*European Journal of Neuroscience*

WILEY

EJN European Journal of Neuroscience FENS

RESEARCH REPORT OPEN ACCESS

# Exploring Changes in Primary Motor Cortex Organization and Associations With Changes in Motor-Sensory Tests Over Time in Relation to Low Back Pain Recovery. A Longitudinal Study

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**Received:** 25 September 2024 | **Revised:** 24 January 2025 | **Accepted:** 24 February 2025

**Associate Editor:** Francisco Alvarez

**Funding:** This work was supported by the Netherlands Organization for Scientific Research 016.Vidi.178.014, 023.010.068.

**Keywords:** brain mapping | low back pain | rehabilitation, motor control, pain | transcranial magnetic stimulation

## ABSTRACT

The evidence for primary motor cortex reorganization in people with low back pain varies and is conflicting. Little is known about its association with motor and sensory tests, and recovery. We investigated primary motor cortex (re)organization and its associations with motor and sensory tests over time in people with ($N = 25$) and without ($N = 25$) low back pain in a longitudinal study with a 5-week follow-up. Participants with low back pain received physical therapy. Primary motor cortex organization, including the center of gravity and area of the cortical representation of trunk muscles, was evaluated using neuronavigated transcranial magnetic stimulation, based on individual magnetic resonance imaging. A motor control test (spiral tracking test) and sensory tests (quantitative sensory testing, graphaesthesia, and 2-point discrimination) were administered. Multivariate mixed models with a 3-level structure were used. In non-recovered participants, the center of gravity of longissimus L5 moved significantly anterior, and their temporal summation of pain decreased significantly more than in people without low back pain. The spiral tracking path length decreased significantly in participants without low back pain, which differed significantly from the increase in recovered participants. Significant associations were found between center of gravity and area with quantitative sensory tests and the spiral tracking test. We found a limited number of significant changes and associations over time, mainly related to longissimus L5. For some of these findings, no logical explanation seems currently available. Hence, it is unclear whether meaningful changes in cortical organization occur in people with low back pain over a 5-week period.

**Abbreviations:** CoG, center of gravity; EMG, electromyography; LBP, low back pain; MEP, motor evoked potential; MRI, magnetic resonance imaging; MVC, maximum voluntary contraction.

## 1 | Introduction

Reorganization of the primary motor cortex has been reported in people with low back pain (LBP) (Chang et al. 2019; Elgueta-Cancino et al. 2018; Jenkins et al. 2022, 2023; Klerx et al. 2024; Schabrun et al. 2017; Tsao et al. 2008, 2010, 2011). For various trunk muscles, differences were observed in cortical map volume (i.e., the cortical volume from which a muscle can be stimulated) (Chang et al. 2019; Tsao et al. 2008, 2011) and center of gravity locations (CoG, the center of the cortical area from which a muscle can be stimulated) (Elgueta-Cancino et al. 2018; Klerx et al. 2024; Li et al. 2021; Schabrun et al. 2017; Tsao et al. 2008, 2011). Although cortical reorganization of the primary motor cortex has been demonstrated, variability in findings is common, and findings may even conflict (Chang et al. 2019; Elgueta-Cancino et al. 2018; Klerx et al. 2024; Schabrun et al. 2017; Shraim et al. 2024; Tsao et al. 2008, 2011).

Only a small number of longitudinal studies investigating reorganization of the primary motor cortex have been conducted in people with LBP. Findings from these studies include changes after motor control interventions (Li et al. 2024; Massé-Alarie et al. 2016; Tsao et al. 2010). For example, an earlier activation of the transversus abdominis was observed following 2 weeks of motor training compared to self-paced walking (Tsao et al. 2010). This earlier activation was associated with an anterior and medial shift of the CoG of the transversus abdominis (Tsao et al. 2010). Furthermore, corticospinal excitability decreased and intracortical inhibition increased after a 3-week daily practice of isometric contraction of the deep multifidus in people with LBP (Massé-Alarie et al. 2016). In addition, 2 weeks of trunk motor control exercises, five times a week, resulted in a medial shift of the CoG for the multifidus muscle, and an anterior shift for the transversus abdominis and obliquus internus muscles (Li et al. 2024). Another study revealed no associations between a motor test and cortical excitability and intracortical mechanisms (facilitation and inhibition) after motor control training (Shraim et al. 2023). Noteworthy, no association was found between changes in pain intensity and shifts in CoG after 2 weeks of trunk motor control training (Li et al. 2022; Tsao et al. 2010). Taken together, these findings suggest that measures of cortical organization of the primary motor cortex may change after training.

Somatosensory impairments, as an aspect of impairments in motor control (Chiba et al. 2016), have been shown in people with LBP (Adamczyk et al. 2018; Biely et al. 2014; Elgueta-Cancino et al. 2015; Jung et al. 2020; Luomajoki and Moseley 2009; Tong et al. 2017; Wand et al. 2010) and may be associated with changes in the organization of the primary motor cortex. While no association was found between a motor test, a sensory test, and cortical map volume and CoG of the longissimus muscle (Elgueta-Cancino et al. 2018), the pressure pain threshold and CoG of longissimus L5 were associated (Elgueta-Cancino et al. 2018). A recent study revealed an association between a vibration test and the CoG of the longissimus L3 and obliquus internus muscle, and between the 2-point discrimination threshold and the CoG of the longissimus L5 (Klerx et al. 2024). Despite conflicting evidence, it may that various aspects of motor control in patients with LBP relate to the reorganization of the primary motor cortex.

To the best of our knowledge, there are a limited number of studies into the longitudinal associations between changes in the organization of the primary motor cortex and recovery in people with LBP. A longitudinal association was found between a smaller cortical map volume during the acute stage of LBP and a higher pain intensity at 6-month follow-up (Jenkins et al. 2022). However, after considering confounding factors, such as inflammation biomarkers, psychological variables, and mechanical pain sensitization, this association was no longer significant (Jenkins et al. 2022). Furthermore, a smaller map volume of the L3 region of the longissimus muscle was a predictor of the presence of LBP at a 6-month follow-up, whereas the CoG did not show predictive value (Jenkins et al. 2023). While there is some evidence suggesting longitudinal associations between the organization of the primary motor cortex and recovery in individuals with LBP, the available evidence remains limited.

In conclusion, there is limited information regarding the longitudinal aspects of reorganization of the primary motor cortex in people with LBP, and it is unclear how this longitudinal aspect of reorganization is related to changes in motor and sensory tests and recovery. Therefore, we explored the reorganization of the primary motor cortex of trunk muscles, as well as changes in motor and sensory test performance over time, within and between people with LBP (both those who recovered and did not recover) and without LBP. In addition, we explored the associations between reorganization of the primary motor cortex and changes in motor and sensory test performance over time.

## 2 | Material and Methods

In this longitudinal study in people with and without LBP, we assessed quantitative sensory tests, motor and sensory tests, and the organization of the primary motor cortex with transcranial magnetic stimulation (TMS). Participants were assessed at baseline and after five (±1) weeks. During this period, the people with LBP received physiotherapy care. The study was registered in the Open Science Framework (DOI 10.17605/OSF.IO/5C8ZG) and a protocol has been published elsewhere (Klerx et al. 2022). We adhered to the STROBE checklist for observational studies. Ethical approval was granted by METC Brabant (NL70934.028.19). All participants provided written informed consent prior to participating in the study.

### 2.1 | Participants & Intervention

#### 2.1.1 | Experimental Group

People who sought physical therapy care for LBP, which interfered with their daily activities, were recruited from five primary care physiotherapy clinics in the Netherlands. Twenty-five people with LBP were included in the study. All participants had a history of LBP. Eleven participants experienced chronic LBP with a flare-up duration of median (interquartile range [IQR]) of 6 (7) days ($n = 8$; for three participants these data from the questionnaire were missing), while 14 people had a recurrence of LBP with a median (IQR) of 14 (22) days. The flare-up or recurrent episode of LBP had to exceed 24 h. With this short minimum duration of the current episode or flare-up and without

a maximum duration, we aimed for and anticipated to achieve variability in recovery. Exclusion criteria were self-reported spinal pathology (e.g., ankylosing spondylitis), history of lumbar radiculopathy or spinal surgery, cardiovascular diseases, or pregnancy and the 6-month postpartum period, younger than 18 or older than 65 years of age, or not meeting the safety criteria for magnetic resonance imaging (MRI) or TMS (Rossi et al. 2011).

Participants with LBP received usual care physical therapy at a primary care clinic. The therapists received information about motor control exercise options and sensory accuracy training, but had the freedom to design the intervention, duration, and intensity. The clinicians could not use the tests that served as outcome measures during the therapy sessions. The frequency of therapy was, in most cases ($n = 19$), one time per week during the five ($\pm 1$) week time interval, for six cases (one participant in the recovered and five participants in the non-recovered group), there was only one therapy session. All participants received motor control and sensory accuracy training during their therapy and were instructed to perform home exercises. Other interventions were mobilization of the thoracic and lumbar spine ($n = 17$; recovered: $n = 10/13$; non-recovered: $n = 7/12$), pain education ($n = 6$; recovered: $n = 2/13$; non-recovered: $n = 4/12$), other forms of exercise ($n = 10$; recovered: $n = 3/13$; non-recovered: $n = 7/12$), and dry needling ($n = 2$; recovered: $n = 1$; non-recovered: $n = 1$).

#### 2.1.2 | Control Group

Twenty-five age- and sex-matched participants without LBP were recruited from friends or relatives of the people with LBP. The same exclusion criteria applied. People in the control group received no intervention.

#### 2.1.3 | Sample Size

The sample size was determined considering a cross-sectional comparison between two groups for the primary outcome CoG of the longissimus muscle (mean difference: 0.60 with a pooled standard deviation of 0.68) (Schabrun et al. 2017). The calculation yielded a sample size of $N = 21$ per group (power: 0.80; $\alpha$: 0.05). To account for a potential dropout rate of 15%–20%, the adjusted sample size per group was set at 25. This sample size calculation was deemed satisfactory for the longitudinal analysis of the primary outcome between two groups. However, despite the large number of observations used for the longitudinal analysis, splitting one of the groups into recovered and non-recovered resulted in a sample size that was relatively low.

