



# Passive intervertebral restraint is different in patients with treatment-resistant chronic nonspecific low back pain: a retrospective cohort study and control comparison

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## Abstract

**Purpose** In vivo studies of continuous lumbar sagittal plane motion have found passive intervertebral motion to be more uneven in patients with chronic nonspecific low back pain (CNSLBP) than healthy controls, but the mechanisms are unclear. This study aimed to compare patients with CNSLBP with a matched group of pain-free controls for intervertebral restraint during passive recumbent bending.

**Methods** Seventeen patients with CNSLBP and minimal disc degeneration who had quantitative fluoroscopy investigations were matched to 17 healthy controls from a database acquired using the same imaging protocol. The entire database ( $n = 136$ ) was examined for clustering of peaking times, magnitudes and ROM of the first derivatives of the intervertebral angle/motion curves (PTFD, PMFD and ROM) during flexion and return that might introduce confounding. The groups were then compared for differences in these variables.

**Results** There were significant segmental ROM differences among clusters in the database when PMFD and ROM were used as clustering variables, indicating heterogeneity. However, in the patient–control study, it was PTFD (velocity) that differentiated the groups. At L5-S1, this was at 10.82% of the motion path compared with 25.06% in the controls ( $p = 0.0002$ ). For L4-5, PTFD was at 23.42% of the motion path in patients and 16.33% in controls ( $p = 0.0694$ ) suggesting a reduced initial bending moment there. There were no significant differences for PMFD or ROM.

**Conclusion** Peaking time of passive intervertebral velocity occurs early at L5-S1 in patients with CNSLBP; however, these findings should be treated with caution pending their replication. Future studies should explore relationships with altered disc pressures and biochemistry. Usefulness for monitoring regenerative disc therapies should be considered.

**Keywords** Back pain · Lumbar spine · Kinematics · Fluoroscopy · Passive restraint

## Background

Nonspecific low back pain is a multifaceted disorder with the highest population impact on Years Lived with Disability [1]. Mechanical abnormalities linked to degeneration are suspected of playing a part, but there has been little objective evidence of this in terms of the usual measures of mechanical disruption (i.e. reduced disc pressure, increased range of motion (ROM), translation and laxity) [2–4]. However, lesser disruption, resulting in disco-ligamentous sub-failure, has been suggested as an underlying contributor to pain [5]. In a review of the role of biomechanics in intervertebral disc degeneration and regenerative therapies, Iatridis et al. emphasised the importance of disc pressure loss and the need for safe and minimally invasive interventions that may mitigate or repair structural defects at earlier stages of

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degeneration, where instability has been found to be more prevalent [6, 7]. However, how early-stage loss of intervertebral restraint would be monitored in lesser degenerative states is unclear.

Exploration of the microinjury concept in chronic back pain has prompted studies of relationships between abnormal intervertebral velocities and disc pressures and the material properties of passive spinal tissues [8–11]. There is evidence from histologic studies that the disc annulus undergoes greater damage under rapid loading than under quasistatic loading, signalling the importance of velocity in intervertebral kinematics and the need to take account of this in vivo [12]. A finite element study by Mithani et al. [13] found that changes to the material properties of passive spinal tissues elicit compensatory changes in lumbar intervertebral ranges, “underscoring the significance of passive tissue properties in regulating segmental mobility and geometric compensation to maintain spinal congruency”. This has also been proposed as a plausible mechanism underlying the development of low back pain.

Two studies of passive lumbar flexion have revealed a biomarker for chronic, nonspecific low back pain (CNSLBP) in the form of motion sharing inequality (MSI) across the range in patients with CNSLBP during passive recumbent motion. This also suggests the involvement of passive intervertebral restraint [2, 14]. MSI is measured using quantitative fluoroscopy (QF). Moving vertebral images are digitised semi-automatically and processed using a custom algorithm to output the intervertebral motion patterns in terms of rotation, translation and finite centre of rotation [15, 16]. MSI is a measure that has been added to this and is fully described in Breen 2018 [14]. It consists of the average difference between the largest and smallest shares of segmental motion that is accepted by intervertebral levels from L2-S1 across the whole bending sequence. When applied during passive recumbent motion, it is a summary measure of the evenness of intervertebral passive restraint.

The QF technology responds to the need to reduce measurement variability when comparing small amounts of intervertebral displacement [17–20]. Early weight-bearing fluoroscopic studies explored the inflexion points of intervertebral rotation curves in small numbers of healthy participants and proposed normal patterns for these as a top-down cascade during flexion [21, 22]. Recently, four significantly different spatiotemporal clusters of peak intervertebral rotation velocities were found in a sample of healthy controls during standing QF (n=127) [23]. Reminiscent of the previous studies, the greatest proportion of these also exhibited a top-down cascade of peak velocities during standing flexion.

The MSI variable, measured in the passive recumbent configuration, is highly correlated with age and degree of disc degeneration, but in CNSLP patients only, indicating a biomarker for CNSLBP [14]. In addition, a multivariate

analysis of continuous passive intervertebral motion data comparing CNSLBP sufferers and controls confirmed the presence of an acceleration/deceleration principal component in the measurement of passive restraint between vertebrae, supporting the prospect of an additional kinematic biomarker [24].

As a basis for conducting patient-specific comparisons, two open-source reference databases of standardised, continuous lumbar intervertebral rotational motion (presented as midplane angles) in 136 healthy volunteers during flexion and extension have been published [25]. One was recorded using QF during passive recumbent motion and the other during weight-bearing active motion in the same population. The present study investigated the prospect of making patient-specific comparisons based on spatiotemporal interactions, based on ranges and velocities, between levels compared with the passive recumbent database. It was first, however, necessary to determine if there are spatiotemporal clusters of movement patterns in the database, suggesting inhomogeneity.

The main purpose of this study was, therefore, to compare a matched subgroup of healthy controls to a group of patients with treatment-resistant CNSLBP who received the same passive recumbent QF examination in an investigation to inform their management. The aims were: (1) to assess the passive recumbent database for the absence of significant clusters indicating heterogeneity and (2) to compare the degree of altered passive restraint in a population of CNSLBP patients compared to healthy controls for velocity and range peaking points. The hypotheses were that there would be (1) no significant clusters in the passive recumbent normative database and (2) statistically significant differences between patients and controls for peaking points within intervertebral levels.

## Methods

### Participants

One hundred and thirty-six healthy volunteers were recruited from staff, students and visitors at our institution and received passive recumbent and weight-bearing active quantitative fluoroscopy (QF) scans. Radiographic disc degeneration was assessed from the fluoroscopic images for all participants using the Kellgren and Lawrence scale [26]. Seventeen of those in the passive recumbent study were matched in pairs to a group of 17 patients with CNSLBP and minimal disc degeneration for age, sex and BMI for a sub-study of spatiotemporal differences between patients and controls. The study received a favourable ethical opinion (National Research Ethics Service South-West 3, REC reference 10/H0106/65).

## Inclusion criteria

All participants were males and females aged 18–71 with minimal radiographic evidence of disc degeneration, no medical radiation exposure of  $> 8$  mSv in the previous 2 years, no pregnancy (females) and having given informed consent. Controls had to have been free of any back pain that limited their normal activity for more than 1 day in the previous year. Patients had to have been referred to investigate treatment-resistant back pain of more than 3 months' duration as specified by the referrer. Patients whose pain was associated with nerve compression or serious spinal pathology were excluded.

