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Original experimental

Influence of paravertebral muscles training on brain plasticity and postural control in chronic low back pain

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HIGHLIGHTS

- Isometric vs. global exercises of multifidus muscles had different effects.
- Isometric exercise influenced brain plasticity and fastened postural adjustment.
- Changes persisting after 3-week training and long-term effects are questioned.

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ABSTRACT

Background and purpose: Isometric activation (ISOM) of deep multifidi muscles (MF) can influence postural adjustments and primary motor cortex (M1) function in chronic low back pain (CLBP). In order to better understand how ISOM impacts on CLBP condition, the present study contrasted ISOM after-effects on M1 function, MF postural activation and pain with another training, the global activation of paravertebral muscles (GLOB, hip extension). The main objective of this study was to compare the effects of ISOM and GLOB (3-week training each) on MF postural activation and M1 function in a CLBP population.
Methods: Twenty-four people with CLBP were randomly allocated to ISOM and GLOB groups for a 3-week daily practice. Pre/post-training after-effects were assessed by the onset of superficial MF (MF-S) activation during ballistic limb movements (bilateral shoulder flexion in standing; unilateral hip extension in prine lying), MF-S corticomotor control tested by transcranial magnetic stimulation of M1, and assessment of pain, kinesiophobia and disability by standardized questionnaires.
Results: Both ISOM and GLOB improved pain and disability. However, only ISOM influenced M1 function (decreased corticospinal excitability and increased intracortical inhibition), fastened MF-S postural activation and decreased kinesiophobia.
Conclusions: Changes of corticospinal excitability and of MF-S postural adjustments suggest that ISOM better influenced brain plasticity. Future studies should further test whether our novel findings relate to an influence of the exercises on the lumbopelvic control of different muscles and on cognitive function. Clinically, individual's evaluation remains warranted before prescribing one or the other of these two conventional exercises for reducing pain.
Implications: This original study presents how motor control exercises can influence brain plasticity and postural control in chronic low back pain. This knowledge will impact on the decision of clinicians to prescribe specific exercises with a view of improving motor control in this musculoskeletal condition.

1. Introduction

Chronic low back pain (CLBP) is common [1] and affects up to 10% of people worldwide [2,3]. The impairment of posturo-motor control of trunk muscles has been proposed as a factor contributing to the persistence of pain [4]. In line, studies reported an overactivation of superficial paravertebral muscles in some individuals with CLBP [5–8] and a delay of the anticipatory postural adjustments

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Table 1
Descriptive characteristics of participants at baseline (mean ± SD).

Groups	GLOB	ISOM	*p*
Participants (*n*)	11	11	–
Gender (M:F)	8:3	6:5	0.66[a]
Age (years)	45.4 ± 18.1	35.1 ± 11.4	0.13
Height (cm)	169.7 ± 7.5	174.1 ± 11.4	0.30
Weight (kg)	76.0 ± 19.8	78.1 ± 14.2	0.78
BMI (kg/m^2)	26.2 ± 6.1	25.6 ± 2.7	0.75
GPAQ (METS)	2640.0 ± 2432.7	3265.5 ± 2185.4	0.53
Sedentarity (h)	8.9 ± 2.1	8.5 ± 2.7	0.66
Pain duration (mo)	51.6 ± 44.8	38.5 ± 23.4	0.40
Pain side (right:left)	7:4	4:7	0.40[a]

GLOB: global exercise; ISOM: isometric exercise; BMI; body mass index; GPAQ: Global Physical Activity Questionnaire; mo: months; METS; metabolic equivalent; *p*: bilateral unpaired *t*-test.
[a] Bilateral Fisher's exact test.

(APA) of some trunk muscles (usually transverse abdominis or TrA and lumbar multifidus or MF) [9–12]. Studies using transcranial magnetic stimulation (TMS) of the primary motor cortex (M1) showed that this APA delay was correlated with a shift of M1 maps [13] and concomitant to a loss of M1 inhibitory mechanism usually involved in motor planning [14]. Precisely, M1 areas controlling erector spinae and MF muscles overlapped in CLBP whereas distinct in pain-free subjects [15,16].

