Is the Organization of the Primary Motor Cortex in Low Back Pain Related to Pain, Movement, and/or Sensation?

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Aim/Background: Primary motor cortex (M1) organization differs between individuals with and without chronic low back pain (CLBP), in parallel with motor and sensory impairments. This study investigated whether movement behaviour and tactile/pain sensation are related to M1 organisation in CLBP.

Methods: Transcranial magnetic stimulation (TMS) was used to map the M1 representation of the erector spinae and multifidus muscles in 20 participants with and without CLBP. Cortical organisation was quantified by: map volume; center of gravity (CoG); number of peaks; and primary and secondary peak location. Movement behaviour was assessed as the ability to dissociate lumbar from thorax motion and sensory function as two-point discrimination, pressure pain thresholds, and pain intensity (visual analogue scale).

Results: People with CLBP showed more anterior location of the CoG than controls. Map peaks were more numerous in CLBP participants who performed the movement task good than those with poor performance. In CLBP, smaller map volume correlated with greater pain during the movement task. Movement behaviour was not linearly correlated with M1 features.

Conclusions: This study confirms that M1 maps differ between people with and without CLBP, but these changes are variable within the CLBP group and are not related to motor and sensory features in a simple manner.

Key Words: low back pain, motor cortex organization, movement pattern, two-point discrimination

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Chronic low back pain (CLBP) is associated with changes in the brain's structure and function. Structural brain changes include decreased thickness of the gray matter of the insula, thalamus, and prefrontal cortex.[1] Functional brain differences include lower excitability,[2] modified location,[3] and greater overlap[4] of trunk muscle representations in the motor cortex (M1) relative to controls, plus modified location of sensory cortex (S1) activation in response to afferent input from the back.[5,6] There is early evidence for a relationship between brain changes, movement, and pain. For example, a shift of the M1 representation of the transversus abdominis muscle correlates with the amplitude of delayed activation of this muscle during rapid arm movements.[3] Further, the amplitude of shift of the S1 representation correlates with pain duration.[6] Detailed investigation of the relationship between cortical changes and sensorimotor functions is necessary.[7]

It is plausible that convergence of the normally separate M1 representations (ie, "smudging"[4]) of the back muscles in CLBP could have behavioral relevance.[8–10] For example, altered M1 function could translate to reduced ability to individually control separate fascicles of the back muscles.[9,11] This observation appears relevant to the common clinical presentation of a reduced ability to dissociate movement of the lumbar (an action of the shorter back muscles) and thoracic (an action of the longer back muscles) regions of the spine (ie, "thoracolumbar dissociation").[12] Less independent function of discrete components of the back muscles and less independence of cortical organization (loss of separate motor cortex representation) in CLBP appears congruent. Although a relationship is plausible, this possibility has not been tested.

Distortion of body schema, as evidenced by reduced ability to discriminate 2 points of tactile stimulation, is related to deficits in lumbopelvic control in some people with CLBP.[13] Poor ability to discriminate between 2 sensory stimuli applied to the back might be related to both convergence of M1 representations and reduced ability to move spine regions independently. Further, although some characteristics of pain such as duration[6,14], and intensity[15], have been related to reorganization of M1 and/or S1, there has been limited attention to other pain characteristics such as hypersensitivity to mechanical stimuli.

The objective of this study was to evaluate the relationship between measures of M1 organization and tests of motor behavior or sensory (including pain) function. We aimed to: (1) compare M1 organization, and motor and sensory function between individuals with and without CLBP; (2) evaluate the relationship between M1 and a motor behavior test; (3) evaluate the relationship between M1 and sensory function; and (4) evaluate the relationship between tests of motor and sensory function. Our primary hypothesis was that the representation of the trunk muscles at M1 (eg, number of peaks,[16] map volume,[15] location of map peak[3]) would correlate with the ability to dissociate lumbar and thoracic movement and discrimination of 2 simultaneously applied stimuli.

METHODS

Participants

A convenience sample was used in this study and the number of participants was selected to balance the risk to

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participants against the potential to observe differences and relationships in the data. The sample size was similar to that used in studies that have observed changes in cortical organization with similar methodology.[15] Twenty individuals with a history of nonspecific CLBP lasting for more than 3 months who reported limited function or required intervention from a health care professional (32 ± 9 y, 9 males/11 females) participated. Each CLBP participant was asked to identify which side was more painful; in case of bilateral location the dominant side was chosen for further assessments. A group of 20 age-matched and gender-matched pain-free participants with no history of CLBP (28 ± 5 y) were also recruited.

Participants were excluded from the study if they had major spinal pathology (eg, tumor, infection, fracture, inflammatory disease), pregnancy, nerve root compromise, previous spinal surgery, or major surgery scheduled. Participants completed a transcranial magnetic stimulation (TMS) safety questionnaire[17] and were excluded if they did not fulfil the criteria for safety considerations to receive TMS.[18] Participants in the control group were excluded if they presented with any history of chronic neck, lower back or leg pain that was sufficient for them to seek treatment or modify function. The institutional Medical Research Ethics Committee approved the study and all participants provided written, informed consent.

Motor Cortex Organization

The region of the primary motor cortex with inputs to lumbar paraspinal muscles was mapped using TMS and surface electromyography (EMG). Pairs of surface electrodes (Ag/AgCl) were placed in a longitudinal direction over the erector spinae (ES) 3 cm lateral to the spinous processes of L3 and 1 cm adjacent to L5 on both sides.[19] EMG data were preamplified 2000 times, band-pass filtered (20 to 1000 Hz) and sampled at 2000 Hz using a Power 1401 Data Acquisition System with Signal 2 software (Cambridge Electronic Design, CED, UK). Data were exported and analyzed with Matlab 6.5 (The Mathworks).