## Data collection and image analysis

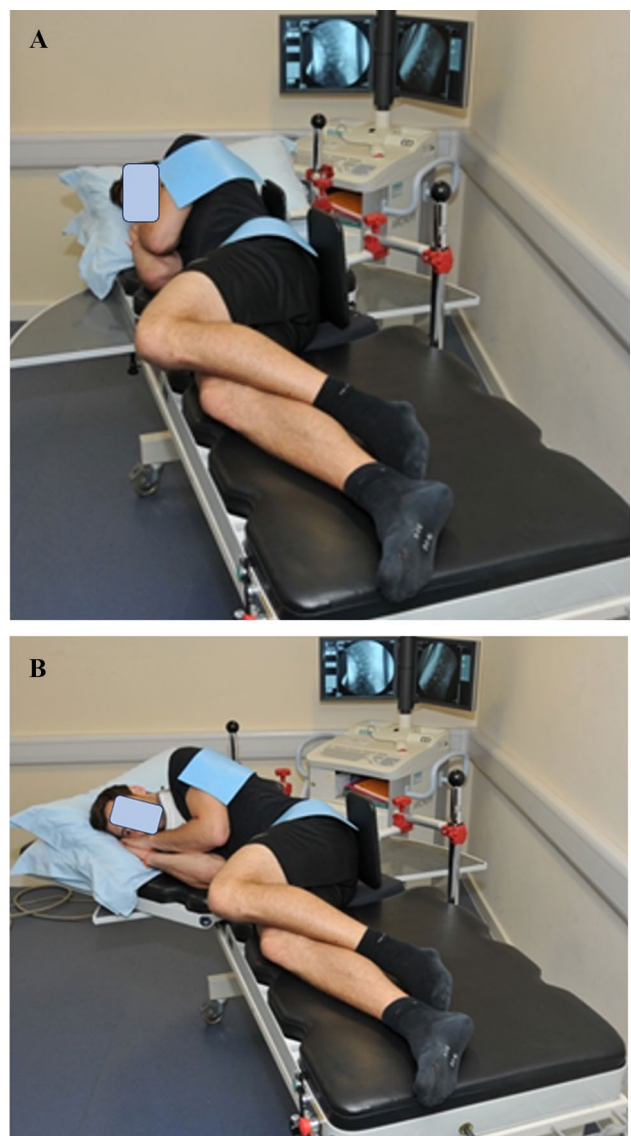
All participants received the same standardised passive recumbent flexion and return lumbar fluoroscopy examination as previously described [14] (Fig. 1). The image analysis involved a semi-automated tracking process to determine the position of each vertebra (L2, L3, L4, L5 and S1) in each recorded image during the flexion and return motion. The midplane angles of all vertebrae were then extracted and smoothed using a Tikhonov regularisation to reduce noise in the output [27].

## Kinematic analysis

The kinematic analysis of the passive recumbent midplane angles database followed a similar protocol to the weight-bearing active one [23]. The spatiotemporal variables chosen for comparison at each level from L2-3 to L5-S1 were in terms of the peak intervertebral ranges and velocities as follows: (1) the peak range of motion (ROM) ( $^{\circ}$ ), wherever it occurred in the sequence, (2) the time in the sequence (%) of the peaking of the first derivative (PTFD) of the angle/velocity motion curve (velocity) and (3) the peak magnitude ( $^{\circ}$ ) of the first derivative (PMFD)(velocity) of the peak velocity across the sequence wherever it occurred.

## Statistical analysis

A custom algorithm was used to cluster the passive recumbent normative study participants based on these three variables to investigate the possible existence of clusters as was found in the weight-bearing normative study of the same participants [23]. The Shapiro–Wilk test was used to assess normality in the patient–control populations. Normally distributed spatiotemporal data were compared using two-sided paired *t*-tests and non-normal data using the Wilcoxon



**Fig. 1** Participant positioned for passive recumbent flexion motion recording: **a** neutral position and **b** fully flexed ( $40^{\circ}$ ) position (from Breen and Breen [2])

rank-sum test. All statistical analyses were performed using SPSS software (version 27, Chicago, IL).

Peaking times and magnitudes of the first derivative (velocity) of the rotational motion of each motion segment taken separately (PTFD), along with the ranges of motion (ROM and PMFD), were calculated and compared between the 17 patients with CNSLBP and 17 matched controls from the normative study during flexion and return motion. Statistical parametric mapping (SPM) was used to test the significance of differences between patients and controls' time-series data (spm1d.stats.ttest) using the open-source software package: (<https://www.spm1d.org>) [28].

## Results

There were 136 healthy volunteers in the recumbent reference database (68 males, mean age 43 (sd 13) and mean BMI 25 (sd 2.33); 68 females, mean age 43 (sd 13) and mean BMI 23 (sd 3.05)). The results of the analyses for motion clusters of the three spatiotemporal variables for both outward and return motion are shown in Supplementary Material. Although there were several spatiotemporal clusters for ROM, PTFD and PMFD, none of the PTFD clusters was significant ( $p > 0.05$ ), indicating

greater population homogeneity for this variable than in the weight-bearing database [23].

The matching demographics of reference, normative and sub-study populations are shown in Table 1. There were no significant differences between patients and controls in terms of age, sex, height, weight or BMI. However, two of the patients and two of the controls in the sub-study had a small amount of disc degeneration at one or two levels.