### 2.2 | Assessments

#### 2.2.1 | Questionnaires

At baseline and at 5-week follow-up, the participants with LBP completed the following reliable and validated self-reported questionnaires: a Numeric Pain Rating Scale (0–10) for pain intensity (Williamson and Hoggart 2005), Oswestry Disability Index (Van Hooff et al. 2015), Pain Anxiety Symptom Scale (Lundberg et al. 2011) and Central Sensitization Inventory (Scerbo et al. 2018). In addition, they indicated their overall level of recovery at 5-week follow-up on a Global Perceived Effect scale (GPE-Dutch Version, 7-point Likert scale) (Kamper et al. 2010). Participants without LBP reported whether they were still free of LBP. The assessments have been detailed elsewhere (Klerx et al. 2022) and are described briefly below. See Figure 1 for a flowchart of the study.

### 2.3 | Primary Motor Cortex Organization

For precise targeting of TMS (Ruohonen and Karhu 2010), each participant underwent a T1-weighted MRI scan of the brain using a Siemens Magnetom Vida-XQ-32 Numaris/X VA20A-04 ML (3Tesla) scanner. Whole-brain grey matter segmentation was performed using SPM12 (SPM, https://www.fil.ion.ucl.ac.uk/spm/software/spm12) for neural navigation purposes (Neural Navigator 3.4, BrainScience Tools, the Netherlands).

Surface electromyography (EMG) was employed bilaterally to monitor muscle activity of the longissimus muscle at the levels of L3 and L5, as well as the obliquus externus and internus. Disposable bipolar pregelled rectangular ECG electrodes (AG/AgCl Ambu Blue Sensor N, Medicotest, Ølstykke, Denmark) were positioned in accordance with SENIAM recommendations (SENIAM n.d.). EMG signals were recorded using a 16-channel Porti EMG device (Twente Medical Systems International B.V., Enschede, the Netherlands). To facilitate the elicitation of motor evoked potentials (MEPs), the threshold at which MEPs could be evoked was lowered, using preactivation at 20% of maximum voluntary contraction (MVC) of the longissimus muscle during the measurements, with the participant sitting upright (Cavaleri et al. 2020; Elgueta-Cancino et al. 2018; Jenkins et al. 2022; Schabrun et al. 2017; Tsao et al. 2011). A feedback line indicating the percentage of MVC exerted by the participant was displayed on the computer screen alongside the target line representing the 20% of the participant's MVC.

A Magstim 2002 stimulator (Magstim Company Ltd., Whitland, Dyfed, UK), equipped with a figure-of-eight coil featuring 70-mm windings, was employed to administer single-pulse TMS to the hemisphere contralateral to the side exhibiting the highest intensity of LBP. This was matched for the control group. The coil orientation was set at a 45° angle to the sagittal plane (Jin et al. 2022). A protocol was employed involving 100 stimulations delivered at pseudorandom positions with an interstimulus interval of approximately 4 s (Cavaleri et al. 2020; Van De Ruit et al. 2015). The stimulations covered the motor cortex using a predefined 7 × 7-cm grid, originating from the midline of the vertex. If MEPs were detected at the grid boundaries, additional stimulations were administered in the surrounding areas to ensure comprehensive coverage of the stimulable region. All measurements were conducted in accordance with the TMS checklist for methodological quality (Chipchase et al. 2012).

The neural navigation data and EMG recordings were analyzed using Matlab (R2019b) according to procedures outlined by Jin et al. 2022. EMG data were high-pass filtered at 30 Hz. We segmented the EMG data to be epoched 500 ms after the stimulus, after which we checked for MEPs in this epoch. These MEPs had to have an onset between 5 and 50 ms of stimulation, and

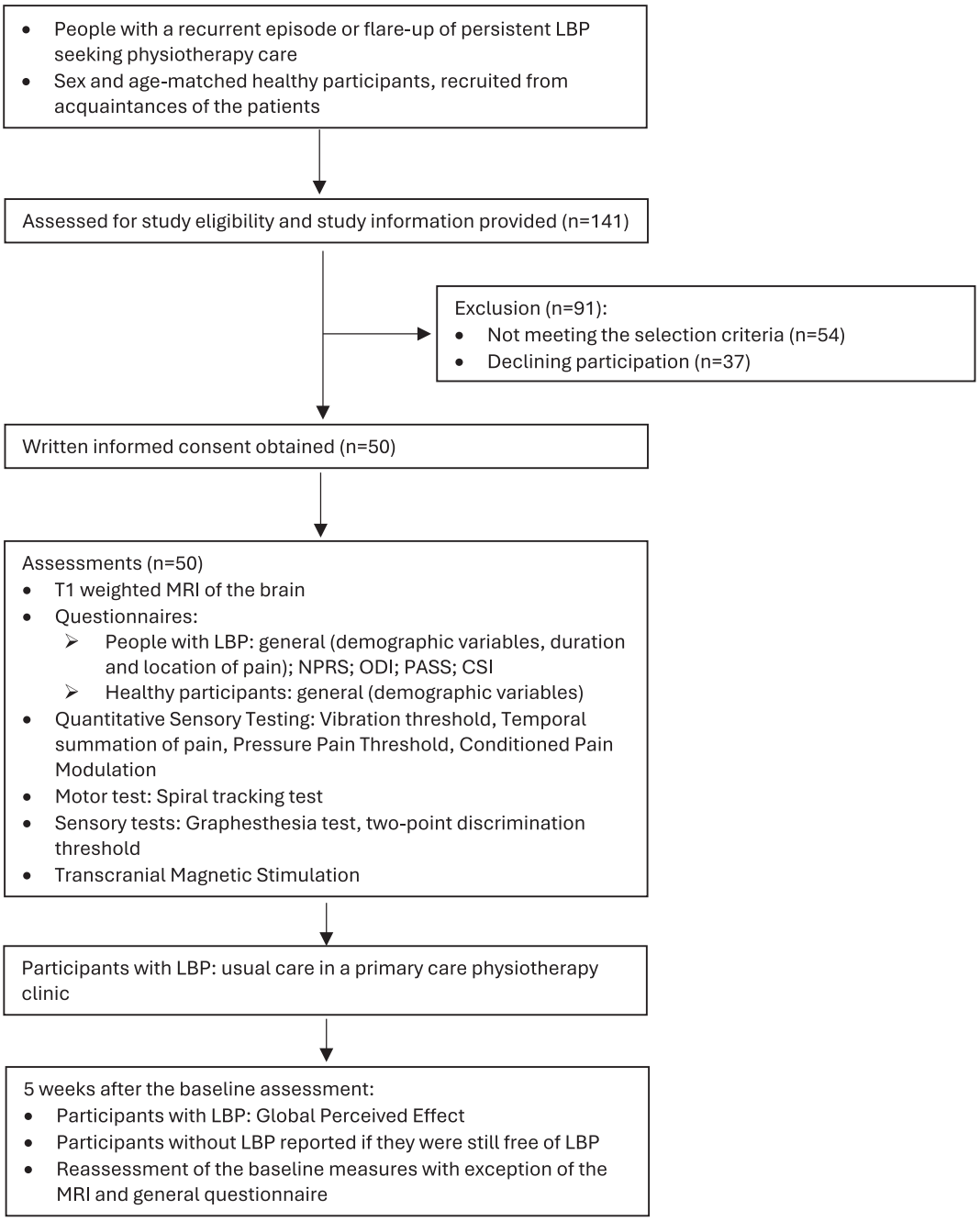


**FIGURE 1** | Flowchart of the study. LBP, low back pain; MRI, magnetic resonance imaging; NPRS, Numeric Pain Rating Scale; ODI, Oswestry Disability Index; PASS, Pain Anxiety Symptom Scale; CSI, Central Sensitization Inventory.

a duration of $<35$ ms, where the peak-to-peak amplitude exceeded 50 μV. Responses below 25% of the peak were discarded to ensure accuracy. This automatic identification was visually inspected. To account for interindividual differences in brain morphology, individual stimulation sites were normalized to a standard Montreal Neurological Institute space template (Kraus and Gharabaghi 2016). Subsequently, for each muscle on the most painful side (longissimus at levels L3 and L5, obliquus externus, and internus), the CoG was computed using the formula: $CoG = \Sigma\ (Vi \times Xi) / \Sigma vi;\ \Sigma\ (Vi \times Yi) / \Sigma vi;\ \Sigma\ (Vi \times Zi) / \Sigma vi$, where Vi represents the MEP amplitude at site i with corresponding coordinates Xi, Yi, and Zi (Tsao et al. 2011). Additionally, the cortical area responsive to stimulation was determined using a custom algorithm (Jin et al. 2022) available at https://github.com/marlow17/surfaceanalysis.

### 2.3.1 | Quantitative Sensory Testing

Four tests from the quantitative sensory test battery were conducted following established protocols (German Research Network on Neuropathic Pain 2010; Rolke et al. 2006). (1) Vibration sense over the spinous process of L4 with a Rydel-Seiffer tuning fork (64 Hz, 8/8 scale; US Neurologicals, WA). The vibration threshold was determined as the mean of three repetitions (Whitton et al. 2005). (2) Pressure pain threshold was

determined over the paraspinal musculature at L5 on the most painful side using a hand-held algometer (Wagner Instruments FDX-25, Greenwich, USA). The pressure was increased at ~5 N/s. The participant was asked to indicate when the sensation of pressure changed to a sensation of painful pressure. The threshold was calculated based on the mean of three repetitions. (3) Conditioned pain modulation was assessed using the cold pressor test. Pressure pain thresholds (as described above) were measured both before and during immersion of the right hand in cold water (10°C). The relative and absolute conditioned pain modulation effects were computed as per recommended methods (Reezigt et al. 2021; Yarnitsky et al. 2015). (4) Temporal summation of pain was assessed using a single stimulus followed by a train of 10 stimuli over the paraspinal musculature at L5 on the most painful side using a 256-mN pinprick (MRC-systems GmbH, Heidelberg). This procedure was conducted five times. The outcome was determined by subtracting the mean Numeric Pain Rating Scale score of a single stimulus from the mean Numeric Pain Rating Scale score of the train of 10 stimuli.