TMS was delivered using a single-pulse monophasic Magstim 200[2] (Magstim Company, UK). A figure-of-eight coil was placed with the crossover position over the target scalp site and orientated along the sagittal plane. Although it was possible to evoke motor evoked potentials (MEP) in ES using TMS for all participants, it was not possible to provide standardized stimulation at 120% of motor threshold as this generally exceeded the 100% output of the stimulator. Thus, stimulator output was set at 100% for all participants. Stimulation was delivered at points aligned to a 5×7 cm grid over each hemisphere (starting at the midline to 5 cm lateral to this point, and from 6 cm anterior to 1 cm posterior to the vertex). TMS mapping was guided using a Brainsight 2 navigation system based on reference points obtained from the location of the vertex, determined using an International 10/20 electrode placement system. Five stimuli were delivered at each intersecting point on the grid (interstimulus interval: ~5 s) during submaximal muscle activation.

Before commencement of the trial, participants performed 3 maximum voluntary contractions (MVC) of the paraspinal muscles (~3 s duration). This involved extension of the back with the participant sitting upright in a chair with a backrest at 90 degrees. With the arms crossed and the feet fixed on the floor the participants extended isometrically against manual resistance applied to the shoulders, with no movement of the trunk. The trunk posture was identical to that used for the remainder of the testing session. The maximum amplitude across the trials for L5 ES was recorded.

For the experimental trials, participants activated the paraspinal muscles by leaning forward with a straight back to match a visual target indicating 20% MVC root mean square (RMS) EMG amplitude of the L5 ES recording. Approximately 10% variation of the value estimated for the 20% of their MVCs was allowed. This was monitored by the experimenter by observation of the target and performed force on the computer monitor. Verbal feedback was provided to the participant to make adjustments if necessary. All procedures adhered to the TMS checklist for methodological quality.[20]

Motor Behavior Measurement

Coordination of spine movement was evaluated using a clinical test of the ability to dissociate motion of the lumbar spine from that of the thoracic spine. This test is based on the observation that some subgroups of patients with CLBP have difficulty with this maneuver and the hypothesis that this might be related to smudging of the M1 representation of the lumbar muscles in CLBP. Motion was assessed with clinical criteria using the "Clinical test of thoracolumbar dissociation" that has been validated previously.[12] This test is scored from 0 to 10 based on the quality and consistency of performance of the task and a score of 5.5 has been established as the cutoff for good/poor performance. The test was assessed by a trained rater with known reliability for this specific test.[21] Test scores are used in the analysis as the proportion of participants in each group who presented with good and bad performance.

Sensory Function Measurement

Pain and tactile sensation were assessed using pressure pain thresholds (PPT) and two-point discrimination (TPD), respectively. TPD was assessed on both sides of the back between the L1 and the iliac crest with a calliper. Threshold for TPD was identified as the shortest distance between calliper points that the participant could accurately identify as 2 (rather than 1) points. Stimuli were applied with decreasing and increasing aperture of 0.5 cm from a starting separation of 10 or 1 cm, respectively. With each sequence of application, after the initial presentation at the maximum or minimum aperture, the order of apertures was generally presented in sequential stimuli delivered out of order (± 4 increments from the next expected stimulus). The average threshold from 3 sequences of aperture change was calculated. Stimuli were varied between alignment in the vertical and horizontal directions.

PPT was assessed with a pressure algometer (1 cm^2 rubber tip) applied to the back (at the site of worst pain reported by the participant or a matched side for the pain-free participants) and a remote site (thumbnail). Participants indicated when the sensation of pressure first changed to one of pain[22] by depressing a button that produced an audible sound. The algometer was applied perpendicular to the skin and pressure applied manually with increasing force.

Participants also reported the intensity of their low back pain during the TMS and test of motor behavior on a 10-cm visual analog scale, anchored with "no pain" at zero and "worst pain imaginable" at 10. Pain was reported immediately after TMS and after the motor behavior test.

Data Analysis

Maps of M1 were generated from the surface EMG recordings from ES at L3 and L5. EMG was full-wave rectified, trials at each scalp site averaged, and the onset and

offset of the MEP were visually determined. MEP amplitude was quantified as the RMS EMG amplitude for the period between onset and offset of the MEP, and the background RMS EMG amplitude recorded before the TMS pulse (55 to 5 ms before stimulation) was subtracted. The RMS EMG amplitudes of the MEP were superimposed over a grid of respective scalp sites to produce a topographical map of the amplitude of responses recorded with the L3 and L5 ES EMG. Response amplitude was normalized to the amplitude of the greatest MEP amplitude or "primary peak" response and values under 25% of the peak were removed.[4] Parameters of cortical organization (eg, map volume, center of gravity [CoG] location) were calculated from normalized maps. The maps were averaged across participants with data aligned in 2 configurations. First, maps for each participant were aligned by anatomic landmarks based on the 5×7 cm grid orientated to the vertex. Second, maps for each participant were aligned to the stimulation site with the greatest MEP amplitude. Maps were also considered separately for participants in each group who achieved "good" ($>5.5/10$) or "poor" (≤ 5.5) performance on the clinical test of thoracolumbar dissociation.

Map volume (a measure of the total excitability of the cortical representation) was calculated as the sum of the normalized MEPs recorded across all scalps sites where MEPs exceeded the 25% threshold. The location of the CoG was calculated using the formula $= \sum z_i x_i / \sum z_i, \sum z_i y_i / \sum z_i$ (For scalp sites x_i (medial–lateral), y_i (anterior–posterior), and z_i (amplitude))[23] and expressed as x-coordinate and y-coordinate. The number of discrete peaks in the M1 representation of the ES muscles was determined using a published criteria that define a peak as a scalp site where the MEP amplitude is $>60\%$ of the greatest MEP amplitude for the whole map and that was separated from other "peak" in the anteroposterior direction by a reduction in MEP amplitude of at least 20%.[15] The locations of the primary (greatest amplitude) and secondary (second greatest amplitude) peaks in the motor maps were defined using the x-coordinate and y-coordinate and the vector length between each peak and the vertex of the scalp (coordinates 0,0).