**Table 1** Matching demographics for patients and controls (M=10, F=7 per group) for age, height, weight and BMI

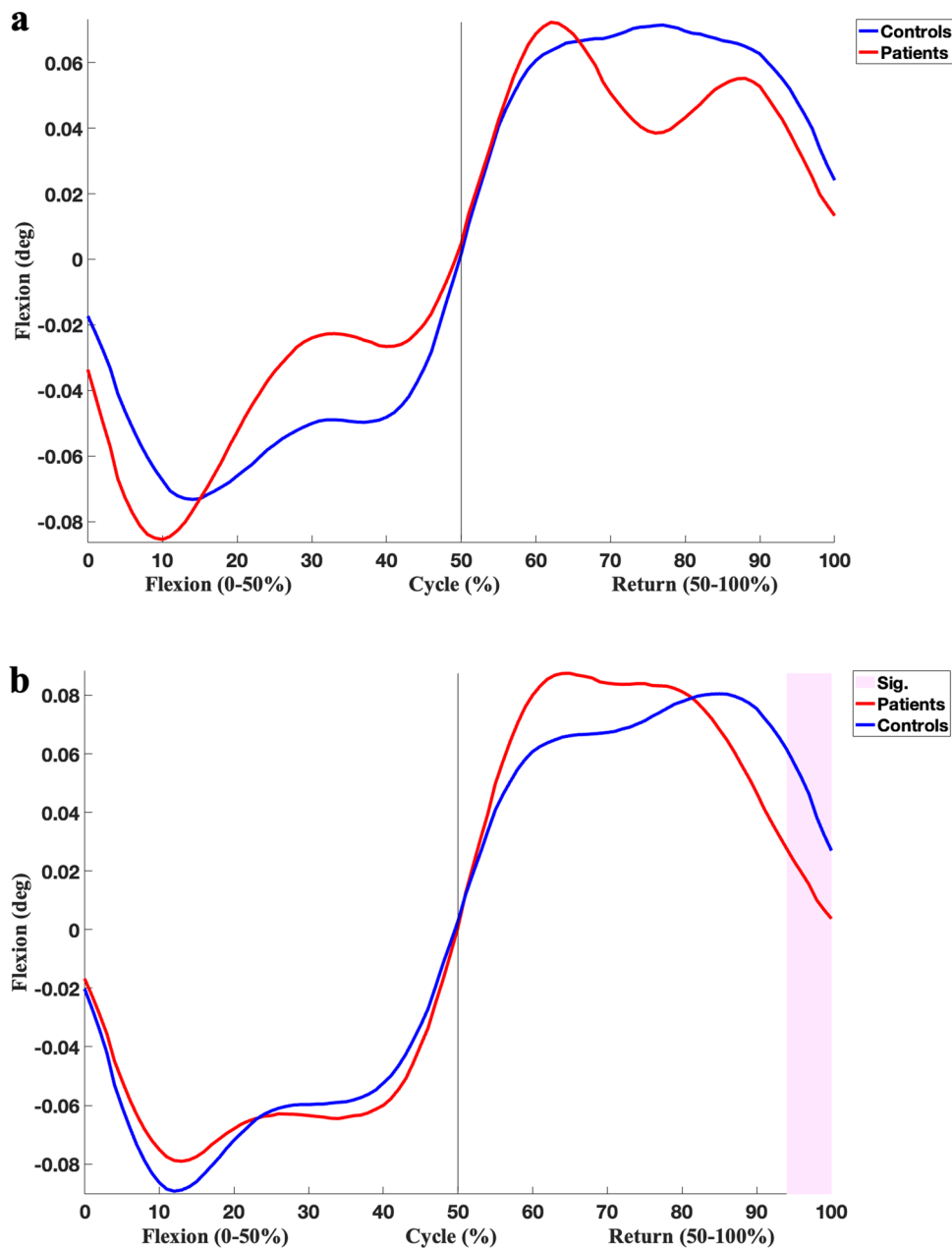
	Age			Height			Weight			BMI		
	Median	Min	Max	Median	Min	Max	Median	Min	Max	Median	Min	Max
All patients	51.00	20.00	75.00	1.77	1.55	1.98	76.20	53.98	104.00	24.32	19.26	42.29
All controls	50.00	21.00	66.00	1.73	1.59	1.87	71.70	47.60	92.10	24.32	16.87	27.17
<i>p</i>	0.235			0.363			0.1			0.532		
Male patients	50.50	22.00	74.00	1.79	1.55	1.98	84.50	63.00	104.00	24.55	19.88	42.29
Male controls	50.00	22.00	65.00	1.76	1.65	1.87	77.50	65.00	92.10	25.28	21.97	27.17
<i>p</i>	0.121			0.475			0.241			0.799		
Female patients	49.00	20.00	75.00	1.74	1.62	1.77	64.00	53.98	82.55	21.14	19.26	28.35
Female controls	51.00	21.00	66.00	1.73	1.59	1.78	57.00	47.60	76.20	21.38	16.87	26.34
<i>p</i>	1.000			0.686			0.225			0.500		

Wilcoxon rank-sum test

**Table 2** Spatiotemporal comparisons of patients ( $n = 17$ ) and matched controls ( $n = 17$ )

Patients and controls ( $n = 17$ )												
Variables	Segments	Flexion (0–50%)					Return (51–100%)					
		Patients		Controls			Patients		Controls			
		Mean/median	SD/IQR	Mean/median	SD/IQR	<i>p</i>	Mean/median	SD/IQR	Mean/median	SD/IQR	<i>p</i>	
ROM (°)	L5-S1	5.32/	2.94/	5.15/	1.94/	0.825	4.95/	2.68/	5.62/	2.46	0.4133	
	L4-5	6.14/	2.44/	5.15/	2.00/	0.935	7.01	3.27	7.01	7.09	0.9999	
	L3-4	4.50/	1.51/	4.87/	1.68/	0.478	4.74/	1.49/	4.91/	1.49/	0.7191	
	L2-3	3.29/	1.34/	3.88/	1.58/	0.136	3.34/	1.29/	4.12/	1.57/	0.0785	
PTFD (%)	L5-S1	<b>10.82/</b>	<b>5.09/</b>	<b>25.06/</b>	<b>12.64/</b>	<b>0.0002</b>	71.76/	11.94/	74.71/	11.81/	0.4974	
	L4-5	23.42	16.33	13.24	0.60	0.0694	77.76	16.54	84.02	18.36	0.1009	
	L3-4	22.82/	10.95/	21.76/	9.60/	0.7669	76.35/	9.47/	78.27/	10.95/	0.2302	
	L2-3	25.82/	14.40/	25.23/	12.26/	0.8855	78.58/	10.81/	74.11/	11.47/	0.2302	
PMFD (°)	L5-S1	0.11/	0.06/	0.09/	0.35/	0.2817	0.09	0.08	0.09	0.03	0.7819	
	L4-5	0.11/	0.04/	0.10/	0.03/	0.5834	0.11/	0.04/	0.09/	0.02/	0.0808	
	L3-4	0.08/	0.03/	0.07/	0.03/	0.8350	0.07/	0.02/	0.07/	0.02/	0.7725	
	L2-3	0.06/	0.02	0.07/	0.02/	0.1425	0.05	0.02	0.06	0.03	0.2842	

ROM: range of motion clustering; PTFD: peaking time of first derivative; PMFD: peaking magnitude of first derivative and IQR: interquartile range; significant: bolded text. Analysis: normally distributed; two-way paired *t*-test and non-normally distributed; two-way Wilcoxon rank-sum test



**Fig. 2** Ensemble means of flexion and return intervertebral velocities of 17 patients and matched controls: **a** L5-S1, **b** L4-5, **c** L3-4 and **d** L2-3. (Pink shading = region of significant difference (SPM))

**Comparison of spatiotemporal variables of patients and controls**

Table 2 shows that the median velocity peaking time for flexion PTFD for L4-5 was at 23.42% of the motion in patients and 16.33% of the motion in controls ( $p=0.0694$ ). For L5-S1, the mean velocities were at 10.82% in patients

and 25.06% in controls ( $p=0.0002$ ). There were no significant differences for any variable during the return phase, although a slightly greater mean value for L4-5 PMFD in patients approached significance ( $p=0.0808$ ).

Figure 2a–d shows the ensemble means of the intervertebral velocities in patients and controls from L2-3 to L5-S1 throughout passive recumbent flexion and return