#### 2.3.2 | Sensory Tests

To test graphaesthesia (Klerx et al. 2022; Wand et al. 2010), participants were positioned prone. They were asked to identify 20 numbers written on their lower back using the back of the monofilament holder (Wand et al. 2010). The outcome measure was determined by calculating the error rate, obtained by dividing the number of incorrect responses by 20. Sensory discrimination was further evaluated by establishing the 2-point discrimination threshold at six locations paraspinal to L1, L3, and L5, using a 2-point discriminator (Carolina Biological Supply Company, Burlington, NC, USA), with participants lying prone (Ehrenbrusthoff et al. 2016; Klerx et al. 2022). The mean threshold across the six locations was used in the analyses.

#### 2.3.3 | Motor test

Movement precision was evaluated using a spiral tracking test (Klerx et al. 2023). A movement sensor comprising an inertial measurement unit (MPU9250) and a microcontroller (SAMD21G18A) were attached to the skin over the spinous process of T12. This sensor's orientation was represented by a green point on a computer monitor, while a red target point moved anticlockwise along the lines of a spiral displayed on the screen. Participants were instructed to track the red target as precisely as possible with the green point by moving their trunk forward, backward, left, and right. The tracking error (in degrees) was calculated based on the absolute difference between the target angle and the actual inclination angle of the trunk in the sagittal (x) and transversal (y) axis (Willigenburg et al. 2013). For motor control assessment, three outcome measures were calculated: (1) the mean of the closest 90% tracking errors; (2) the mean percentage of the total time spent at an angular distance closer than 0,9° from the red target point; and (3) the path, the total distance in degrees travelled over one trial (Klerx et al. 2023), see Figure 2. Data from the sensors were analyzed using custom-written Matlab scripts (R2014B, The MathWorks, Natick, MA). A detailed description of the outcome measures has been published elsewhere (Klerx et al. 2023).

### 2.4 | Statistical Analysis

To analyze the differences between groups over time, multivariate mixed model analyses were employed using a 3-level structure. The analysis encompassed two main areas: (1) primary motor cortex organization, focusing on CoG and area measurements of trunk muscles (i.e., longissimus at levels L3 and L5, externus, and internus obliquus muscles) and (2) motor and sensory tests.

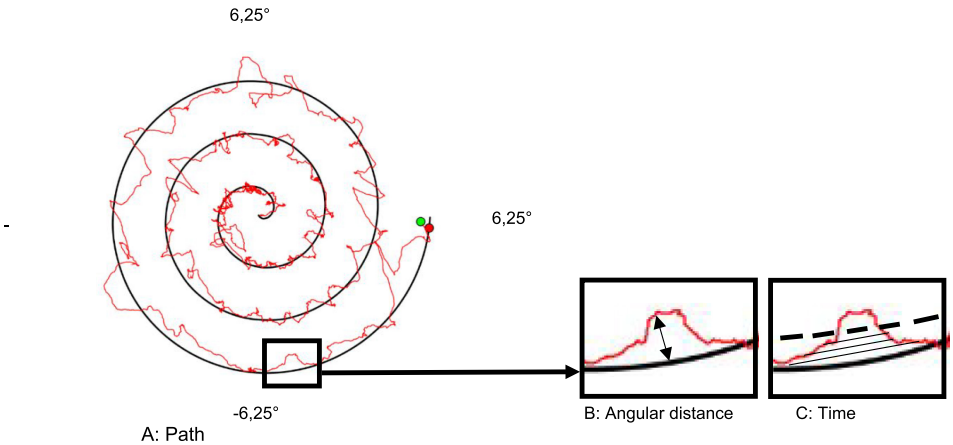


**FIGURE 2** | Parameters measured in the spiral tracking test: reprinted and modified with permission from Klerx et al. (2023). The tracking error was calculated based on the absolute difference between the target angle and the actual angle of the trunk in the frontal (x) and sagittal (y) axis of motion in degrees. The orientation of the sensor in degrees of the x and y axis was converted on a two-dimensional screen, calculated as $\sqrt{\left(\left(target_x - actual_x\right)^2 + \left(target_y - actual_Y\right)^2\right)}$. The spiral on the screen was set at 13,5°×13,5° (the x axis −6,25° to 6,25° and the y axis −6,25° to 6,25°). Panel (A) path, the red squiggly line represents the sum of all differences between the target position and the actual position. Panel (B) angular distance, the black arrow represents the error as the distance in degrees from the red target point (the spiral). Panel (C) time, the lines till the dashed lines represent the area of the time spent in 0,9° distance from the red target point (the spiral).

The choice of multivariate mixed model analysis was motivated by correlations observed among the outcomes on the different tests within each participant. To account for the correlation, a random intercept on the subject level was included in the model. The model included the following variables: group (LBP recovered, LBP non-recovered, and people without LBP), test (indicating the specific test outcome), and time (baseline and follow-up), as well as their interactions. For the analysis of primary motor cortex organization, separate models were created for CoG and area measurements. Within these models, the Test variable incorporated the different trunk muscles (i.e., longissimus at levels L3 and L5, externus, and internus obliquus muscles).

Regarding the sensory accuracy tests, the test variable included vibration, graphaesthesia, and 2-point discrimination threshold. For quantitative sensory testing, the test variable included temporal summation of pain, pressure pain threshold, and conditioned pain modulation, relative and absolute. Lastly, for the spiral tracking test, the test variable involved parameters such as angular distance, angular distance closer than 0,9°, and path.

To examine the association between the organization of the primary motor cortex in trunk muscles and motor control as well as sensory tests, the difference between follow-up and baseline for the primary motor cortex organization was the test variable (multivariate outcome). These associations were analyzed in relation to each difference between follow-up and baseline for the motor and sensory test variables. All multivariate multilevel analyses were performed using STATA (version 17).

## 3 | Results

### 3.1 | Participants and Missing Data

Based on the Global Perceived Effect scale at 5-week follow-up, 13 out of the 25 participants with LBP had recovered (mean [SD] age: 44 [15] years, nine males and four females) and 12 had not recovered (36 (14) years, three males and nine females). All 50 participants participated at follow-up, see Table 1.

As MEPs could not be elicited for all muscles in all participants, some cortical organization data were missing. Specifically, 29 muscle outcomes per model (four models: area and CoG in three directions) were missing across 18 participants. This corresponds with 7.3% of the entire dataset. Among the five participants with LBP who had recovered, missing data included the longissimus at L3 in three participants, the longissimus at L5 in two participants, the obliquus externus in one participant, and the obliquus internus in one participant. In five participants with LBP who had not recovered, the missing outcomes were the longissimus at L3 in two participants, the longissimus at L5 in one participant, and the obliquus internus in two participants. Among the eight participants without LBP, missing outcomes included the longissimus at L3 in eight participants, the longissimus at L5 in three participants, and the obliquus internus in four participants. Because we used mixed model analysis for the research questions regarding differences in outcomes of the organization of the primary motor cortex and the clinical tests, missing data were handled appropriately (Twisk et al. 2013). For the association analysis, we used the delta between follow-up

**TABLE 1** | Characteristics of the groups.

| | Participants with LBP ($n=25$) | | | |
|---|---|---|---|---|
| | All | Recovered $N=13$ | Non-recovered $N=12$ | Participants without LBP ($n=25$) |
| Age | 40 (15) | 44 (15) | 36 (14) | 41 (14) |
| Sex M:F | 12:13 | 9:4 | 3:9 | 12:13 |
| BMI | 26 (3) | 27 (1) | 25 (2) | 25 (3) |
| Hemisphere L:R | 9:16 | 3 (10) | 6 (6) | 9:16 |

| | Questionnaires for participants with LBP | | | | | |
|---|---|---|---|---|---|---|
| | Baseline | | | Follow-up | | |
| | All | Recovered | Non-recovered | All | Recovered | Non-recovered |
| NPRS—current | 4 (2) | 4 (2) | 3 (1) | 2 (2) | 1 (1) | 2 (2) |
| Max past week | 7 (2) | 8 (1) | 6 (2) | 4 (3) | 2 (2) | 5 (2) |
| Average past week | 4 (1) | 5 (1) | 3 (1) | 2 (2) | 1 (1) | 4 (3) |
| ODI | 18 (12) | 22 (12) | 13 (9) | 8 (9) | 5 (4) | 11 (11) |
| PASS | 45 (18) | 40 (14) | 50 (20) | 45 (18) | 43 (15) | 47 (22) |
| CSI | 26 (10) | 23 (8) | 29 (11) | 21 (10) | 21 (6) | 29 (12) |

*Note:* LBP, experiencing a flare-up or recurrence of pain (> 24 h) between the lower rib margins and the buttock creases; recovered, participants with LBP at baseline and recovered at follow-up; non-recovered, participants with LBP at baseline who are not recovered at follow-up. Recovered and non-recovered were based on the Global Perceived Effect scale.

and baseline outcomes. Consequently, there were 26 missing data points, distributed as described above. For one participant without LBP, the follow-up trial of the spiral tracking test was missing.

## 3.2 | Multivariate Analyses

### 3.2.1 | Changes Over Time

**3.2.1.1 | Organization of the Primary Motor Cortex.** In non-recovered LBP participants, the location of the CoG of the longissimus moved significantly anterior over time (see Figure 3, Table 2). No other significant changes over time were found for cortical area or CoG, see Table 2.

**3.2.1.2 | Clinical tests.** In non-recovered LBP participants, temporal summation of pain decreased significantly more over time than in participants without LBP (see Figure 3). Participants without LBP had a significant decrease in path length of the spiral tracking test over time (see Figure 3). This decrease differed significantly from the increase of path length over time of the participants with LBP who recovered (see Figure 3, Table 3).

## 3.3 | Association Between the Changes in the Organization of the Primary Motor Cortex and the Changes in Performance on Clinical Tests

Increases in the vibration threshold over time were significantly associated with increases in cortical area over time. This association was significant for both the recovered and non-recovered LBP groups. Increases in conditioned pain modulation absolute and relative score over time (which corresponds with a decrease in inhibition of pain) were significantly associated with decreases in cortical area of the obliquus externus and a lateral shift of the CoG of the longissimus L5 over time.