Statistical Analysis

Normal distribution of all variables was tested with the Shapiro-Wilk test. To address aim 1, M1 map variables (map volume, CoG, number of peaks, and peak location) and sensory function variables (TPD, PPT) were compared between groups (CLBP vs. pain-free) and levels (L3 vs. L5) using repeated-measures analysis of variance and Duncan test for post hoc analyses. Motor map volumes at the L3 and L5 EMG recording site were transformed (square root method) to achieve normal distribution. The proportion of participants in each group who displayed poor performance on the motor behavior test were compared with a χ^2 test.

Two analyses were conducted to address aim 2. First, the relationship between motor map variables at L3/L5 and measures of motor behavior were examined using the Spearman rank test. Second, differences in the number of map peaks between participants in each group who displayed good/poor performance on the test of motor behavior were assessed with χ^2 tests.

Aim 3 was addressed by the relationship of motor map volumes and measures of sensory function (including pain). We also assessed the correlation between M1 measures and pain experienced during the TMS and motor behavior test. For all analyses the Spearman rank test was used.

To address aim 4, the relationship between the tests of motor behavior and sensory function were assessed with the Spearman rank test. For all analyses the significance level was set at $P \leq 0.05$. All analyses were performed using the statistical software Stata 12. Data are presented as mean ± SD throughout the text and figures.

RESULTS

Comparison of M1 Organization Between Groups

The location of the CoG for each motor map (regardless of the number of peaks) was more anterior in the CLBP group (y-coordinate—main effect: group—$P=0.02$) and this was observed for ES EMG recordings at both levels (main effect: level—$P=0.26$; interaction: group×level—$P=0.93$). No differences in CoG location were found in the mediolateral direction (x-coordinate main effect: group—$P=0.74$, level—$P=0.23$, interaction: $P=0.21$; Table 1).

Map volume was smaller at L5 than L3 (main effect: level—$P=0.03$), and although not significant, there was a tendency for a smaller map volume in those with CLBP than pain-free controls (main effect: group—$P=0.07$) that did not differ between L5 and L3 (interaction: group×level—$P=0.90$).

When TMS maps of ES EMG recorded at L3 and L5 were aligned by the anatomic reference (vertex) and averaged across participants, a single discrete peak was identified for each group and each muscle (Fig. 1). In contrast, when TMS maps were averaged across participants with the maps aligned to the location of the greatest peak (Fig. 2), multiple peaks were identified in the average map for the recording made at L3 for the pain-free controls, but only a single peak was identified in the CLBP group (Fig. 2). For the L5 EMG recording, the pain-free group showed a single peak (primary peak) in the M1 motor maps with a tendency toward a second peak, but this did not meet our a priori defined criteria. Although the CLBP group had 2 peaks in the motor maps of L5, this was very distant from the primary peak and on the edge of the averaged map. Despite the differences observed for the averaged maps in each group, when maps were considered for individual participants according to our conservative criteria for definition of a peak there was no difference between groups. A second peak at L3 was identified for 13/20 and 12/20 of the pain-free and CLBP participants, respectively ($\chi^2=0.107$; $P=0.74$), and 12/20 and 11/20 at L5 ($\chi^2=0.102$; $P=0.75$).

The distance of the primary peak from the vertex (vector length) was significantly different between groups and site of EMG recordings (interaction group×level—$P=0.03$). Post hoc analyses showed that vector length in the pain-free group at L3 level was larger than L5 recordings (Duncan test—$P=0.05$). This difference was not present for CLBP participants.

No significant differences in the vector location of the primary peak of each M1 map were found in the mediolateral direction (x-coordinate interaction: $P=0.26$, main effect: group —$P=0.91$, level—$P=0.89$) or for the anterior-posterior direction (y-coordinate interaction: $P=0.69$, main effect: group—$P=0.26$, level—$P=0.69$; Table 1).

There was no difference in the vector length of the secondary peak between groups or level of EMG recordings (interaction: group×level—$P=0.99$). At L3 level, the secondary peak in the CLBP group showed a nonsignificant tendency to be more anteriorly and laterally located from the vertex than in the pain-free group (main effect: group—$P=0.07$). At L5, the

secondary peak in both groups showed a significantly larger distance from the vertex in the lateral direction (*x*-coordinates—CLBP: 2.8 ± 1.7; pain-free: 2.4 ± 1.6) than anterior (*y*-coordinates—CLBP: 1.4 ± 2.1; pain-free: 0.3 ± 1.8, main effect: direction—$P = 0.003$). The post hoc analysis revealed that this difference was significant only within the pain-free group (Duncan test—$P = 0.0001$).

Comparison of Motor Behavior Between Groups

The proportion of participants who achieved good performance on the clinical test of thoracolumbar dissociation was greater for the pain-free (13/20) than the CLBP group (5/20) ($\chi^2 = 6.46$, $P = 0.011$).

Comparison of Sensory Function Between Groups

Although not significant, CLBP participants showed a tendency (main effect: group—$P = 0.06$) to require a larger vertical distance to detect 2-points than pain-free participants. There were no significant differences between affected and nonaffected sides between groups (interaction: group×side—$P = 0.72$). For the detection of 2 points in the horizontal direction there was no difference between groups or sides (interaction: group×side—$P = 0.12$). PPT had a significant interaction between groups and area of test (interaction: group×area—$P = 0.008$). The CLBP group had a significantly lower threshold than pain-free group at the back (Duncan test—$P = 0.03$). Pain-free participants, but not CLBP participants, had a lower threshold for thumbnail than the back (Duncan test—$P = 0.001$).

Relationship Between Motor Cortex Organization and Motor Behavior

The scores achieved by the participants in the test of motor performance were not correlated in a linear manner or showed trends toward correlation with any of the M1 map measures (all: $P > 0.16$) at either the L3 or L5 level. However, individuals in the CLBP group (Fig. 3A) with good performance on the clinical test showed 2 peaks in the average of the maps aligned to the primary peak, but these were medial-laterally distributed which does not fit the criteria to determine the presence of secondary peak. In contrast, CLBP participants with poor performance had a single peak in the average map. When the pain-free participants were subgrouped by score on the test of motor behavior, TMS maps at L3 (Fig. 3B) showed 2 discrete map peaks, regardless of the score achieved on the clinical test. A single peak was present for both groups regardless of performance on the clinical test for EMG recordings made at L5 (Figs. 3C, D).