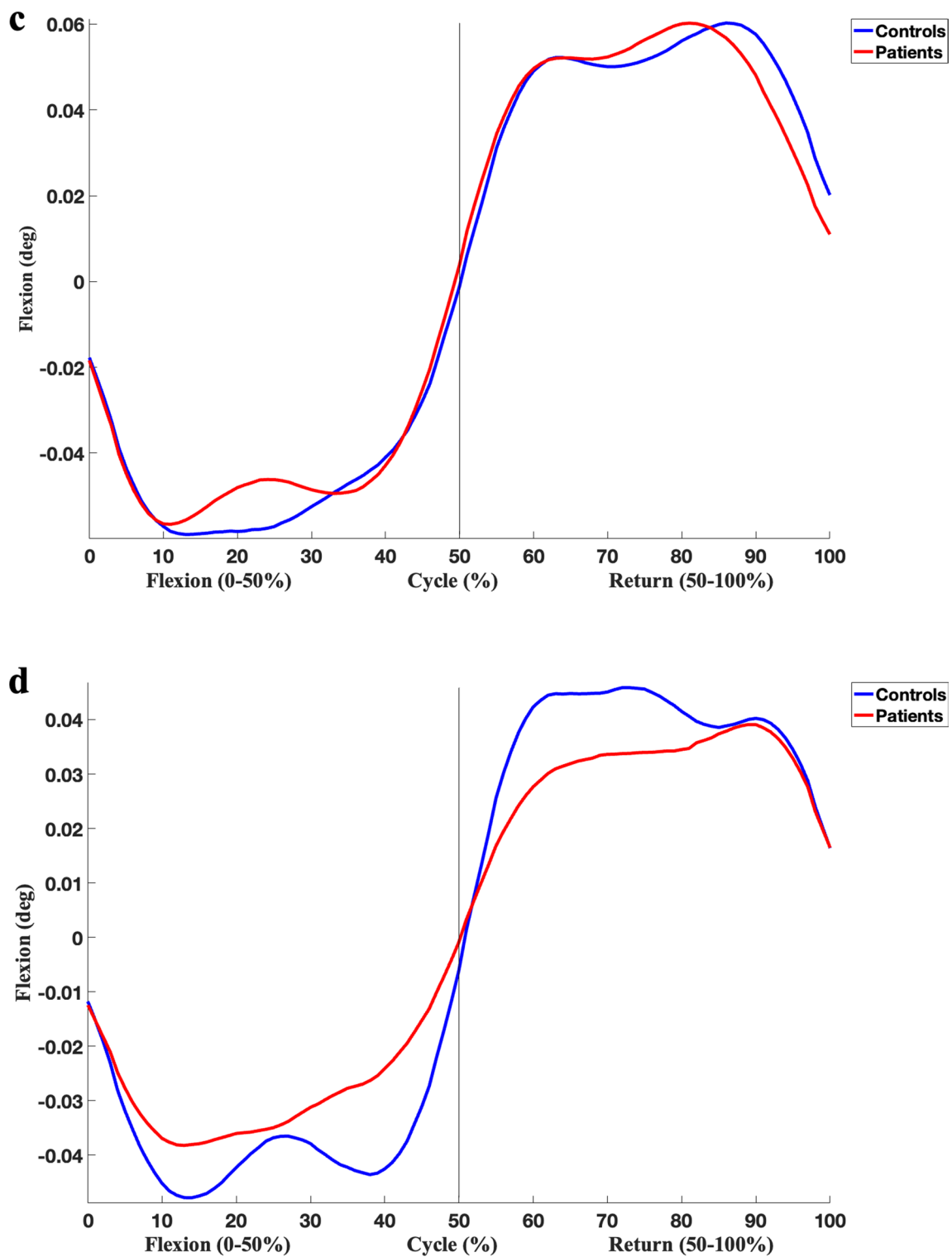
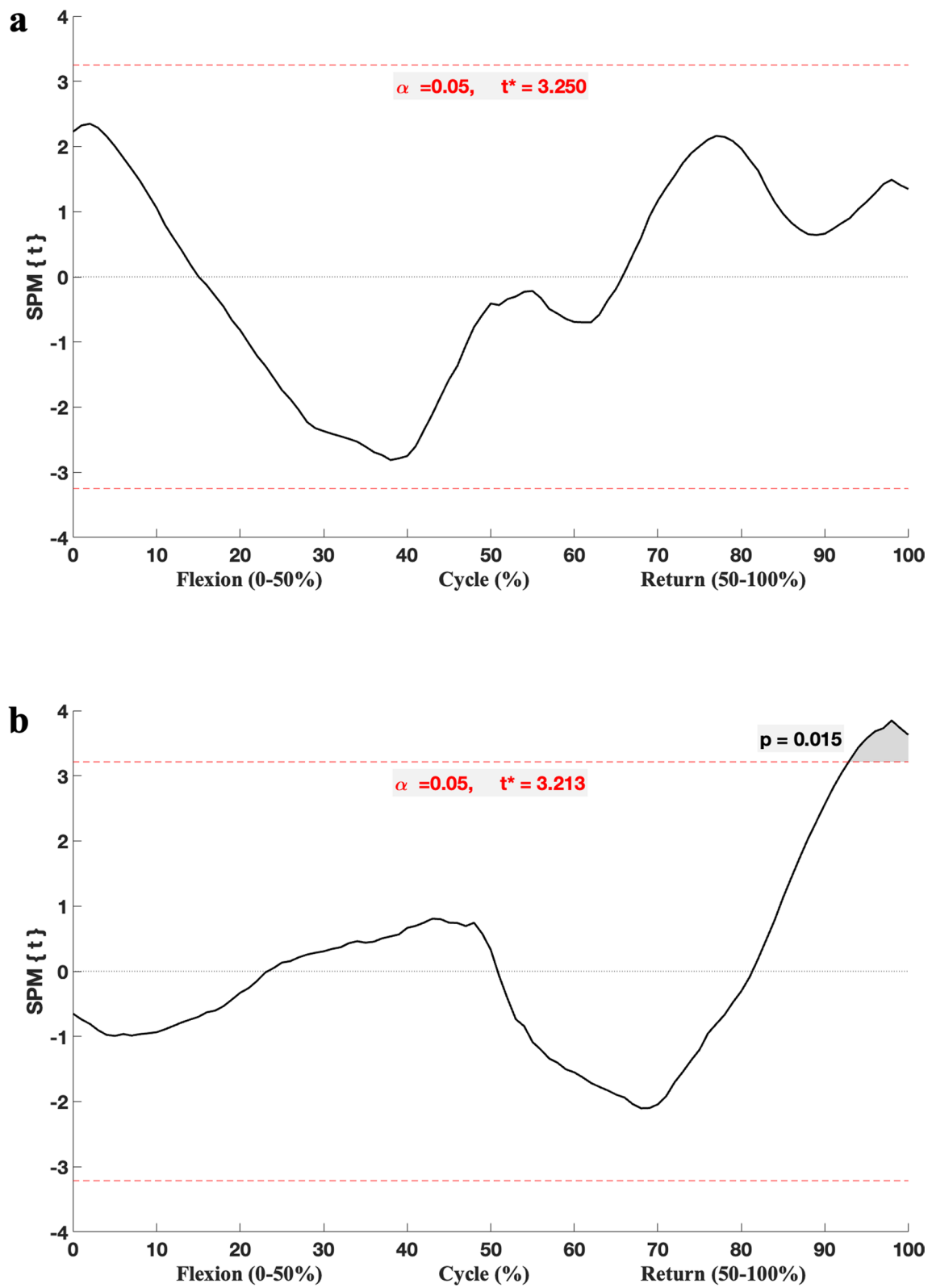


Fig. 2 (continued)

motion in patients and controls. SPM showed that only differences in velocities towards the end of the return phase at L4-5 were statistically significant ( $p < 0.015$ ) (Fig. 3a-d).

Figure 4a-d shows the ensemble means of the magnitudes and locations of the motion ranges of these levels for flexion and return. These found symmetrical patterns





**Fig. 3** Segmental comparison of each intervertebral level for differences in velocities between 17 patients and controls during flexion and return using statistical parametric mapping (SPM): **a** L5-S1, **b**

L4-5, **c** L3-4 and **d** L2-3. (Significance only found towards the end of the return phase at L4-5)