This association was significant in the group of participants without LBP (conditioned pain modulation absolute) and in the group of participants who recovered (conditioned pain modulation relative). Increases in the pain pressure threshold over time were associated with a shift downward lateral of the CoG of the longissimus L5. Subgroup analyses showed this association was significant in the group of participants without LBP and the group with LBP who recovered. In motor testing, increases of the distance error over time were associated with a lateral shift in the CoG of longissimus L5 over time. Subgroup analysis revealed that this association was only present in participants with LBP who recovered. Increases in time scores over time (the mean percentage of the total time spent at an angular distance closer than 0,9° from the red target point) were associated with a medial shift of the CoG of longissimus L5 over time, again, subgroup analysis revealed this association in participants with LBP who recovered. Statistical results of the associations between the changes in the organization of the primary motor cortex over time with changes in performance on clinical tests over time can be found in Appendices 1–4. The significant associations can be found in Table 4 and are plotted in Figure 4.

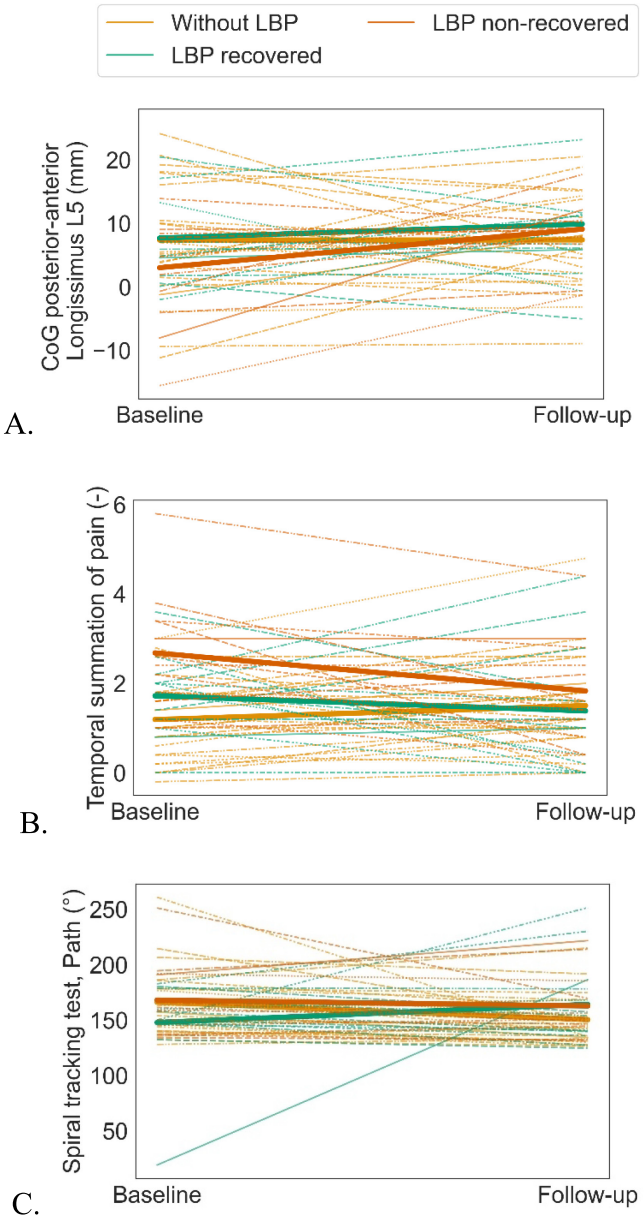


**FIGURE 3** | Significant changes within and between groups over time, from baseline to follow-up, measured after a 5-week interval. The averaged lines represent results from the multivariate mixed model; the individual lines correspond to the original data. (A) Center of gravity of the longissimus L5 in the direction posterior (toward negative value)–anterior (toward positive value). (B) Temporal summation of pain—a higher number indicates a higher pain sensitivity. (C) Path (the sum of all errors, in degrees over one trial) of the spiral tracking test.

## 4 | Discussion

We studied the reorganization of the primary motor cortex, and associations with motor and sensory tests over time in people with LBP, who recovered ($n = 13$) and who did not recover ($n = 12$) in comparison with people without LBP ($n = 25$). Among the statistical analyses conducted, only a few results showed significance in changes in cortical reorganization and clinical tests and their associations. In cortical reorganization, the significant change was only demonstrated in the CoG of the longissimus L5. In the clinical tests, significant

**TABLE 2** | Multivariate analyses of the changes over time within and between groups in TMS measurements.

| Dependent variable | Muscle | Independent variable | $\beta_{changes}$ | 95% CI lower:upper | Independent variable | $\beta_{group \times time}$ | 95% CI lower:upper |
|---|---|---|---|---|---|---|---|
| | | Group | Changes over time within groups | | Between groups | Changes over time between groups | |
| Cortical area | | | | | | | |
| | Longissimus L3 | Without LBP | 516 | −297:1329 | Recovered vs. without LBP | −303 | −1688:1082 |
| | | Recovered | 213 | −908:1334 | Recovered vs. non-recovered | 484 | −1100:2068 |
| | | Non-recovered | −271 | −1389:847 | Non-recovered vs. without LBP | −787 | −2170:596 |
| | Longissimus L5 | Without LBP | −51 | −816:713 | Recovered vs. without LBP | 278 | −1038:1595 |
| | | Recovered | 227 | −844:1298 | Recovered vs. non-recovered | 323 | −1209:1855 |
| | | Non-recovered | −96 | −1190:998 | Non-recovered vs. without LBP | −45 | −1380:1291 |
| | Obliquus externus | Without LBP | 369 | −373:1111 | Recovered vs. without LBP | −976 | −2260:310 |
| | | Recovered | −606 | −1656:443 | Recovered vs. non-recovered | −457 | −1956:1043 |
| | | Non-recovered | −150 | −1220:921 | Non-recovered vs. without LBP | −519 | −1821:784 |
| | Obliquus internus | Without LBP | −651 | −1434:131 | Recovered vs. without LBP | −220 | −1531:1090 |
| | | Recovered | −872 | −1923:179 | Recovered vs. non-recovered | −998 | −2533:537 |
| | | Non-recovered | 126 | −992:1244 | Non-recovered vs. without LBP | 777 | −588:2142 |

(Continues)

**TABLE 2** | (Continued)

| Dependent variable | Muscle | Independent variable | $\beta_{changes}$ | 95% CI lower:upper | Independent variable | $\beta_{group \times time}$ | 95% CI lower:upper |
|---|---|---|---|---|---|---|---|
| Center of gravity | | | | | | | |
| Posterior–anterior | Longissimus L3 | Without LBP | 0.96 | −3.25:5.18 | Recovered vs. without LBP | −1.38 | −8.58:5.81 |
| | | Recovered | −0.42 | −6.25:5.41 | Recovered vs. non-recovered | −2.22 | −10.51:6.07 |
| | | Non-recovered | 1.80 | −4.09:7.70 | Non-recovered vs. without LBP | 0.84 | −6.41:8.09 |
| | Longissimus L5 | Without LBP | 0.03 | −4.03:4.09 | Recovered vs. without LBP | 2.19 | −4.77:9.14 |
| | | Recovered | 2.22 | −3.43:7.86 | Recovered vs. non-recovered | −3.86 | −11.96:4.25 |
| | | **Non-recovered** | **6.07** | **0.26:11.89** | Non-recovered vs. without LBP | 6.04 | −1.04:13.13 |
| | Obliquus externus | Without LBP | 1.84 | −2.13:5.81 | Recovered vs. without LBP | −0.01 | −6.86:6.83 |
| | | Recovered | 1.83 | −3.75:7.40 | Recovered vs. non-recovered | −1.43 | −9.42:6.57 |
| | | Non-recovered | 3.25 | −2.48:8.98 | Non-recovered vs. without LBP | 1.41 | −5.56:8.38 |
| | Obliquus internus | Without LBP | 3.38 | −0.73:7.50 | Recovered vs. without LBP | −0.005 | −6.94:6.93 |
| | | Recovered | 3.38 | −2.21:8.96 | Recovered vs. non-recovered | | −4.11:12.12 |
| | | Non-recovered | −0.63 | −6.52:5.27 | Non-recovered vs. without LBP | 4.00<br>−4.01 | −11.20:3.18 |

(Continues)

**TABLE 2** | (Continued)

| Dependent variable | Muscle | Independent variable | $\beta_{changes}$ | 95% CI lower:upper | Independent variable | $\beta_{group \times time}$ | 95% CI lower:upper |
|---|---|---|---|---|---|---|---|
| Latero-medial | Longissimus L3 | Without LBP | −1.11 | −4.93:2.72 | Recovered vs. without LBP | 1.48 | −5.04:8.01 |
| | | Recovered | 0.38 | −4.91:5.67 | Recovered vs. non-recovered | 2.93 | −4.54:10.41 |
| | | Non-recovered | −2.55 | −7.84:2.73 | Non-recovered vs. without LBP | −1.45 | −7.98:5.08 |
| | Longissimus L5 | Without LBP | −0.003 | −3.63:3.62 | Recovered vs. without LBP | −3.41 | −3.63:3.62 |
| | | Recovered | −3.42 | −8.48:1.65 | Recovered vs. non-recovered | −4.01 | −11.25:3.24 |
| | | Non-recovered | 0.59 | −4.59:5.78 | Non-recovered vs. without LBP | 0.60 | −5.73:6.92 |
| | Obliquus externus | Without LBP | −0.12 | −3.63:3.40 | Recovered vs. without LBP | 2.09 | −4.00:8.18 |
| | | Recovered | 1.97 | −3.00:6.94 | Recovered vs. non-recovered | 3.80 | −3.31:10.90 |
| | | Non-recovered | −1.83 | −6.91:3.25 | Non-recovered vs. without LBP | −1.71 | −7.89:4.47 |
| | Obliquus internus | Without LBP | 0.81 | −2.89:4.50 | Recovered vs. without LBP | −0.12 | −6.32:6.08 |
| | | Recovered | 0.69 | −4.29:5.66 | Recovered vs. non-recovered | 0.62 | −6.64:7.87 |
| | | Non-recovered | 0.07 | −5.21:5.36 | Non-recovered vs. without LBP | −0.74 | −7.19:5.71 |

