown in Appendix. Figure 3 represents the SWVs throughout the ankle ROM for the 2 lower limbs in both groups.

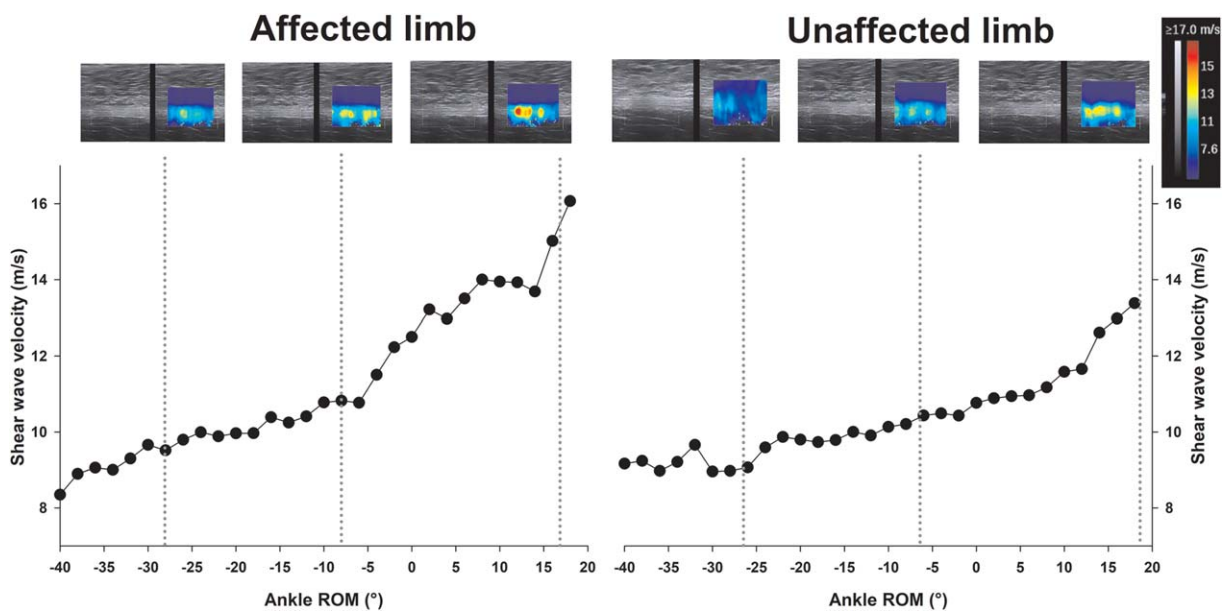
Concerning the within-participant analysis, no significant interaction (limb × ankle ROM) was observed, but a significant main effect was found for limb ($P = .047$) in the low back-related leg pain group. The affected limb on average showed an increase of 11.3% in

Table 2. Clinical Variables for the Participants With Low Back-Related Leg Pain (n = 8)

Variable	Participant								Mean (SD)
	1	2	3	4	5	6	7	8	
Sex	Male	Male	Female	Female	Male	Male	Male	Male	
RMQ, 0–24	8	8	4	6	6	4	7	2	5.6 (2.1)
ODI, %	20	14	18	26	24	4	20	10	17.0 (7.3)
Symptom duration, mo	36	12	156	12	24	60	96	240	79.5 (81.4)
Pain, 10-point NRS	5	4	1	5	2	2	6	4	3.6 (1.8)

NRS indicates numeric rating scale; ODI, Oswestry Disability Index; and RMQ, Roland-Morris Disability Questionnaire.

Figure 2. Sciatic SWV response during ankle dorsiflexion in both the affected (left) and unaffected (right) limbs of a participant (No. 7) with low back-related leg pain. For each graphic, examples of the elastogram are provided for 3 different amplitudes: 30° and 10° of plantarflexion and 15° of dorsiflexion.



the SWV compared to the unaffected limb. In the healthy group, neither significant interactions (limb × ankle ROM) nor limb effects ($P = .658$) were found. Regarding the between-group analysis, no significant interactions (group × ankle ROM) and no significant group effects were detected for both legs (affected limb versus control, $P = .336$; unaffected limb versus control, $P = .878$; see Appendix for further details).