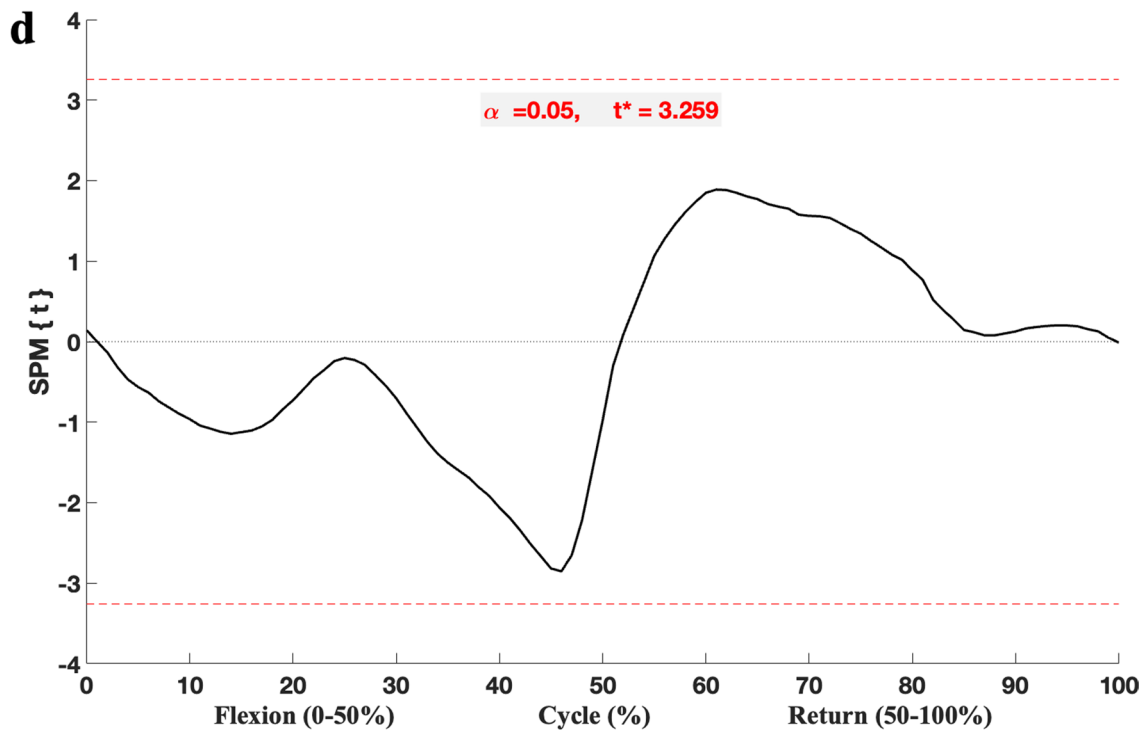
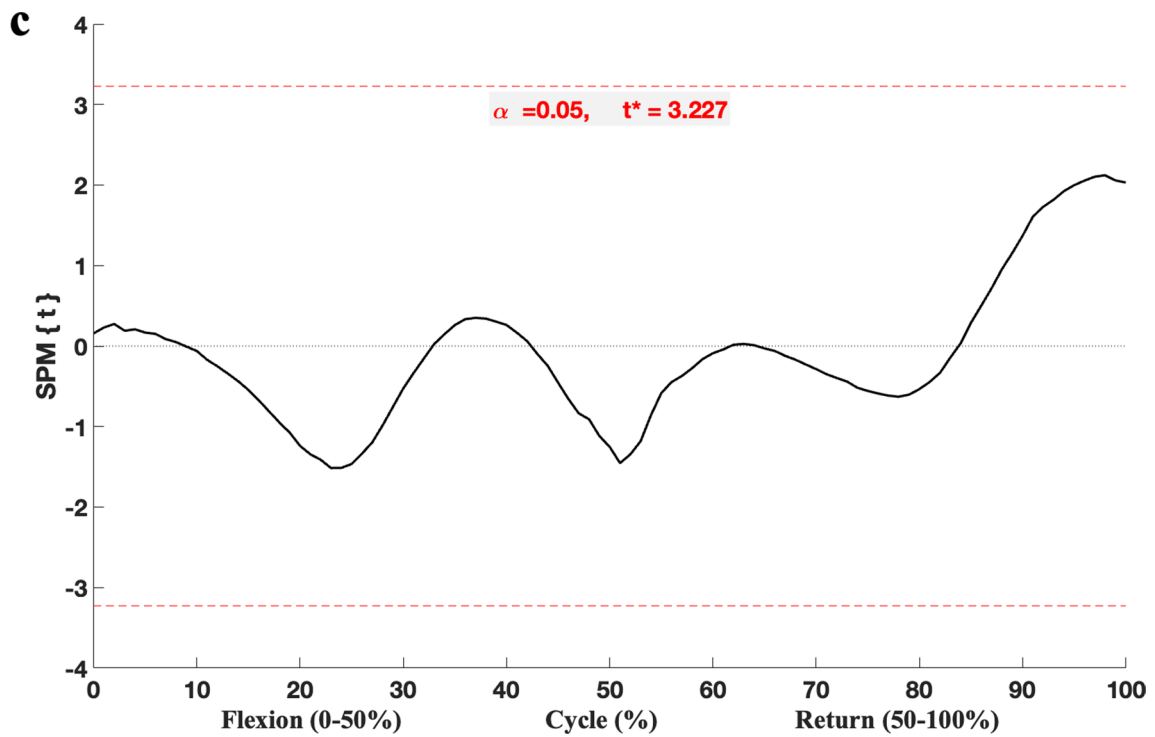
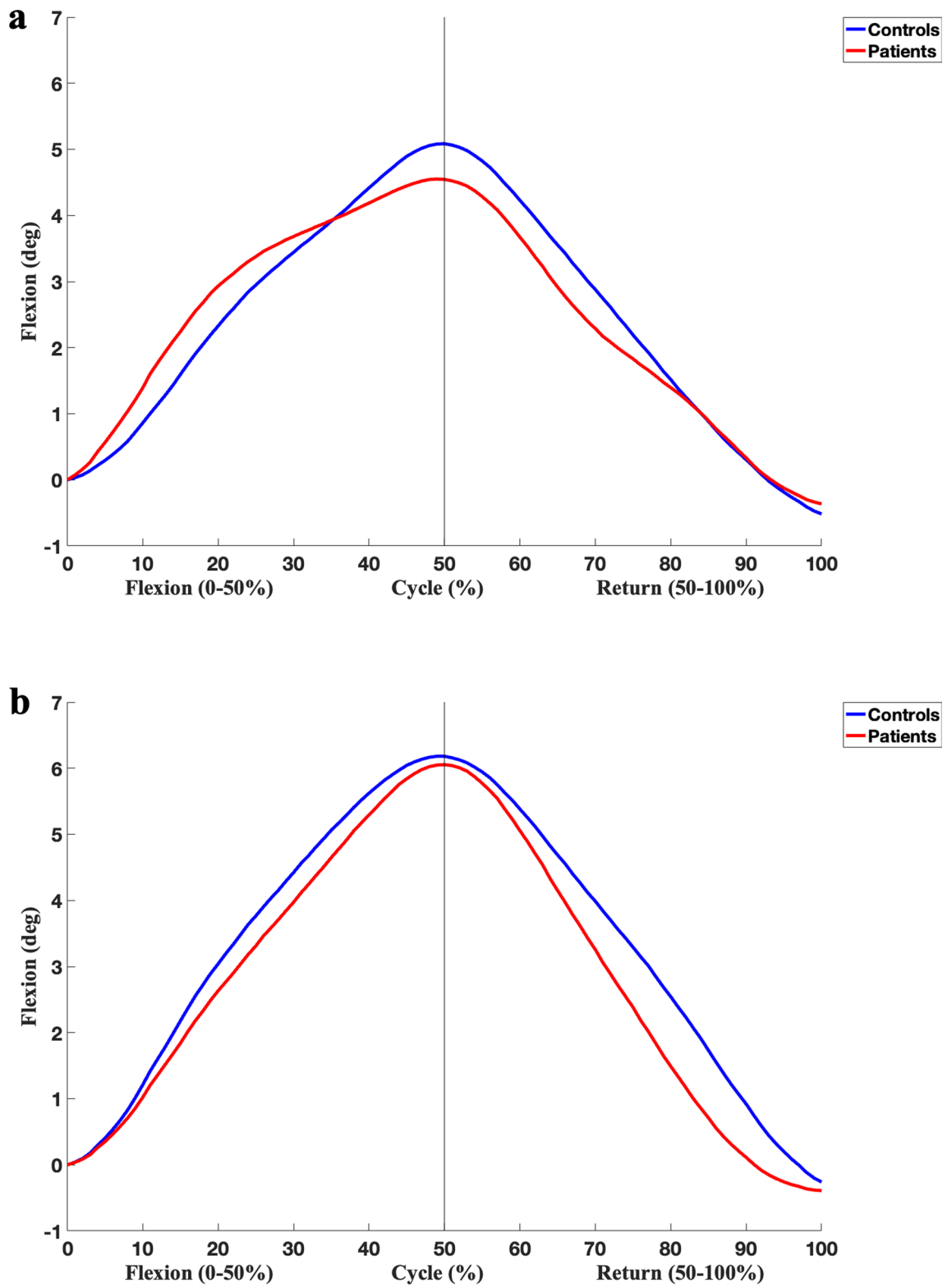