(Continues)

**TABLE 2** | (Continued)

| Dependent variable | Muscle | Independent variable | $\beta_{changes}$ | 95% CI lower:upper | Independent variable | $\beta_{group \times time}$ | 95% CI lower:upper |
|---|---|---|---|---|---|---|---|
| Vertical | Longissimus L3 | Without LBP | −1.11 | −3.28:1.07 | Recovered vs. without LBP | −1.27 | −4.98:2.44 |
| | | Recovered | −2.38 | −5.38:0.63 | Recovered vs. non-recovered | −0.33 | −4.58:3.92 |
| | | Non-recovered | −2.05 | −5.05:0.96 | Non-recovered vs. without LBP | −0.94 | −4.65:2.77 |
| | Longissimus L5 | Without LBP | 0.29 | −1.77:2.35 | Recovered vs. without LBP | −2.96 | −6.51:0.58 |
| | | Recovered | −2.67 | −5.55:0.21 | Recovered vs. non-recovered | −2.62 | −6.74:1.50 |
| | | Non-recovered | −0.05 | −3.00:2.90 | Non-recovered vs. without LBP | −0.34 | −3.94:3.26 |
| | Obliquus externus | Without LBP | −0.44 | −2.45:1.56 | Recovered vs. without LBP | 0.51 | −2.96:3.98 |
| | | Recovered | 0.07 | −2.76:2.90 | Recovered vs. non-recovered | 1.64 | −2.41:5.68 |
| | | Non-recovered | −1.57 | −4.46:1.32 | Non-recovered vs. without LBP | −1.13 | −4.65:2.39 |
| | Obliquus internus | Without LBP | 0.09 | −2.01:2.19 | Recovered vs. without LBP | 1.16 | −2.01:2.19 |
| | | Recovered | 1.25 | −1.58:4.09 | Recovered vs. non-recovered | 0.68 | −3.45:4.81 |
| | | Non-recovered | 0.57 | −2.44:3.58 | Non-recovered vs. without LBP | 0.48 | −3.19:4.15 |

*Note:* Recovered, participants with LBP at baseline and recovered at follow-up; non-recovered, participants with LBP at baseline who are not recovered at follow-up; posterior–anterior, a positive coefficient defines a shift to anterior, a negative coefficient a shift to posterior; latero-medial, a positive coefficient defines a shift to medial, a negative coefficient a shift to lateral; vertical, a positive coefficient defines a shift to the vertex line, a negative coefficient a shift away from the vertex line (to a lower location).

**TABLE 3** | Multivariate analyses of the changes over time within and between groups in clinical assessments.

| Dependent variable | Test | Independent variable | $\beta_{changes}$ | 95% CI lower:upper | Independent variable | $\beta_{group \times time}$ | 95% CI lower:upper |
|---|---|---|---|---|---|---|---|
| | | Group | Changes over time within groups | | Between groups | Changes over time between groups | |
| QST, pain | Temporal summation | Without LBP | 0.31 | −0.29:0.92 | Recovered vs. without LBP | −0.65 | −1.69:0.39 |
| | | Recovered | −0.34 | −1.18:0.50 | Recovered vs. non-recovered | 0.51 | −0.70:1.73 |
| | | Non-recovered | −0.85 | −1.73:0.03 | **Non-recovered vs. without LBP** | **−1.16** | **−2.23:−0.10** |
| | PPT | Without LBP | −4.62 | −16.75:7.52 | Recovered vs. without LBP | 7.20 | −13.55:27.95 |
| | | Recovered | 2.58 | −14.25:19.41 | Recovered vs. non-recovered | 1.07 | −23.22:25.36 |
| | | Non-recovered | 1.51 | −16.01:19.03 | Non-recovered vs. without LBP | 6.13 | −15.18:27.44 |
| | CPM relative | Without LBP | −5.53 | −17.66:6.61 | Recovered vs. without LBP | 4.53 | −16.22:25.27 |
| | | Recovered | −1.00 | −17.83:15.83 | Recovered vs. non-recovered | 6.18 | −18.11:30.47 |
| | | Non-recovered | −7.18 | −24.70:10.33 | Non-recovered vs. without LBP | −1.66 | −22.97:19.65 |
| | CPM absolute | Without LBP | −4.46 | −16.59:7.68 | Recovered vs. without LBP | 7.20 | −13.55:27.94 |
| | | Recovered | 2.74 | −14.09:19.57 | Recovered vs. non-recovered | 2.87 | −21.42:27.16 |
| | | Non-recovered | −0.13 | −17.64:17.39 | Non-recovered vs. without LBP | 4.33 | −16.98:25.64 |

(Continues)

**TABLE 3** | (Continued)

| Dependent variable | Test | Independent variable | $\beta_{changes}$ | 95% CI lower:upper | Independent variable | $\beta_{group \times time}$ | 95% CI lower:upper |
|---|---|---|---|---|---|---|---|
| Sensory accuracy | Vibration | Without LBP | 0.25 | −0.15:0.66 | Recovered vs. without LBP | −0.33 | −1.02:0.36 |
| | | Recovered | −0.08 | −0.64:0.49 | Recovered vs. non-recovered | −0.24 | −1.06:0.57 |
| | | Non-recovered | 0.17 | −0.42:0.75 | Non-recovered vs. without LBP | −0.09 | −0.80:0.63 |
| | Graphaesthesia | Without LBP | −2.00 | −10.11:6.11 | Recovered vs. without LBP | −5.69 | −19.56:8.18 |
| | | Recovered | −7.69 | −18.94:3.56 | Recovered vs. non-recovered | −6.44 | −22.68:9.80 |
| | | Non-recovered | −1.25 | −12.96:10.46 | Non-recovered vs. without LBP | 0.75 | −13.50:15.00 |
| | 2-point discrimination | Without LBP | −5.13 | −13.25:2.98 | Recovered vs. without LBP | −3.46 | −17.33:10.41 |
| | | Recovered | −8.59 | −19.84:2.66 | Recovered vs. non-recovered | −1.44 | −17.68:14.80 |
| | | Non-recovered | −7.15 | −18.86:4.56 | Non-recovered vs. without LBP | −2.02 | −16.27:12.23 |
| Motor test; | Path | **Without LBP** | **−15.73** | **−28.40:−3.06** | **Recovered vs. without LBP** | **32.13** | **10.61:53.64** |
| | | Recovered | 16.40 | −0.99:33.79 | Recovered vs. non-recovered | 21.79 | −3.31:46.88 |
| | | Non-recovered | −5.39 | −23.48:12.71 | Non-recovered vs. without LBP | 10.34 | −11.75:32.44 |

(Continues)

**TABLE 3** | (Continued)

| Dependent variable | Test | Independent variable | $\beta_{changes}$ | 95% CI lower:upper | Independent variable | $\beta_{group \times time}$ | 95% CI lower:upper |
|---|---|---|---|---|---|---|---|
| Spiral tracking test | Angular distance near | Without LBP | −0.06 | −0.19:0.07 | Recovered vs. without LBP | 0.04 | −0.19:0.07 |
| | | Recovered | −0.02 | −0.19:0.22 | Recovered vs. non-recovered | −0.03 | −0.22:0.28 |
| | | Non-recovered | −0.05 | −0.23:0.13 | Non-recovered vs. without LBP | 0.01 | −0.21:0.23 |
| | Time near | Without LBP | 3.14 | −9.53:15.81 | Recovered vs. without LBP | −1.45 | −22.96:15.81 |
| | | Recovered | 1.70 | −15.69:19.09 | Recovered vs. non-recovered | 1.80 | −23.29:26.90 |
| | | Non-recovered | −0.11 | −18.20:17.99 | Non-recovered vs. without LBP | −3.25 | −25.34:18.84 |

*Note:* Path, the total distance travelled over one trial, in degrees; angular distance near: the mean of the closest 90% tracking errors; time near: the percentage of time spent at an angular distance closer than 0,9° from the red target point; recovered, participants with LBP at baseline and recovered at follow-up; non-recovered, participants with LBP at baseline who are not recovered at follow-up.
Abbreviations: CPM, conditioned pain modulation; PPT, pressure pain threshold; QST, quantitative sensory testing.

changes were only found in temporal summation of pain and spiral tracking test. Among the few significant associations, between cortical reorganization and changes in clinical tests, most were found in the longissimus L5. All in all, our data show that the participants in our study changed only in a few variables over time.

### 4.1 | Reorganization of the Primary Motor Cortex

We found an anterior shift of the CoG of the longissimus L5 over time. This anterior shift was also reported in previous research for the transversus abdominis (Li et al. 2024; Tsao et al. 2010) and obliquus internus muscle (Li et al. 2024) after motor training. However, unexpectedly, the anterior shift we found was only demonstrated in the group of participants who did not recover. Given the role of the primary motor cortex in motor control (Bhattacharjee et al. 2021) and the differences in motor control in people with LBP compared to people without LBP (Hadizadeh et al. 2014; Laird et al. 2014; Rausch Osthoff et al. 2015; Tong et al. 2017; Willigenburg et al. 2013), it is assumed that changes in the organization of the primary motor cortex occur to prevent (further) pain through adapted motor control (Van Dieën et al. 2017). In this context, it seems logical that recovery from pain might involve changes in the organization of the primary motor cortex that move opposite to the baseline measurement, as reflected in cortical area or CoG. Yet, our study found no significant changes in the location of the CoG for participants who recovered from LBP. Instead, changes occurred in participants who did not recover, which cannot be clearly explained.

### 4.2 | Changes Over Time in Clinical Tests

The significantly greater decrease in temporal summation of pain over time in non-recovered participants was unexpected, as a greater decrease over time would be more logical in participants who recover. The significant decrease in path length over time in the spiral tracking test for participants without LBP can be attributed to a learning effect. Furthermore, it is remarkable that the participants who recovered showed an increase in path length over time that differed significantly from the decrease in path length over time in the participants without LBP. However, the angular distance error variable, where the 10% largest errors were removed, showed no significant change in either of the groups. A potential explanation may be using a different strategy between people when experiencing LBP, experiencing a recent history of LBP, or experiencing no (recent history of) LBP (Van Dieën et al. 2010).