TABLE 1 . Between-group Comparisons of Motor Cortex Organization, Motor Behavior, and Sensory Function

	Pain-free Group			CLBP Group				Main Effects	
Variables	**Mean**	**SD**	**n**	**Mean**	**SD**	**n**	**Interaction Effect**	**Group**	**Level/Area/Side**
MEP amplitude L3	0.6	0.3	20	0.5	0.4	20	0.81	0.16	**0.04**
MEP amplitude L5	0.4	0.3	20	0.3	0.3	20	—	—	—
Map volume L3†	9.9	5.4	20	7.4	4.1	20	0.90	0.07	**0.03**
Map volume L5†	8.4	4.2	20	6.3	3.8	20	—	—	—
CoG vector L3	2.6	0.8	20	3.0	0.9	20	0.49	0.20	0.74
CoG vector L5	2.6	0.9	20	2.9	1	20	—	—	—
L3 *x*-coordinates	2.4	0.8	20	2.4	0.8	20	0.21	0.74	0.23
L5 *x*-coordinates	2.4	1	20	2.2	0.9	20	—	—	—
L3 *y*-coordinates	0.7	0.7	20	1.3	1.1	20	0.93	**0.02**	0.26
L5 *y*-coordinates	0.8	0.8	20	1.5	1.1	20	—	—	—
Vector length primary peak—L3	3.1	1.3	20	2.8	1.1	20	**0.03**	0.68	0.38
Vector length primary peak—L5	2.4	1.5	20	3.0	1.4	20	—	—	—
L3 *x*-coordinates	2.4	1.4	20	2.0	1.5	20	0.38	0.67	**0.20**
L5 *x*-coordinates	1.9	1.5	20	1.9	1.7	20	—	—	—
L3 *y*-coordinates	0.5	1.8	20	0.7	1.5	20	0.29	0.25	**0.06**
L5 *y*-coordinates	0.7	1.5	20	1.5	1.7	20	—	—	—
Vector length secondary peak—L3	2.7	1.1	13	3.8	1.6	12	0.99	0.11	0.19
Vector length secondary peak—L5	3.0	1.6	12	3.9	1.5	11	—	—	—
L3 *x*-coordinates	2.0	1.3	13	2.3	1.7	12	0.26	0.91	0.89
L5 *x*-coordinates	2.4	1.6	12	2.8	1.7	11	—	—	—
L3 *y*-coordinates	1.0	1.4	13	2.4	1.9	12	0.69	0.26	0.69
L5 *y*-coordinates	0.3	1.8	12	1.4	2.1	11	—	—	—
Motor behavior (proportion with "good" performance)	5.8	2.4	20	4.7	2.1	20	**0.01***	—	—
TPD—affected side vertical	3.3	1.1	20	3.9	1.4	20	0.72	0.06	0.32
TPD—unaffected side vertical	3.2	0.8	20	3.7	1.1	20	—	—	—
TPD—affected side horizontal	4.8	1.2	20	5.4	1.8	20	0.12	0.73	0.72
TPD—unaffected side horizontal	5.4	1.1	20	5.1	1.6	20	—	—	—
PPT—lumbar	584.6	239.5	18	452.2	171.1	19	**0.008**	0.22	**0.001**
PPT—thumb nail	413.9	185.3	18	411.3	101.5	19	—	—	—

Significant differences highlighted in bold.
*χ^2 test.
†Square root transformation for *t* test as data were not normally distributed.
CLBP indicates chronic low back pain; CoG, center of gravity; MEP, motor evoked potentials; PPT, pressure pain threshold; TPD, two-point discrimination.

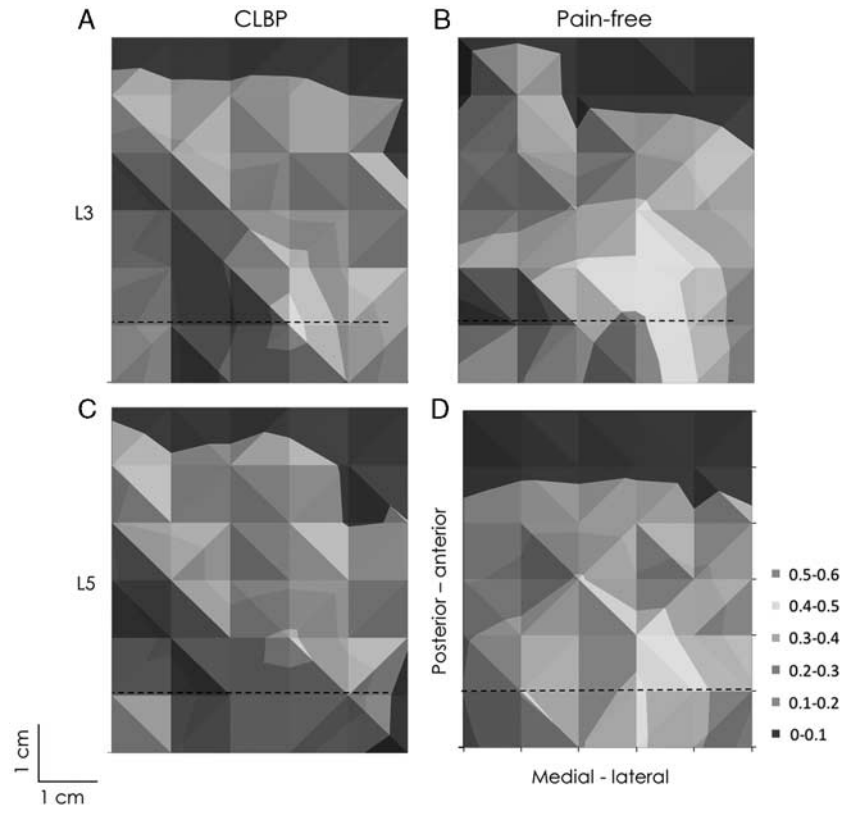

FIGURE 1. Average of the normalized M1 maps aligned to the anatomic reference point (vertex of skull). The dashed lines indicate the location of vertex (vertex 0,0). Data are shown for pain-free (B, D) and chronic low back pain (A, C) groups. L3 electromyography recording sites (A, B) and the L5 (C, D). The colored scale indicates the amplitude as a proportion of the magnitude of the largest motor evoked potential. CLBP indicates chronic low back pain.