Fig. 3 (continued)





**Fig. 4** Ensemble means of flexion and return intervertebral ranges (ROM) in 17 patients and matched controls: **a** L5-S1, **b** L4-5, **c** L3-4 and **d** L2-3

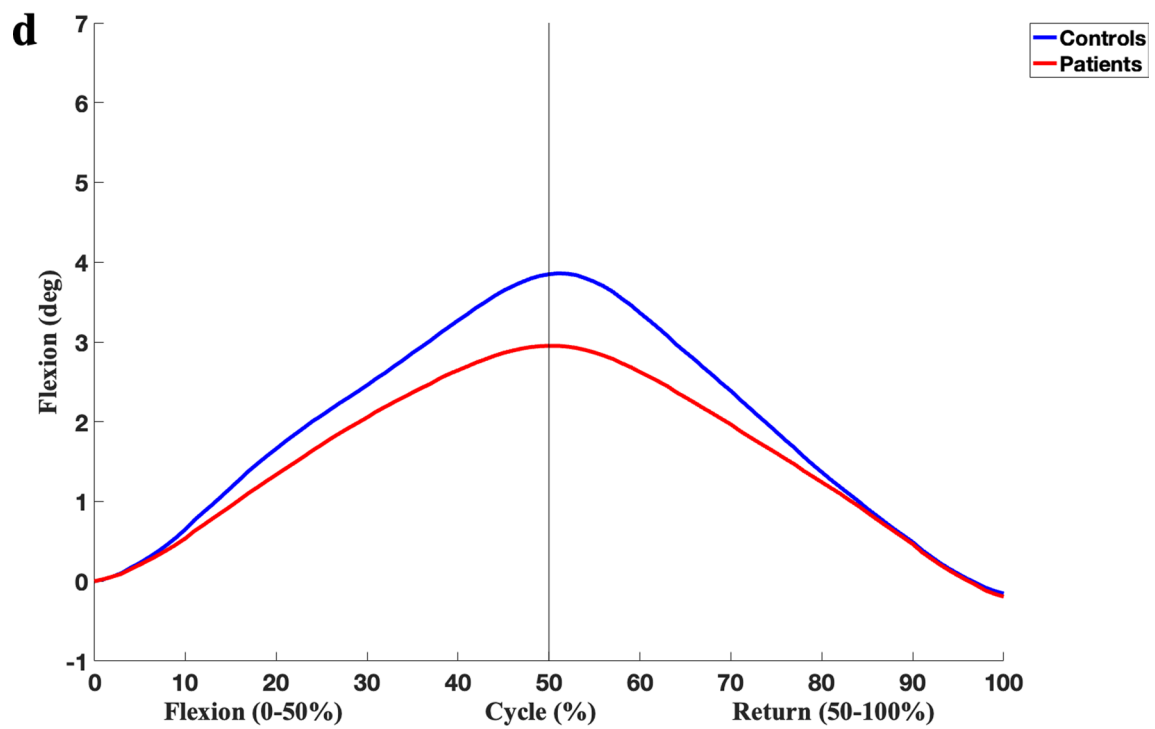
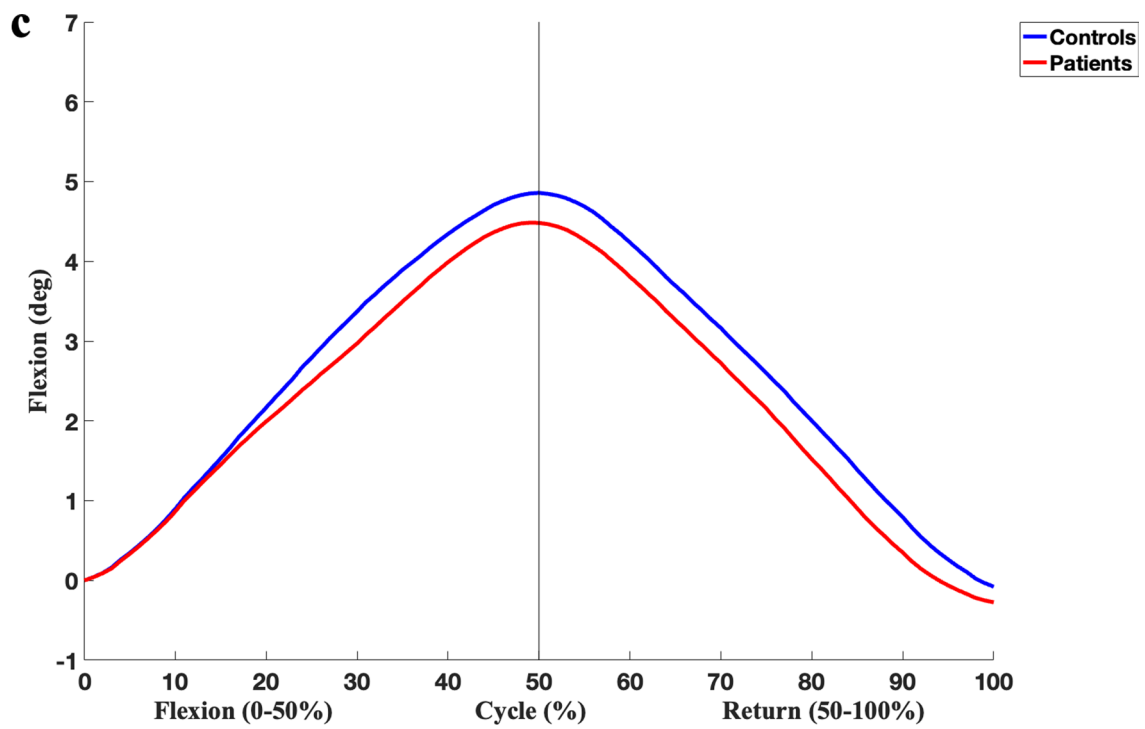
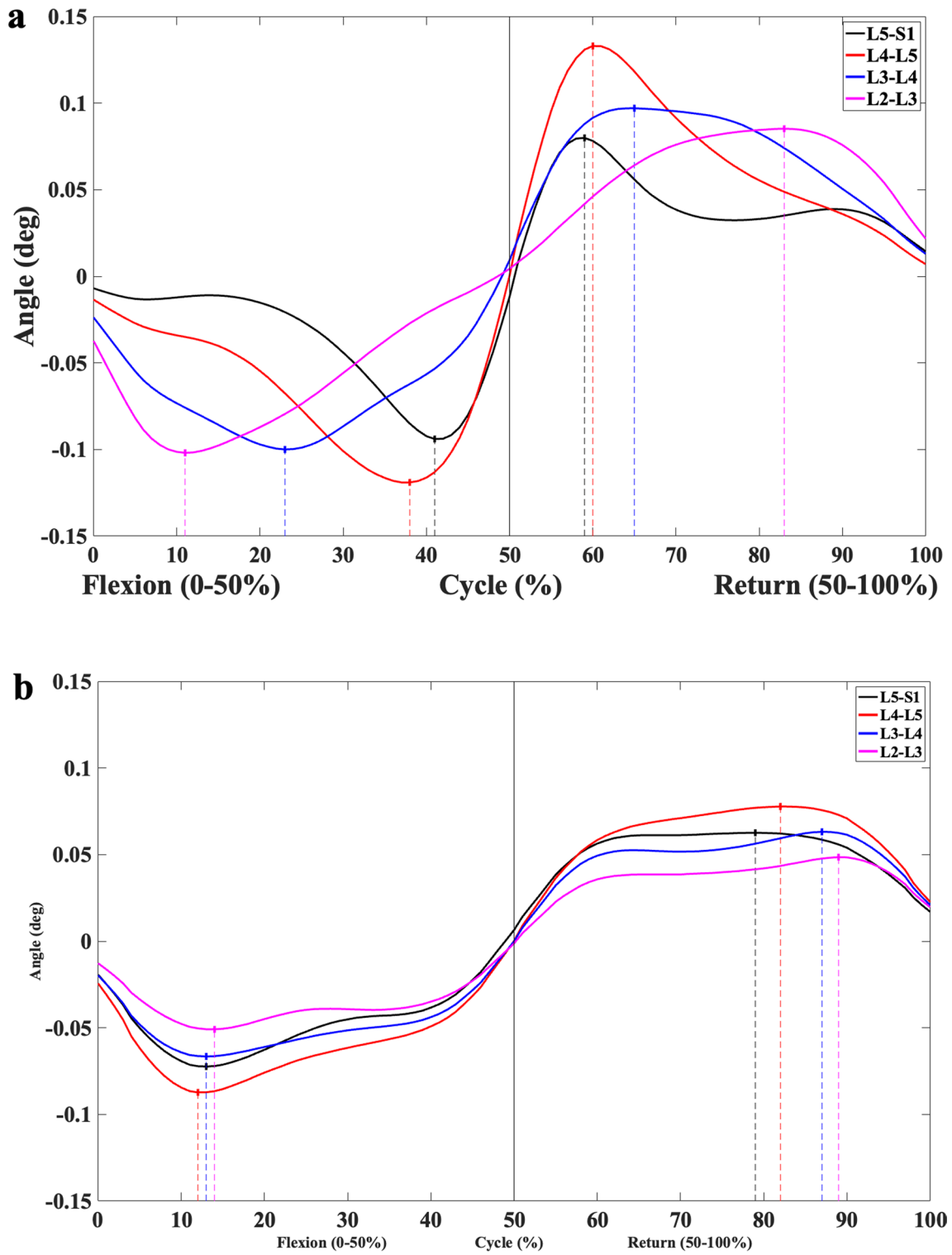
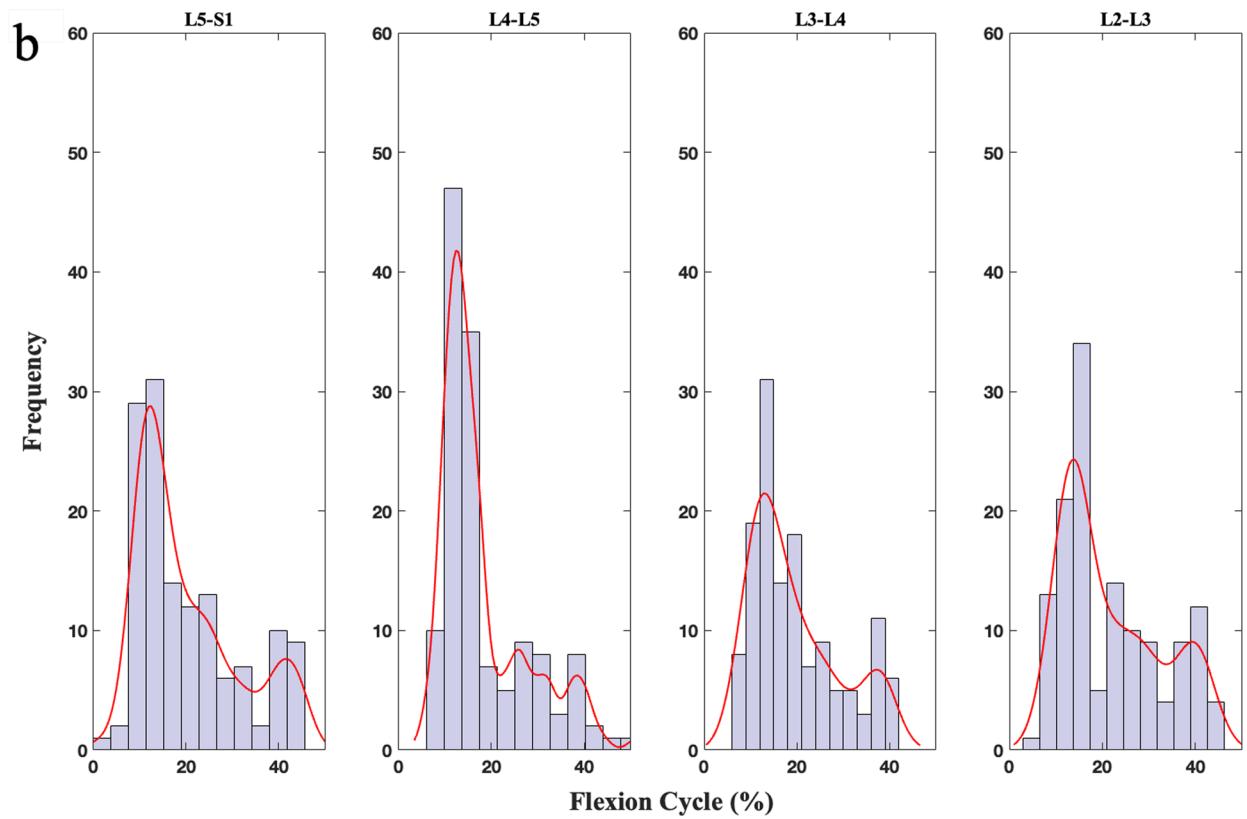
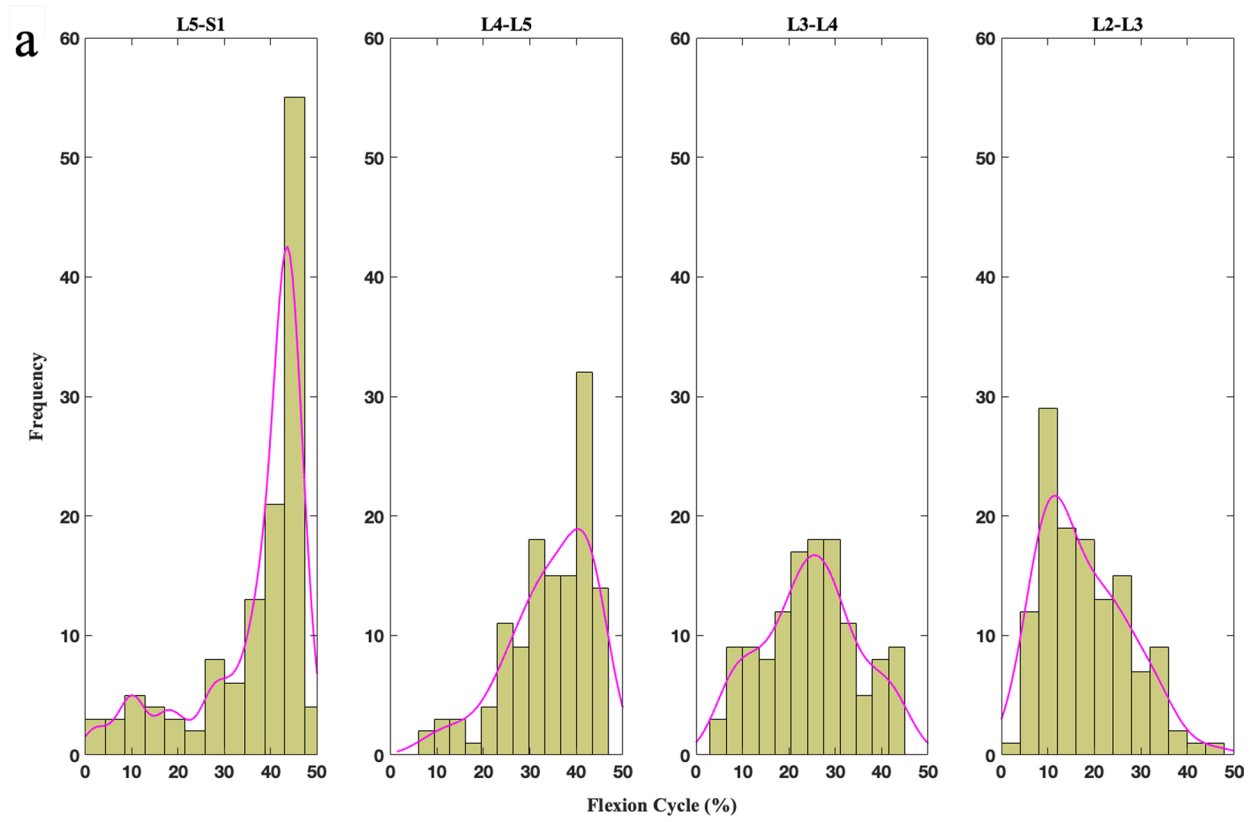