### 4.3 | Associations Between Cortical Reorganization and Changes in Performance on Clinical Tests

Previous research revealed conflicting evidence regarding associations between clinical tests and cortical reorganization (Elgueta-Cancino et al. 2018; Klerx et al. 2024; Shraim et al. 2023). In our study, a few significant associations between changes over time in clinical tests with cortical reorganization (cortical area and CoG) were found and were consistently seen

**TABLE 4** | Multivariate analyses of the significant associations between changes in area, center of gravity, and changes in clinical assessments.

| Dependent variable | Muscle | Independent variable | Independent variable | $\beta_{association}$ | 95% CI lower:upper |
|---|---|---|---|---|---|
| | | Clinical test | Group | | |
| Cortical area | | | | | |
| | Obliquus externus | CPM absolute | **All** | **−44.9** | **−83.0:−6.8** |
| | | | Without LBP | −42.8 | −103.8:18.2 |
| | | | Recovered | −45.3 | −99.8:9.3 |
| | | | Non-recovered | −3.0 | −113:107 |
| | Longissimus L5 | Vibration | **All** | **1794** | **936:2651** |
| | | | Without LBP | 912 | −265:2088 |
| | | | **Recovered** | **3029** | **1565:4493** |
| | | | **Non-recovered** | **2009** | **247:3772** |
| Center of gravity | | | | | |
| Latero-medial | Longissimus L5 | CPM absolute | **All** | **−0.25** | **−0.43:−0.05** |
| | | | **Without LBP** | **−0.35** | **−0.65:−0.05** |
| | | | Recovered | −0.18 | −0.45:0.09 |
| | | | Non-recovered | −0.001 | −0.57:0.56 |
| | Longissimus L5 | CPM relative | **All** | **−0.10** | **−0.19:−0.01** |
| | | | Without LBP | −0.09 | −0.22:0.04 |
| | | | **Recovered** | **−0.22** | **−0.39:−0.05** |
| | | | Non-recovered | 0.02 | −0.14:0.18 |
| | Longissimus L5 | PPT | **All** | **−0.26** | **−0.42:−0.10** |
| | | | **Without LBP** | **−0.33** | **−0.58:−0.07** |
| | | | **Recovered** | **−0.23** | **−0.44:−0.01** |
| | | | Non-recovered | −0.04 | −0.61:0.53 |
| | Longissimus L5 | Angular distance near | **All** | **−13.49** | **−26.43:−0.05** |
| | | | Without LBP | −2.87 | −26.92:21.17 |
| | | | **Recovered** | **−39.69** | **−60.83:−18.54** |
| | | | Non-recovered | 4.83 | −15.01:24.67 |
| | Longissimus L5 | Time near | **All** | **0.25** | **0.04:0.46** |
| | | | Without LBP | −0.004 | −0.44:0.43 |
| | | | **Recovered** | **0.48** | **0.21:0.75** |
| | | | Non-recovered | −0.14 | −0.60:0.31 |
| Vertical | Longissimus L5 | PPT | **All** | **−0.12** | **−0.21:−0.03** |
| | | | Without LBP | −0.11 | −0.26:0.03 |
| | | | Recovered | −0.09 | −0.22:0.03 |
| | | | Non-recovered | −0.07 | −0.39:0.25 |

*Note:* Path, the total distance travelled over one trial, in degrees; angular distance near: the mean of the closest 90% tracking errors; time near: the percentage of time spent at an angular distance closer than 0,9° from the red target point; recovered, participants with LBP at baseline and recovered at follow-up; non-recovered, participants with LBP at baseline who are not recovered at follow-up; posterior–anterior, a positive coefficient defines a shift to anterior, a negative coefficient a shift to posterior; latero-medial, a positive coefficient defines a shift to medial, a negative coefficient a shift to lateral; vertical, a positive coefficient defines a shift to the vertex line, a negative coefficient a shift away from the vertex line (to a lower location).Number of observations, all: $N = 174$, 26 missing; L3: 13; L5:6; obliquus externus: 1: obliquus internus 6. Number of participants per group included longissimus at L3: without LBP: $n = 17$; recovered: $n = 10$; non-recovered: $n = 10$. Longissimus at L5: without LBP: $n = 22$; recovered: $n = 11$; non-recovered: $n = 11$. Obliquus externus: without LBP: $n = 25$; recovered: $n = 12$; non-recovered: $n = 12$; obliquus internus: without LBP: $n = 21$; recovered: $n = 12$; non-recovered: $n = 11$.

Abbreviations: CPM, conditioned pain modulation; PPT, pressure pain threshold; QST, quantitative sensory testing.

in longissimus L5. However, these associations were sometimes contradicting. For instance, increases in conditioned pain modulation absolute and relative score over time (which corresponds with a decrease in inhibition of pain) were significantly associated with decreases in cortical area of the obliquus externus and a lateral shift of the CoG of the longissimus L5 over time. While increases of the pain pressure threshold over time were associated with a shift to downward lateral of the CoG of the

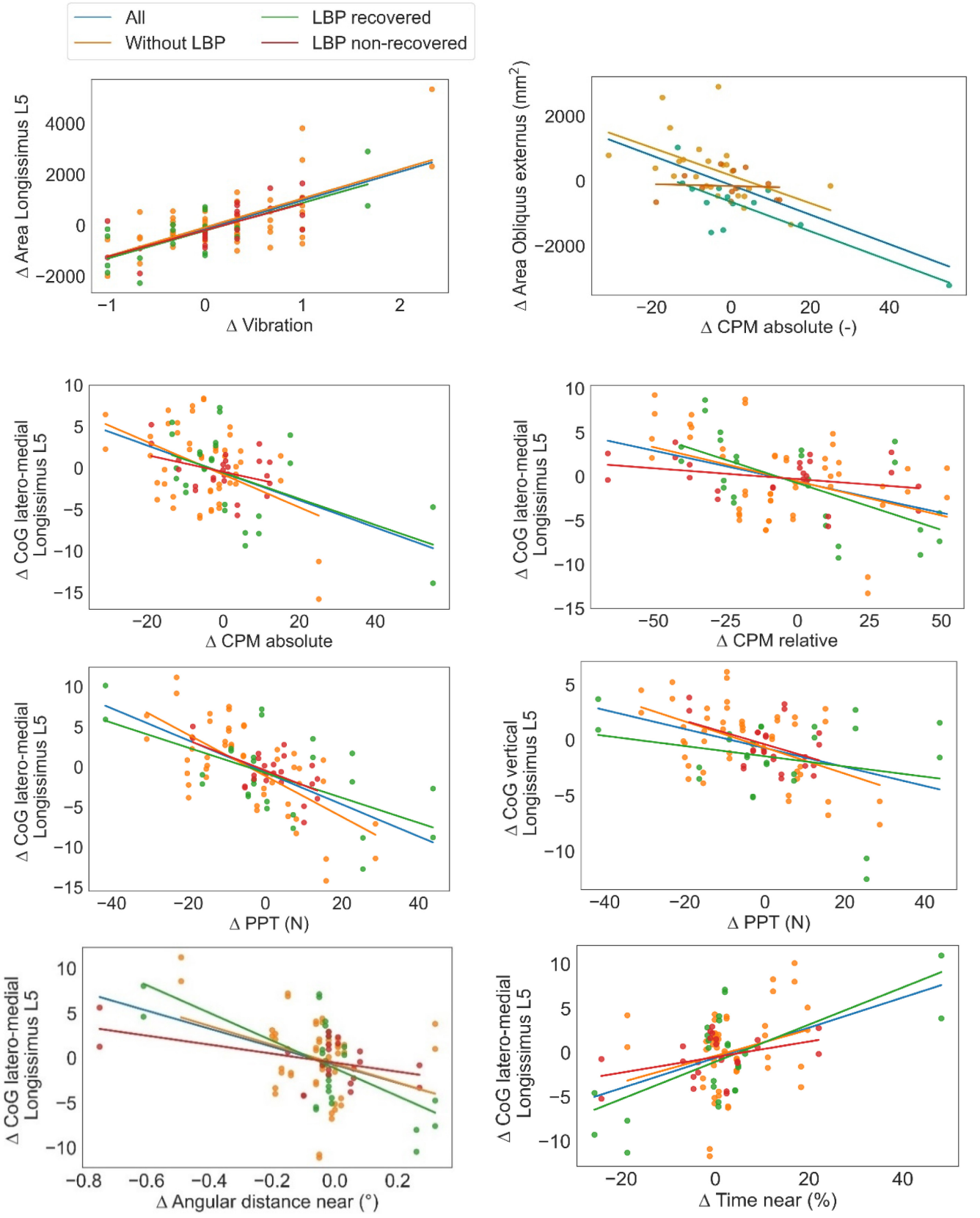


**FIGURE 4** | Legend on next page.

**FIGURE 4** | Significant associations between the changes (Δ) in the organization of the primary motor cortex with changes (Δ) in performance on clinical tests based on multivariate mixed model. Area ($mm^2$), the cortical area from which a muscle can be stimulated; CoG, center of gravity in direction latero- (toward a negative value) medial (toward a positive value), CoG, vertical direction, closer to the vertex line (toward a positive value)—away from the vertex line (toward a negative value); vibration (–), a higher value indicates being able to feel smaller vibrations; CPM absolute and relative (–), a negative value indicates pain inhibition and a positive value indicates pain facilitation; PPT (Newton), a higher value indicates the ability to withstand greater amounts of pressure before it is perceived as painful; angular distance near (°), the mean of the closest 90% tracking errors; time near (%), the percentage of time spent at an angular distance closer than 0,9° from the red target point.

longissimus L5, these findings seem contradictory, and cannot be easily explained. A previous cross-sectional study reported findings that were contradictory to our results. They reported that a lower pain pressure threshold was significantly associated with a more lateral CoG of the longissimus L5 (Elgueta-Cancino et al. 2018). Because the direction of the significant findings could not always be logically explained, the meaning of the findings is uncertain.