Relationship Between M1 Organization and Sensory Function

There was a significant inverse correlation between the distance of the CoG of the motor map from the vertex (vector length, and *x*-coordinate and *y*-coordinate) at L3 and PPT at the lumbar site (vector: $\rho = -0.39$, $P = 0.02$, *x*-coordinate: $\rho = -0.35$, $P = 0.03$; *y*-coordinate: $\rho = -0.03$, $P = 0.88$). That is, the distance of the CoG from the vertex was greater for those with lower PPT (Fig. 4). There were no other relationships between motor maps and PPT (all: $P > 0.09$) and no correlation between any feature of the M1 map and the TPD test (all: $P > 0.08$).

Pain intensities reported during TMS and during movement were related with some map variables. Greater pain intensity reported during TMS testing was correlated with smaller map volume at L3 ($\rho = -0.36$; $P = 0.02$, Fig. 5A) and L5 ($\rho = -0.31$, $P = 0.05$, Fig. 5B) and with longer vector length of the CoG ($\rho = 0.34$; $P = 0.03$, Fig. 5C), *y*-coordinate (anterior-posterior direction) of CoG ($\rho = 0.34$; $P = 0.03$) and longer vector length of the second discrete map peak at L3 ($\rho = 0.50$, $P = 0.01$, Fig. 5D). Greater pain intensity during the movement task was correlated with TMS map volume for both L3 ($\rho = -0.39$, $P = 0.02$, Fig. 5E) and L5 ($\rho = -0.41$, $P = 0.01$, Fig. 5F) EMG recordings. Larger vector length of the CoG ($\rho = 0.35$; $P = 0.03$, Fig. 5G) and secondary peak ($\rho = 0.45$, $P = 0.02$, Fig. 5H) at L3 were also correlated with higher pain intensity during movement. There were no other relationships between M1 measures and pain (all: $P > 0.08$).

Relationship Between Motor Behavior and Sensory Function

The score on the test of motor behavior was inversely correlated with pain intensity during performance of the test ($\rho = -0.34$, $P = 0.03$) and with the PPT at the thumbnail site ($\rho = -0.33$, $P = 0.05$). That is, motor behavior test scores were lower, and thumbnail PPT higher, in those with higher pain. No other significant relationships were observed (all: $P > 0.07$).

DISCUSSION

The findings of this study demonstrate that the M1 representation of back muscles in individuals with CLBP is more complex and in a different location to that of individuals with no history of pain. Differences between groups were also observed in movement performance and sensory function, which provides some evidence of parallel between M1 organization and simple motor and sensory measures. However, these changes were weakly related at best and not in a linear manner. Some features of the motor map did not differ from those of pain-free controls in the manner that has been reported previously or narrowly missed significance. Our correlation analyses suggest some of these features are dependent on pain, which highlights the heterogeneity of the CLBP group. The clinical significance of the change in mapping characteristics of the motor cortex in LBP is largely unknown. This study is the first that has attempted to address this issue giving some insights of the

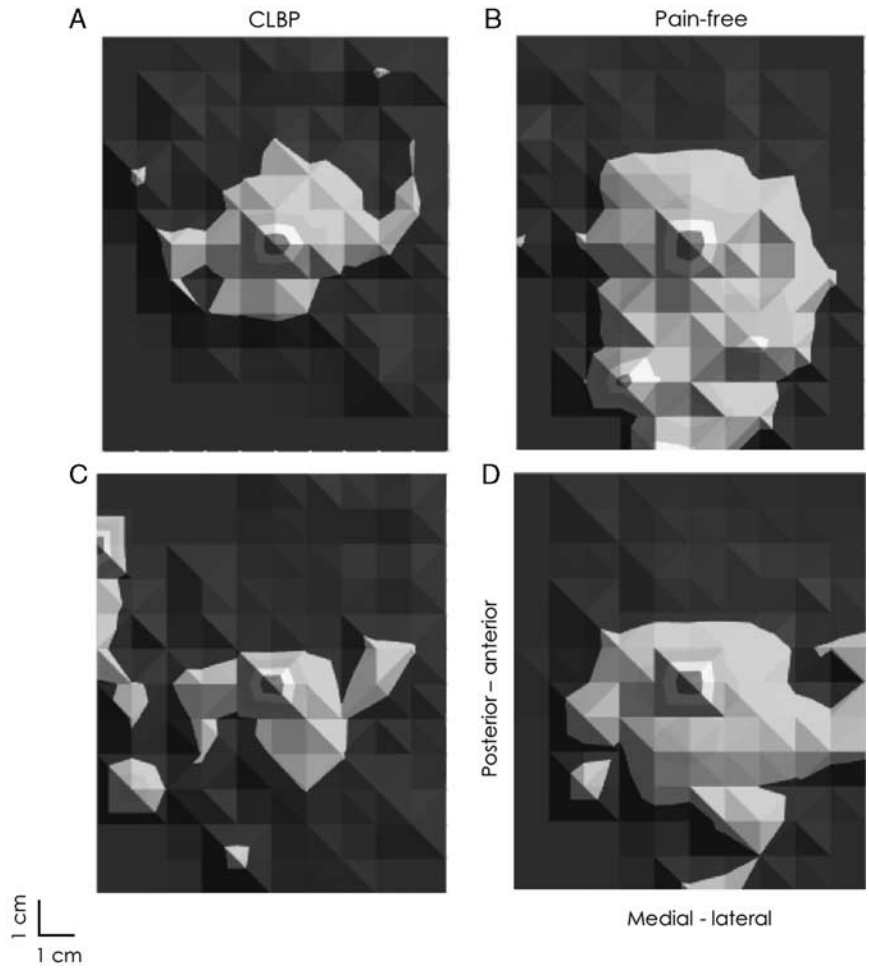

FIGURE 2. Average of normalized M1 maps aligned to the stimulation site that evolved the greatest motor evoked potential (center grid reference in map) obtained for each individual. Data are shown for pain-free (B, D) and chronic low back pain (A, C) groups. L3 electromyography recording sites (A, B) and the L5 (C, D). CLBP indicates chronic low back pain.