Discussion

In this study, we showed that sciatic nerve stiffness of the affected limb of patients with chronic low back-related leg pain is higher than that of the unaffected limb, confirming our hypothesis of interlimb differences regarding sciatic stiffness. However, contrary to our hypothesis, we did not observe differences in sciatic stiffness between people with chronic low back-related leg pain and the control group.

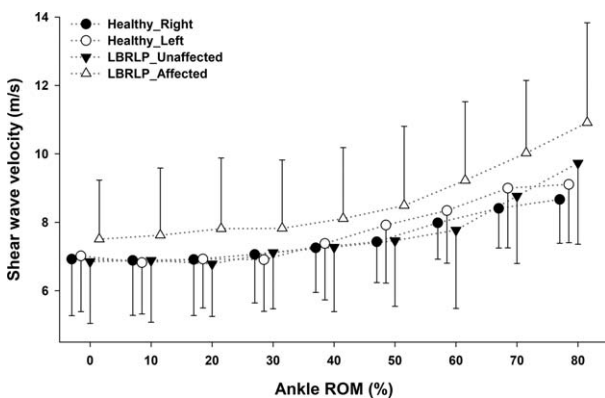
Some neuropathies can affect the mechanical properties of peripheral nerves.^{14,15} For instance, Hough et al¹⁶ concluded that people with carpal tunnel syndrome have lower longitudinal nerve excursion, whereas others have reported increased nerve stiffness as measured by using SWE.⁴ With respect to people with low back-related leg pain, studies reported an increase in the sciatic nerve cross-sectional area of the affected limb^{1,2} and a change in the nerve transverse excursion during a passive straight leg raise.³ However, none of these investigations measured sciatic nerve stiffness in people with chronic low back-related leg pain. In this study, we

observed that sciatic nerve stiffness was higher in the affected limb compared to the unaffected limb. These results demonstrate that, in addition to changes in nerve morphologic characteristics, chronic low back-related leg pain affects the mechanical properties of neural tissues. An explanation for these results may be found in previous research, in which persistent endoneural edema as a result of constant mechanical aggressions led to intraneural fibrosis.^{17,18} Assuming that the affected nerves of the population with chronic low back-related leg pain may be under long-term stress due to a mechanical etiology, we hypothesize that nerve viscoelastic properties could be compromised, which may result in increased nerve stiffness. However, future studies may want to examine whether the asymmetries found between limbs in people with chronic low back-related leg pain are related to a mechanical etiology and whether it evolves as the pathologic condition progresses.

Moreover, we observed no significant differences in sciatic stiffness between people with chronic low back-related leg pain and healthy people. However, the associated effect size for such difference was 0.46, which accordingly to Cohen¹⁹ can be interpreted as medium. In addition, when we look specifically at the difference in the sciatic SWV throughout each ankle ROM percentile, we notice that the between-group difference in the SWV was inferior to the SEM in only 2 of the total 9 percentiles (ie, percentiles 50% and 60%; see Appendix). This finding suggests that the between-group difference is not solely explained by the error of measurement, indicating possible effects of the pathologic condition. Moreover, Frost and Brown¹ measured the sciatic nerve cross-sectional area in people with mild (mean Oswestry Disability Index score, 19.9%) and chronic (mean symptom duration, 126 months) unilateral low back-related leg pain and also found between-limb differences, but not when compared to healthy controls. Our results, together with the ones reported by Frost and Brown,¹ strengthen the hypothesis that the absence of between-group differences may be due to a high variability that naturally occurs in sciatic stiffness of healthy men and women. In addition, the minimal levels of disability reported by the participants with chronic low back-related leg pain may also explain this result. Eventually, people with more severe symptoms and longer durations may have higher sciatic stiffness.