### 4.4 | Strengths and Limitations of the Current Study

We followed established research protocols for setup and used TMS stimulation at 100% of stimulator output (Cavaleri et al. 2020; Elgueta-Cancino et al. 2018; Jenkins et al. 2022; Schabrun et al. 2017; Tsao et al. 2011), as in general setting the intensity at 120% of the motor threshold for the longissimus muscle surpassed the stimulator's capacity. However, this standardized intensity may have led to varied experiences among participants. For some participants, the stimulation intensity may have been too high, while for others, the stimulation intensity may have been too low to induce MEPs, potentially affecting the accuracy of CoG and area estimates. To enhance assessment accuracy, we employed three strategies: (1) individualized whole-brain anatomical MRI navigation to account for brain shape and size variations, which allowed us to analyze the same absolute positions over time; (2) a custom 3D analysis method to calculate the representations of muscles within the primary motor cortex, determining the cortical area responsible for muscle excitability. Importantly, it excluded stimulations without MEPs and avoided assumptions about the underlying geometry; (3) a pseudo-random stimulation protocol for increased spatial resolution (Van De Ruit et al. 2015). Although our protocol aligns with previous research output (Elgueta-Cancino et al. 2018; Schabrun et al. 2017; Tsao et al. 2011), and TMS checklist guidelines (Chipchase et al. 2012), the clinimetric properties of brain mapping in trunk muscles remain unknown.

For the statistical comparison, we divided the LBP group at follow-up into recovered and non-recovered participants based on the Global Perceived Effect scale, using recommended cutoff points (Ostelo and Vet 2005). However, we did not use additional measures of pain or disability as cutoff points. Therefore, the grouping was somewhat arbitrary and may have influenced the results. In our study, we included participants with a history of LBP, but with a current minimum pain duration of 24 h and conducted measurements with a 5-week follow-up. Given the short minimum duration of the current episode or flare-up and the absence of a maximum duration, we anticipated variability in recovery, as marked improvements can occur within 6 weeks following an episode of LBP (Menezes Costa et al. 2012). However, the relatively short duration of the flare-up or recurrence may have attenuated the observed changes in the organization of the primary motor cortex and influenced the number of significant differences in the clinical tests. To our knowledge, it is unknown how long it takes for LBP to induce maladaptive neuroplasticity. The limited changes over time observed in the clinical tests and cortical reorganization may be due to the short follow-up interval. Therefore, investigating a larger group over a longer period may be relevant.

We used multivariate multilevel analysis for our statistical testing. This approach helped to account for multiple testing to some extent, as all estimates were derived from the same model. Therefore, we did not perform an additional adjustment for multiple testing. Moreover, this analysis allowed us to manage dependencies of the observations between the outcomes within the participant, enabling us to draw exploratory meaningful conclusions from our interrelated dataset. However, given that we split the LBP group into participants who recovered and those who did not, our sample was small, which limits the applicability of our findings to exploratory conclusions.

## 5 | Conclusion

Of the analyses conducted, a few results showed significance. These were mainly related to the reorganization of longissimus L5, both in a shift over time and associations with performance on some clinical tests. The direction of these changes and associations varied. Future research should include a large participant group and focus on a group that recovers based on several patient-reported outcomes and clinical measurements over a longer period.

#### Author Contributions

S.P.K., H.K., M.W.C., and A.L.P.-G. designed the study. S.P.K., S.M.B., and A.L.P.-G. designed the TMS procedure. S.P.K. conducted the measurements. S.P.K. and S.M.B. executed the data curation. S.P.K. and J.W.R.T. developed the statistical plan and conducted the statistical analyses. All authors critically read the various drafts of the manuscript and approved the final version of the manuscript.

#### Acknowledgments

Sabrine P. Klerx was funded by the Netherlands Organization for Scientific Research (NWO), grant number 023.010.068. Costs for the MRIs were covered by the Dutch Association for Quality in Physiotherapy and the Vrije Universiteit Amsterdam. Sjoerd M. Bruijn was funded by a VIDI grant (016.Vidi.178.014) from the Netherlands Organization for Scientific Research (NWO). We would like to thank all participants and Lotte Tiessen, Zahir Haddag, Sebastiaan van Osch,

Maurits Eveleens, Maarten van de Beek, and Nils Breebaart who provided assistance during the measurements and Bert Clairbois and Bert Coolen for their technical assistance. We are also thankful to Richard Felius for creating the figures of the results.

### Conflicts of Interest

The authors declare no conflicts of interest.

### Data Availability Statement

Data will be made available on reasonable request.

### Peer Review

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/ejn.70051.

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**Appendix 1**

**Multivariate analyses of the longitudinal association between changes in the cortical area with changes in performance on clinical tests.**

| Dependent variable | Muscle | Independent variable | $\beta_{association}$ | 95% CI lower:upper |
|---|---|---|---|---|
| | | QST pain variables | | |
| Area | Longissimus L3 | Temporal summation | 349.5 | −135.1:834.1 |
| | | PPT | −20.2 | −61.6:21.1 |
| | | CPM relative | −15.0 | −35.6:5.6 |
| | | CPM absolute | −17.7 | −60.6:25.2 |
| | Longissimus L5 | Temporal summation | −162.9 | −598.3:272.4 |
| | | PPT | −13.5 | −47.9:20.9 |
| | | CPM relative | 16.1 | −2.8:35.0 |
| | | CPM absolute | 18.3 | −21.2:57.8 |
| | Obliquus externus | Temporal summation | 34.5 | −401.6:470.7 |
| | | PPT | −17.5 | −50.2:15.2 |
| | | CPM relative | −17.2 | −35.5:1.1 |
| | | **CPM absolute** | **−44.9** | **−83.0:−6.8** |
| | Obliquus internus | Temporal summation | −50.6 | −488.0:386.9 |
| | | PPT | 12.6 | −21.3:46.6 |
| | | CPM relative | −11.1 | −30.1:8.0 |
| | | CPM absolute | −16.4 | −57.9:25.1 |
| | | Sensory accuracy | | |
| Area | Longissimus L3 | 2-point discrimination | −20.62 | −81.44:40.19 |
| | | Graphaesthesia | −19.46 | −63.90:24.99 |
| | | Vibration | 127.24 | −838.63:1093.11 |
| | Longissimus L5 | 2-point discrimination | 11.91 | −46.59:70.40 |
| | | Graphaesthesia | −6.69 | −49.72:36.35 |
| | | **Vibration** | **1793.66** | **935.97:2651.36** |
| | Obliquus externus | 2-point discrimination | −34.90 | −94.94:25.14 |
| | | Graphaesthesia | 47.55 | −1.64:96.75 |
| | | Vibration | 454.03 | −255.21:1163.27 |
| | Obliquus internus | 2-point discrimination | 50.12 | −8.78:109.02 |
| | | Graphaesthesia | −21.20 | −66.39:23.99 |
| | | Vibration | 686.16 | −39.13:1411.45 |
| | | Motor control; spiral tracking test | | |

(Continues)

| Dependent variable | Muscle | Independent variable | $\beta_{association}$ | 95% CI lower:upper |
|---|---|---|---|---|
| Area | Longissimus L3 | Path | −1.53 | −22.1:19.0 |
| | | Angular distance near | −297 | −3543:2950 |
| | | Time near | 19.8 | −38.1:77.7 |
| | Longissimus L5 | Path | 9.25 | −4.11:22.6 |
| | | Angular distance near | −1496 | −4075:1082 |
| | | Time near | 27.1 | −15.2:69.5 |
| | Obliquus externus | Path | −7.24 | −19.1:4.65 |
| | | Angular distance near | −1090 | −3640:1460 |
| | | Time near | 30.9 | −10.3:72.1 |
| | Obliquus internus | Path | −7.18 | −19.1:4.75 |
| | | Angular distance near | 806 | −1749:3360 |
| | | Time near | 2.82 | −38.5:44.2 |

*Note:* Path, the total distance travelled in degrees over one trial; angular distance near: the mean of the closest 90% tracking errors; time near: the percentage of time spent at an angular distance closer than 0,9° from the red target point.
Abbreviations: CPM, conditioned pain modulation; PPT, pressure pain threshold; QST, quantitative sensory testing.

**Appendix 2**

**Multivariate analyses of the longitudinal association between changes in center of gravity posterior–anterior with changes in performance on clinical tests.**

| Dependent variable | Muscle | Independent variable | $\beta_{association}$ | 95% CI lower:upper |
|---|---|---|---|---|
| | | QST pain variables | | |
| CoG, posterior–anterior | Longissimus L3 | Temporal summation | −0.90 | −3.32:1.52 |
| | | PPT | 0.06 | −0.14:0.26 |
| | | CPM relative | −0.01 | −0.11:0.97 |
| | | CPM absolute | −0.06 | −0.28:0.16 |
| | Longissimus L5 | Temporal summation | −1.50 | −3.78:0.79 |
| | | PPT | 0.03 | −0.15:0.21 |
| | | CPM relative | −0.03 | −0.13:0.07 |
| | | CPM absolute | −0.06 | −0.27:0.15 |
| | Obliquus externus | Temporal summation | −0.29 | −2.57:2.00 |
| | | PPT | −0.06 | −0.23:0.12 |
| | | CPM relative | 0.02 | −0.07:0.12 |
| | | CPM absolute | −0.39 | −0.25:0.17 |
| | Obliquus internus | Temporal summation | 1.01 | −1.29:3.29 |
| | | PPT | −0.07 | −0.25:0.11 |
| | | CPM relative | 0.01 | −0.09:0.11 |
| | | CPM absolute | −0.16 | −0.37:0.06 |
| | | Sensory accuracy | | |