Fig. 4 (continued)



**Fig. 5** Ensemble means of intervertebral velocities from L2-S1 during flexion and return in normative database: **a** weight-bearing and **b** recumbent



**Fig. 6** Distribution of velocity peaking times during flexion in the reference database: **a** weight-bearing ( $n=127$ , from Nematimoez 2023) and **b** recumbent ( $n=136$ )

in both patients and controls, but no significant differences between them for range or magnitude ( $p > 0.05$ ).

## Discussion

### Healthy control reference study

The population of healthy controls in this study showed different patterns of velocities in the previous weight-bearing study (Fig. 5a) compared to the recumbent configuration of the same population (Fig. 5b) [23]. The distribution of PTFD/velocity peaking points in the previous weight-bearing study also portrayed a top-down cascade (Fig. 6a), unlike the similar peaking points at all levels in the current recumbent reference study (Fig. 6b). The passive recumbent population also showed no statistically significant spatiotemporal clusters for PTFD, where there were significantly different peaking times at L4-5 and L5-S1 between patients and controls (Table 2). This means that the passive recumbent method for measuring restraint confers greater homogeneity for PTFD and is less likely to result in confounding when making comparisons with other population groups and supports Hypothesis 1 for this variable.

### Patient–control sub-study

The patient/control sub-study was equally represented in terms of age, gender and BMI. The significant differences in PTFD (velocity peaking times) at L5-S1 between patients and controls during passive recumbent flexion thus represent a further biomarker for CNSLBP in populations with minimal disc degeneration, which, like the MSI measure, is based on pure restraint. However, the ranges of motion (ROM) and peak magnitudes of the velocities (PMFD) were not significantly different in patients at any level, and no significant differences were found during the return phase.

These findings, together with the uneven motion sharing biomarker found previously, suggest that early peaking of passive flexion velocity at L5-S1 and (probably) late peaking at L4-5 occur more frequently in people with CNSLBP and are associated with reduced restraint of flexion at L5-S1, supporting Hypothesis 2. This seems consistent with the microstructural sub-failure concept of chronic back pain and the higher frequency of disc degeneration at these levels in older populations [29]. It also seems consistent with a reduction in intradiscal pressure at L5-S1, resulting in a

compensatory reduction in passive stiffness in the neutral zone and a compensatory delay in peak velocity at L4-5 above [13].

Experiments in the rat model found that a stab lesion to the disc annulus resulted in significantly reduced peak stiffness, peak moment and hysteresis in all directions [30]. However, while this provides evidence of links between disc injury and biomechanical changes, it may have less in common with the more intrinsic mechanisms that might be expected in the less destructive disc microstructural changes that may have been present in this study.

### Deconstructing the biomarker

Imaging studies of disc deformation, biochemical change and the environment for neuropathic pain generation have suggested links to disc disruption in back pain and its kinematics [3, 31–33]. Recent in vivo intervertebral kinematic studies have advocated comparison of the functional integrity of motion segments in symptomatic and asymptomatic populations: For example, it has been shown that in pain-free populations, there is no correlation between ROM, laxity or MSI and degree of disc degeneration up to moderate levels [34]. However, in patients with treatment-resistant CNSLBP, there is a high correlation between disc degeneration and passive recumbent MSI, significantly higher levels of MSI and (in the present study), earlier peak L5-S1 passive flexion velocities [2, 14]. These findings suggest a biomarker for CNSLBP and prompt the question of whether the early peaking of L5-S1 velocity in CNSLBP patients is also accompanied by lowered intradiscal pressure [35]. If so, this would confirm a further relationship between kinematics and early structural disruption in vivo and may provide a way of monitoring the clinical course of CNSLBP and/or the outcome of regenerative disc therapies [6].

### Limitations and further work

This is the first study to compare intervertebral spatiotemporal interactions in patients and controls in vivo in terms of pure restraint. However, its findings should be treated with caution, and it would be advisable to replicate the sub-study to ensure that the findings are robust. This could be achieved by matching an additional patient cohort with minimal disc degeneration to a further set of controls from the same database, which is publicly available [25]. If they are, the next step would be to generate hypotheses around its relationship between these altered peak velocities, and some of the factors described above [35]. What mainly remains to be understood is what drives the relationships between CNSLBP, velocity peaking time (PTFD) during passive recumbent intervertebral motion, MSI and early disc degeneration. Another route for further research could, therefore, be to

investigate possible relationships between indicators of lowered intradiscal pressure, increased neutral zone slope and length (measured as laxity or initial attainment rate in vivo) and lowered L5-S1 velocity peaking times in patients [36, 37]. This may confirm or otherwise relationships between kinematics and early structural disruption in vivo. Such investigations could use MRI to assess biochemical markers and QF the kinematic markers. Together, these could constitute additional minimally invasive methods to better understand and monitor disc health, regeneration and repair.

## Conclusion

This study found that in vivo intervertebral rotational velocity during passive recumbent flexion in healthy controls to be homogeneous across the motion sequence for velocity peaking time and thus unlikely to confound clinical studies that depend on this variable for normative values. In patients with CNSLBP, rotational velocity reaches its peak significantly earlier at L5-S1 than in healthy controls. This may be due to changes in intervertebral disc structure and function and indicate relationships between passive disc restraint and the mechanisms of CNSLBP. These findings could be used to help guide future research into the relationships between intervertebral kinematics, disc microstructure and CNSLBP, as well as to monitor the mechanical effects of therapies that target the disc.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s00586-024-08249-y>.

## Declarations

**Conflict of interests** The authors have no relevant financial or non-financial interests to disclose.

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