possible relationships present. Although we provide some evidence of relationships, the interaction between cortex changes and clinical observations of motor behavior and sensory function appears to be more complex than predicted.

Motor Cortex Organization in Individuals With CLBP

Our data show that the M1 representation of back muscles in individuals with CLBP is located more anterior than that of pain-free individuals. Although a shift in the CoG was expected based on previous studies of paraspinal[4] and abdominal[2] muscles, the direction was opposite to the more posterior location identified in some previous work for similar muscles.[4] This outcome might be explained by differences in the muscles recorded and in the EMG recording technique used. Previous work in CLBP has used intramuscular EMG (fine-wire) electrodes, that record activity from individual fascicles of the multifidus muscle.[16] Using that method, different locations have been observed for the site of peak cortical excitability for short/deep and long/superficial fascicles (each recorded with separate, fine-wire electrodes). Our data were collected with surface electrodes, that record more generalized activity from a larger area and include activity from multiple muscle fascicles within the same recording. Our surface electrode recording at L5 (1 cm lateral to the spinous process) would have included contribution from both deep and superficial fibers of multifidus, and the surface electrode at L3 (3 cm lateral to the spinous process) would likely include contribution from multifidus and the more lateral longissimus/iliocostalis. Thus, the properties of the M1 map estimated from each recording site would reflect the net response of multiple muscles (including those not recorded in the earlier study) and the response of individual muscles would be impossible to isolate. These features could explain the difference to earlier work such as the anterior (rather than posterior) shift of the CoG, and differences in the number of map peaks in the data for our CLBP group. Alternatively, these differences could also relate to features such as differences in the intensity of pain; Schabrun et al[15] showed a relationship between some features of the M1 representation and current pain.

Our data replicate the observation of 2 peaks in the M1 map of pain-free participants and 1 peak in the M1 map (smudging) in CLBP[4], but only at the L3 recording site and only when data were averaged across participants with individual maps aligned to the location of the primary peak. This supports the hypothesis that smudging may be related

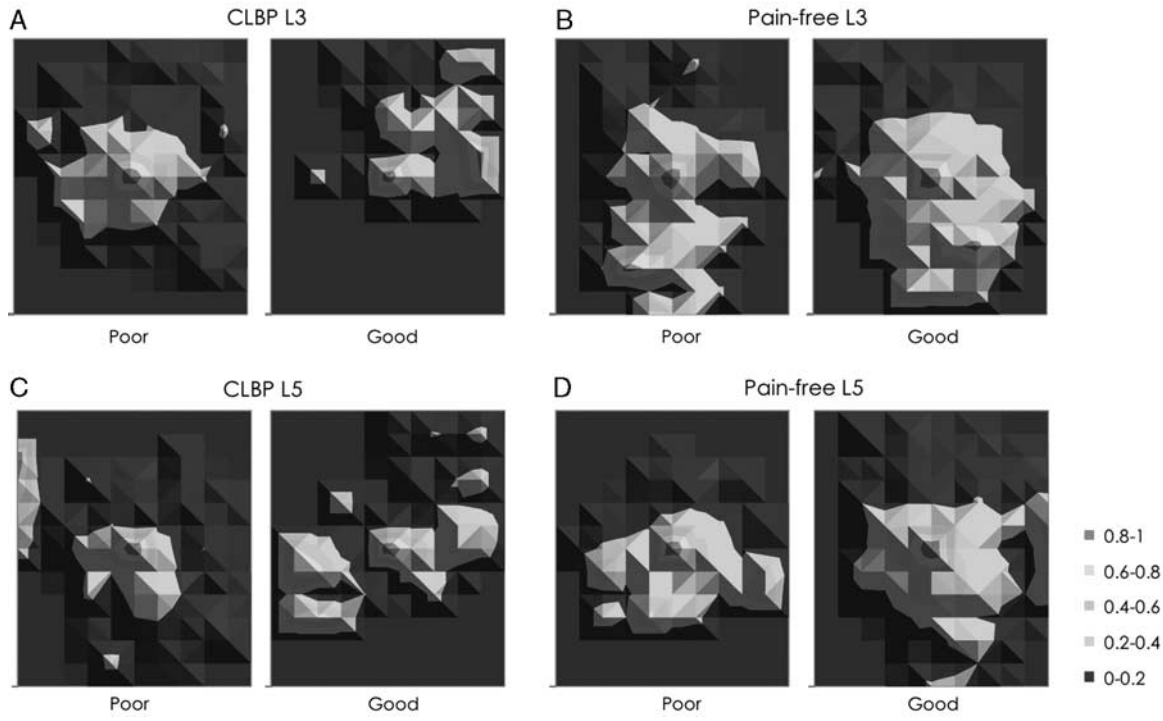

FIGURE 3. Average of normalized M1 maps aligned to the stimulation site that evoked the greatest motor evoked potential (center grid reference in map) averaged for participants with poor (< 5.5) and good (> 5.5) performance on the motor behavior test. Data are shown for participants with chronic low back pain (CLBP) at L3 (A) and L5 (C) electromyography recording sites, and for pain-free participants at L3 (B) and L5 (D).