As limitations of this study, we should mention that sciatic stiffness was measured in only a single site, which

Figure 3. Between-group and within-participant comparisons of the sciatic SWV (mean and SD) throughout the ankle ROM percentiles. Significant differences were found between the affected and unaffected limbs of the low back-related leg pain (LBRLP) group.



is described as a location with good ultrasound visibility and where the sciatic nerve is more superficial.²⁰ Additional measurement sites may allow one to determine whether a difference exists between healthy populations and those with chronic low back-related leg pain. We hypothesize that measurements closer to the roots of the sciatic nerve would yield even higher stiffness values, given that measurements would be closer to the affected region of the nerve. We also observed tibialis anterior EMG values that were slightly superior to the 2% threshold defined for muscle inactivity.²¹ However, we noticed that the EMG values, for all muscles, remained unchanged throughout the dynamic ankle motion. This finding suggests that muscular EMG activity had minimal (or perhaps no) influence on the sciatic nerve stiffness assessment. Moreover, generalizations of the results retrieved by very focused descriptive studies, such as ours, should be made with caution, especially when addressing people with different clinical characteristics from the participants in this study (eg, people with non-radicular low back pain or other lower body quadrant neuropathies).

In conclusion, this study provides evidence of inter-limb differences regarding sciatic stiffness, in people with low back-related leg pain. This finding may indicate chronic changes to nerve mechanical properties. Health professionals should feel confident in using SWE as a safe, noninvasive, and reliable method for assessing sciatic stiffness.

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Appendix
 Descriptive Statistics for Within-Participant and Between-Group Sciatic SWV (m/s) Throughout the Ankle ROM Percentiles

%ROM	SEM	Leg Pain						Healthy						Leg Pain vs Healthy								
		Unaffected			Affected			Left			Right			Leg Pain			Healthy			D	ES	P
		Mean	SD		Mean	SD		Mean	SD		Mean	SD		Mean	SD		Mean	SD				
		Mean	SD	P	Mean	SD	P	Mean	SD	P	Mean	SD	P	Mean	SD	P	Mean	SD	P			
0	0.27	6.85	1.81	7.51	1.73	0.66	0.37	0.47 ^a	6.93	1.65	7.02	1.63	0.07	0.05	.658 ^b	7.51	1.73	7.02	1.63	0.49	0.29	.336 ^c
10	0.41	6.89	1.81	7.62	1.96	0.73	0.39	6.89	1.61	6.82	1.50	0.05	0.04	0.04	0.04	7.62	1.96	6.82	1.50	0.80	0.46	
20	0.23	6.79	1.54	7.81	2.07	1.03	0.56	6.91	1.64	6.93	1.43	0.01	0.01	0.01	0.01	7.81	2.07	6.93	1.43	0.88	0.49	
30	0.50	7.12	1.64	7.82	2.00	0.70	0.38	7.06	1.42	6.91	1.51	0.10	0.10	0.10	0.10	7.82	2.00	6.91	1.51	0.91	0.51	
40	0.57	7.27	1.88	8.11	2.07	0.83	0.42	7.26	1.30	7.38	1.65	0.08	0.08	0.08	0.08	8.11	2.07	7.38	1.65	0.73	0.39	
50	0.60	7.46	1.92	8.49	2.32	1.03	0.48	7.43	1.19	7.92	1.69	0.30	0.34	0.34	0.34	8.49	2.32	7.92	1.69	0.57	0.28	
60	0.94	7.77	2.29	9.22	2.30	1.45	0.63	7.98	1.06	8.34	1.54	0.29	0.27	0.27	0.27	9.22	2.30	8.34	1.54	0.88	0.45	
70	0.59	8.77	1.97	10.03	2.12	1.26	0.62	8.41	1.16	9.00	1.74	0.54	0.40	0.40	0.40	10.03	2.12	9.00	1.74	1.03	0.53	
80	0.88	9.73	2.37	10.91	2.92	1.18	0.44	8.67	1.28	9.11	1.70	0.35	0.29	0.29	0.29	10.91	2.92	9.11	1.70	1.80	0.75	

D indicates difference; and ES, effect size.

^aDifference between unaffected and affected limbs of participants with low back-related leg pain.

^bDifference between left and right limbs of healthy participants.

^cDifference between affected limbs of participants with low back-related leg pain and right limbs of healthy participants.