(Continues)

| Dependent variable | Muscle | Independent variable | $\beta_{association}$ | 95% CI lower:upper |
|---|---|---|---|---|
| CoG, posterior–anterior | Longissimus L3 | 2-point discrimination | 0.07 | −0.25:0.39 |
| | | Graphaesthesia | 0.08 | −0.16:0.32 |
| | | Vibration | 0.53 | −4.20:5.26 |
| | Longissimus L5 | 2-point discrimination | −0.01 | −0.32:0.31 |
| | | Graphaesthesia | −0.03 | −0.26:0.21 |
| | | Vibration | −0.11 | −4.52:4.30 |
| | Obliquus externus | 2-point discrimination | 0.07 | −0.24:0.39 |
| | | Graphaesthesia | 0.12 | −0.13:0.37 |
| | | Vibration | −0.42 | −4.39:3.55 |
| | Obliquus internus | 2-point discrimination | −0.04 | −0.35:0.28 |
| | | Graphaesthesia | −0.01 | −0.25:0.23 |
| | | Vibration | 2.43 | −1.59:6.45 |
| | | Motor control; spiral tracking test | | |
| CoG, posterior–anterior | Longissimus L3 | Path | −0.02 | −0.12:0.07 |
| | | Angular distance near | −2.50 | −19.0:14.0 |
| | | Time near | 0.17 | −0.11:0.45 |
| | Longissimus L5 | Path | −0.03 | −0.11:0.04 |
| | | Angular distance near | 4.47 | −10.3:19.2 |
| | | Time near | 0.01 | −0.23:0.25 |
| | Obliquus externus | Path | −0.01 | −0.08:0.06 |
| | | Angular distance near | 7.68 | −6.98:22.3 |
| | | Time near | −0.01 | −0.25:0.23 |
| | Obliquus internus | Path | −0.04 | −0.11:0.03 |
| | | Angular distance near | −4.28 | −18.9:10.4 |
| | | Time near | 0.21 | −0.03:0.44 |

*Note:* Path, the total distance travelled in degrees over one trial; angular distance near: the mean of the closest 90% tracking errors; time near: the percentage of time spent at an angular distance closer than 0,9° from the red target point; posterior–anterior, a positive coefficient defines a shift to anterior, a negative coefficient a shift to posterior; latero-medial, a positive coefficient defines a shift to medial, a negative coefficient a shift to lateral; vertical, a positive coefficient defines a shift to the vertex line, a negative coefficient a shift away from the vertex line (to a lower location).
Abbreviations: CPM, conditioned pain modulation; PPT, pressure pain threshold; QST, quantitative sensory testing.

**Appendix 3**

**Multivariate analyses of the longitudinal association between changes in center of gravity latero-medial with changes in performance on clinical tests.**

| Dependent variable | Muscle | Independent variable | $\beta_{association}$ | 95% CI lower:upper |
|---|---|---|---|---|
| | | QST pain variables | | |
| CoG, latero-medial | Longissimus L3 | Temporal summation | −0.96 | −3.26:1.33 |
| | | PPT | −0.04 | −0.23:0.15 |
| | | CPM relative | −0.03 | −0.13:0.07 |
| | | CPM absolute | −0.02 | −0.22:0.19 |
| | Longissimus L5 | Temporal summation | 0.90 | −1.17:2.98 |
| | | **PPT** | **−0.26** | **−0.42:−0.10** |
| | | **CPM relative** | **−0.10** | **−0.19:−0.01** |
| | | **CPM absolute** | **−0.24** | **−0.43:−0.05** |
| | Obliquus externus | Temporal summation | −1.12 | −3.20:0.96 |
| | | PPT | −0.14 | −0.29:0.01 |
| | | CPM relative | −0.04 | −0.13:0.04 |
| | | CPM absolute | −0.09 | −0.27:0.09 |
| | Obliquus internus | Temporal summation | 0.48 | −1.60:2.56 |
| | | PPT | −0.07 | −0.23:0.09 |
| | | CPM relative | −0.05 | −0.14:0.05 |
| | | CPM absolute | −0.08 | −0.28:0.12 |
| | | Sensory accuracy | | |
| CoG, latero-medial | Longissimus L3 | 2-point discrimination | 0.21 | −0.08:0.50 |
| | | Graphaesthesia | −0.01 | −0.22:0.21 |
| | | Vibration | −0.58 | −5.34:4.17 |
| | Longissimus L5 | 2-point discrimination | 0.12 | −0.16:0.40 |
| | | Graphaesthesia | 0.02 | −0.19:0.22 |
| | | Vibration | 2.24 | −2.01:6.49 |
| | Obliquus externus | 2-point discrimination | −0.10 | −0.38:0.19 |
| | | Graphaesthesia | −0.14 | −0.37:0.10 |
| | | Vibration | −1.41 | −4.97:2.15 |
| | Obliquus internus | 2-point discrimination | −0.06 | −0.35:0.22 |
| | | Graphaesthesia | −0.09 | −0.30:0.13 |
| | | Vibration | −0.07 | −3.70:3.57 |
| | | Motor control; spiral tracking test | | |

(Continues)

| Dependent variable | Muscle | Independent variable | $\beta_{association}$ | 95% CI lower:upper |
|---|---|---|---|---|
| CoG, latero-medial | Longissimus L3 | Path | 0.04 | −0.06:0.14 |
| | | Angular distance near | 4.29 | −11.6:20.2 |
| | | Time near | −0.10 | −0.38:0.18 |
| | Longissimus L5 | Path | 0.001 | −0.07:0.07 |
| | | **Angular distance near** | **−13.5** | **−26.4:−0.55** |
| | | **Time near** | **0.25** | **0.04:0.46** |
| | Obliquus externus | Path | 0.04 | −0.03:0.10 |
| | | Angular distance near | −6.76 | −19.6:6.06 |
| | | Time near | 0.09 | −0.12:0.30 |
| | Obliquus internus | Path | 0.02 | −0.04:0.09 |
| | | Angular distance near | −8.15 | −21.0:4.68 |
| | | Time near | 0.13 | −0.08:0.34 |

*Note:* Path, the total distance travelled in degrees over one trial; angular distance near: the mean of the closest 90% tracking errors; time near: the percentage of time spent at an angular distance closer than 0,9° from the red target point; posterior–anterior, a positive coefficient defines a shift to anterior, a negative coefficient a shift to posterior; latero-medial, a positive coefficient defines a shift to medial, a negative coefficient a shift to lateral; vertical, a positive coefficient defines a shift to the vertex line, a negative coefficient a shift away from the vertex line (to a lower location).
Abbreviations: CPM, conditioned pain modulation; PPT, pressure pain threshold; QST, quantitative sensory testing.

**Appendix 4**

**Multivariate analyses of the longitudinal association between changes in center of gravity vertical with changes in performance on clinical tests.**

| Dependent variable | Muscle | Independent variable | $\beta_{association}$ | 95% CI lower:upper |
|---|---|---|---|---|
| | | QST pain variables | | |
| CoG, vertical | Longissimus L3 | Temporal summation | −0.15 | −1.42:1.12 |
| | | PPT | −0.04 | −0.15:0.06 |
| | | CPM relative | −0.01 | −0.07:0.05 |
| | | CPM absolute | −0.02 | −0.14:0.09 |
| | Longissimus L5 | Temporal summation | 1.05 | −0.11:2.22 |
| | | **PPT** | **−0.12** | **−0.21:−0.03** |
| | | CPM relative | −0.02 | −0.08:0.03 |
| | | CPM absolute | −0.07 | −0.18:0.04 |
| | Obliquus externus | Temporal summation | −0.38 | −1.55:0.79 |
| | | PPT | −0.05 | −0.14:0.04 |
| | | CPM relative | −0.004 | −0.05:0.05 |
| | | CPM absolute | −0.01 | −0.11:0.10 |
| | Obliquus internus | Temporal summation | 0.37 | −0.80:1.55 |
| | | PPT | −0.06 | −0.15:0.03 |
| | | CPM relative | −0.04 | −0.09:0.02 |
| | | CPM absolute | −0.01 | −0.12:0.10 |
| | | Sensory accuracy | | |

(Continues)

| Dependent variable | Muscle | Independent variable | $\beta_{association}$ | 95% CI lower:upper |
|---|---|---|---|---|
| CoG, vertical | Longissimus L3 | 2-point discrimination | 0.07 | −0.10:0.23 |
| | | Graphaesthesia | 0.02 | −0.11:0.14 |
| | | Vibration | 0.35 | −2.25:2.96 |
| | Longissimus L5 | 2-point discrimination | 0.10 | −0.06:0.26 |
| | | Graphaesthesia | 0.04 | −0.08:0.16 |
| | | Vibration | 0.64 | −1.72:3.01 |
| | Obliquus externus | 2-point discrimination | −0.04 | −0.20:0.12 |
| | | Graphaesthesia | −0.01 | −0.14:0.12 |
| | | Vibration | −0.06 | −2.09:1.97 |
| | Obliquus internus | 2-point discrimination | 0.01 | −0.15:0.17 |
| | | Graphaesthesia | 0.01 | −0.11:0.14 |
| | | Vibration | −0.42 | −2.48:1.65 |
| | | Motor control; spiral tracking test | | |
| CoG, vertical | Longissimus L3 | Path | 0.03 | −0.03:0.08 |
| | | Angular distance near | −3.83 | −12.7:5.02 |
| | | Time near | 0.06 | −0.10:0.21 |
| | Longissimus L5 | Path | −0.02 | −0.06:0.02 |
| | | Angular distance near | −6.16 | −13.6:1.28 |
| | | Time near | 0.09 | −0.03:0.22 |
| | Obliquus externus | Path | 0.02 | −0.01:0.06 |
| | | Angular distance near | −5.73 | −13.1:1.64 |
| | | Time near | 0.07 | −0.05:0.19 |
| | Obliquus internus | Path | 0.01 | −0.02:0.05 |
| | | Angular distance near | −5.27 | −12.7:2.12 |
| | | Time near | 0.07 | −0.05:0.19 |

*Note:* Path, the total distance travelled in degrees over one trial; angular distance near: the mean of the closest 90% tracking errors; time near: the percentage of time spent at an angular distance closer than 0,9° from the red target point; posterior–anterior, a positive coefficient defines a shift to anterior, a negative coefficient a shift to posterior; latero-medial, a positive coefficient defines a shift to medial, a negative coefficient a shift to lateral; vertical, a positive coefficient defines a shift to the vertex line, a negative coefficient a shift away from the vertex line (to a lower location).
Abbreviations: CPM, conditioned pain modulation; PPT, pressure pain threshold; QST, quantitative sensory testing.