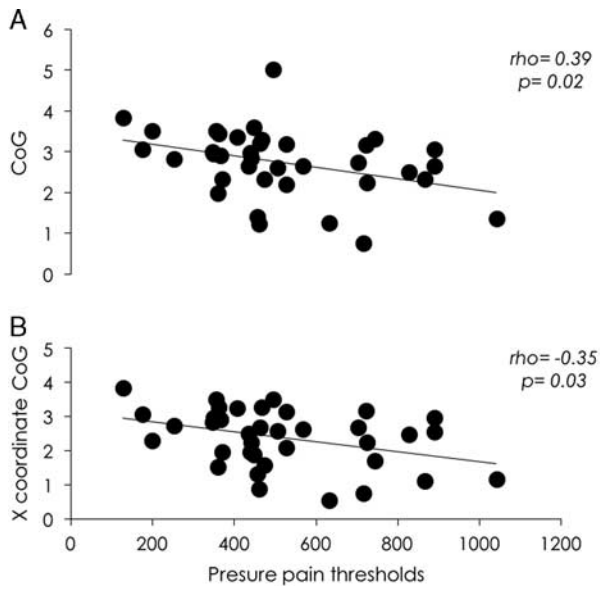

FIGURE 4. Relationship between motor cortex organization and pressure pain threshold (PPT) at lumbar site. A, Correlation between PPT and with the distance of the center of gravity (CoG) of the motor map from the vertex. B, Relationship between PPT and the *x*-coordinate (mediolateral) of the CoG. Lower pressure pain thresholds were related to a location of the CoG that was further from the vertex.

to deficits in control of the back muscles. However, inspection of individual data revealed 2 peaks for most participants and the number did not differ between groups. This differs from previous work[15] where the smudging of the representation of back muscles in M1 was consistent with the fewer secondary peaks between LBP participants. Our observation is best explained by variation in the location of the second peak relative to the primary peak that resulted in removal of the second peak from the average. This proposal is supported by the longer average and greater SD of the vector length for the CLBP group (pain-free: 1.1 vs. CLBP: 1.6). Other observations also support the greater variation in CLBP participants. For instance, the length of the vector for the primary peak differed between L3 and L5 recording sites for the pain-free but not CLBP participants.

The increase in volume of M1 representation in muscles related to improvement of motor skills after specific training[24–26] leads to hypothesize that the decrease of the volume of M1 representations in CLBP would influence detriment of motor skills. Although the tendency to present lower volume of the averaged cortical maps of paraspinal muscles in the CLBP group concurs with smaller motor map volume in earlier studies of CLBP and shoulder pain[4,14,19] and could relate to reduced gray matter volume[1] and activation of glial cells in cortical motor regions in CLBP.[27] The functional relevance of reduced volume is unclear. The correlation between higher levels of pain and smaller map volume in CLBP participants demonstrates that the characteristics of the CLBP group were not homogenous in this study. This might explain the inability to show differences

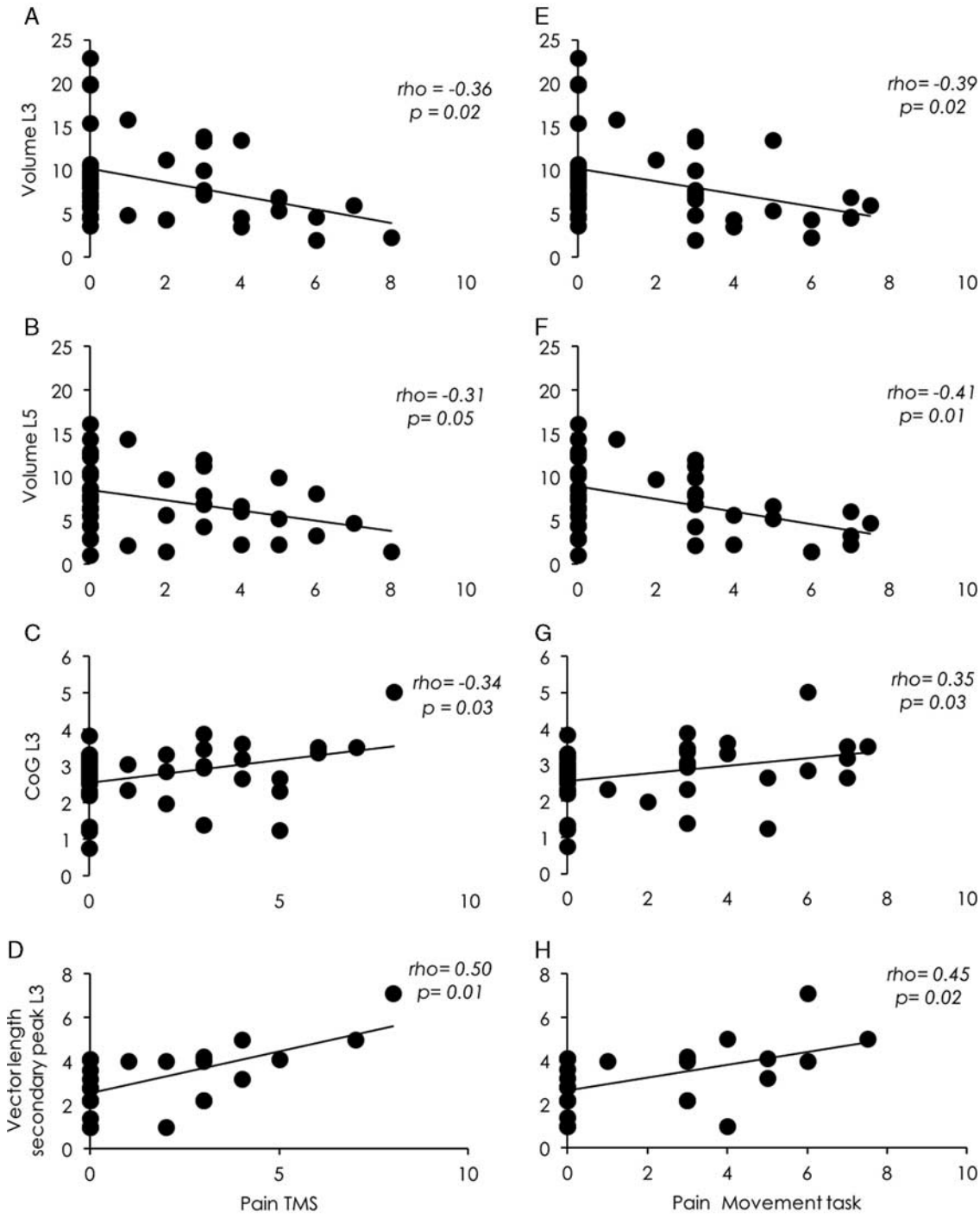

FIGURE 5. Relationship between motor cortex organization variables and pain intensity. Left panels show the relationship of pain reported during TMS and (A) volume of the map at L3 electromyography recording site, (B) volume of the map at L5 electromyography recording site, (C) centre of gravity of the map at L3 electromyography recording site, and (D) vector length of the secondary peak of the map at L3 electromyography recording site. Right panels show relationships of pain reported during movement task with (E) volume of the map at L3 electromyography recording site, (F) volume of the map at L5 electromyography recording site, (G) centre of gravity of the map at L3 electromyography recording site, and (H) vector length of the secondary peak of the map at L3 electromyography recording site.

between groups and suggests that a comparison that includes CLBP participants with higher levels of pain might show a clearer difference in features of the motor cortex map relative to pain-free individuals.

It is unclear whether differences in M1 organization precede or follow pain development as all patients in the present study reported current pain. The presence of a single map peak in some healthy participants could be a precursor

to pain, but this is as yet untested in longitudinal studies. Previous studies have involved participants with current pain[15] and during symptom remission.[28] It is plausible that variation between the findings of these studies (eg, location and number of peaks in the M1 map) may be explained by time-dependent processes. For instance, nerve growth factor injection into the wrist extensor muscles induces elbow pain for several days and is accompanied by increased map volume.[29] This contrasts the decreased volume observed with longer periods of pain, as shown in the present and earlier work.[15] Whether these differences represent different events in the continuum from acute to chronic/recurrent pain requires investigation.

Motor Behavior and Sensory Function in CLBP

Consistent with previous studies of some motor tasks,[13] the thoracolumbar dissociation task was performed poorly by more participants with CLBP than pain-free in the present study. Although most participants with CLBP scored below the cutoff (75%), and most pain-free scored above this value (65%), this was not uniform across the groups. This concurs with the view that CLBP is heterogenous, including subgroups that present with specific movement patterns. The inability to move the lumbar spine and pelvis separately from the thorax has been identified in a specific subgroup of CLBP in the clinical literature.[30–32] A similar motor pattern in some pain-free participants could reflect a risk factor for future development of pain or may suggest the motor behavior is not problematic. This requires further investigation.

Sensory function is commonly modified in CLBP using both painful and nonpainful stimuli in the area of pain.[33,34] Our data show weak evidence for impaired tactile acuity (ability to discriminate between 2 points) of the back in CLBP which concurs with findings of a recent systematic review of sensory changes in CLBP.[35] As expected, PPTs were lower in the lumbar area of our CLBP cohort, but there was no evidence of more generalized central sensitization as PPTs were not modified at the thumbnail.

Relationships Between Motor Cortex Organization and Motor or Sensory Function

Contrary to our hypothesis, we found no simple linear relationship between differences in M1 organization and either the ability to dissociate movement between spine regions or the ability to discriminate between simultaneous sensory inputs. However, we did observe a single peak in the averaged M1 map (consistent with "smudging" of the cortical representations) in the subgroup of patients with poor performance on the motor task and 2 peaks in the group with good performance. Taken together, this indicates that there is a relationship, but it is not linear.

Several studies in humans and animals have correlated changes in brain organization with motor variables. The amplitude of delay in feedforward activation of the abdominal muscles correlates with the shift in their cortical representation in CLBP during rapid arm movements.[3] The ability to activate the multifidus muscle voluntarily correlates with the amplitude of reduced short interval intracortical inhibition and active motor threshold in people with CLBP.[36] Further, skilled movement and motor skill learning modify the topography of M1 maps in rats[37,38] and humans.[24–26] Although these studies show a relationship between skilled movements and changes in M1 organization, it is unclear why these features have been more consistently related to features of M1 organization than the motor behavior tested here. Some features of sensory function/pain were related to M1 organization. First, motor map volume was smaller in participants with higher pain intensity, which aligns with previous studies.[19,39] Pain intensity has also been shown to relate to the density or thickness of the gray matter.[39,40] Second, anterior shift in the CoG location was correlated with PPT in the painful region, which implies a relationship between pain intensity and M1 organization.

We aimed to investigate the clinical significance of a key change in the motor cortex map, but also uncovered some other characteristics of the variation in the map organization. This included, correlation between variation of the location of secondary peak and CoG with sensory variables, and smudged representation of back muscles only in people with CLBP with poor performance. This suggests the nervous system may adopt a variety of strategies in the presence of CLBP. Although, it is too early to understand the clinical significance of minor and variable differences in map organization, we do provide evidence of some parallels between map and behavior. More research is needed to unravel these phenomena.

Motor Behavior was not Related to Tactile Discrimination

Previous work has reported a positive correlation between motor behavior and sensory function in CLBP.[41] In that work, individuals with poor tactile acuity also exhibited poorer performance on motor tests. Although tactile acuity and motor behavior were different between groups in our study, we found no relationship between the ability to discriminate 2 points and the motor task assessed.

CONCLUSIONS

These data show that M1 organization varies in participants with and without CLBP. However, the representation of back muscles of CLBP participants is more complex, smaller, and differently located than in pain-free controls. Some map features were related to altered sensory function, specifically pain intensity and PPT, but not linearly with performance of the movement task. These data suggest that assessment of sensory and motor features that can be measured clinically using the tests described here, cannot be used as a surrogate for measures of organization of the motor cortex.

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