It was shown that a single session of isometric motor control exercises (ISOM, i.e. specific activation of deep trunk muscles) immediately reduced APA delay of the muscle trained [17,18] and that improvement persisted after a 3-week training program [19,20]. This was correlated with M1 map normalization [19] and accompanied by a reactivation of M1 inhibitory processing [21]. These improvements were not observed after a single session of global activation of trunk muscles (GLOB, maintenance of a specific posture) [22] that however significantly reduced APA delay after one-year training [23,24].

A different influence of ISOM and GLOB on APA and pain and persistence of after-effects after several training sessions could be related to a different impact on M1 plastic phenomena but this has never been tested. Studies in neuropathic pain and using noninvasive brain stimulation to influence M1 plasticity indeed showed that the level of reactivation of M1 inhibitory circuits (dynamic plastic changes) was correlated with a reduction of neuropathic pain [25]. Therefore, the primary objective of this study was to compare the effects of ISOM and GLOB (3-week training each) on MF APA and M1 function in a CLBP population. The working hypothesis was on a greater influence of ISOM on M1 and APA. In support, ISOM represents a motor skill-focused training that influences more M1 plasticity than a less-skill focused training [26,27] and that requires high-level attention and cognitive demand, with larger impact on APA than GLOB has [17–19,22].

2. Methods

2.1. Participants

Twenty-four individuals with lateralized CLBP (pain ≥3 months, one side more painful, see Section 2.6), mainly members of Université Laval community having responded to the study advertisement sent by emailing lists, were randomly allocated to two different groups, ISOM or GLOB, using statistical software (see Table 1 for group characteristics). A member of the laboratory not involved in the study prepared a random list where each new participant was allocated to an exercise group. The participants and the therapist could not be blinded to the intervention given the design of the study. However, all data were codified so that the investigator in charge of data analysis remained blinded until completion of the analyses.

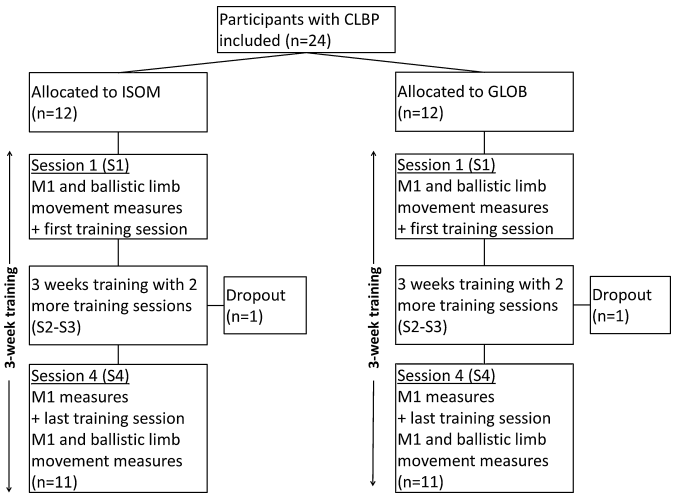

Fig. 1. Flowchart of the study design. CLBP: chronic low back pain; ISOM: isometric contraction of multifidus muscles (MF); GLOB: global activation of paravertebral muscles; M1: primary motor cortex; APA: anticipatory postural adjustment.

The exclusion criteria were non-mechanical LBP (e.g. fracture, malignancy, infection), more than 2 radicular signs, lumbar infiltration in the last 6 months, facet denervation, lumbar surgery, other chronic pain pathology, litigation, specific training of trunk muscles, any major circulatory, respiratory, neurological or cardiac disease, severe orthopaedic troubles (e.g. scoliosis with gibbosity >8 mm), cognitive deficit, or recent/current pregnancy. Exclusion criteria related to TMS testing are reported elsewhere [28] and mainly concerned brain surgery, lesion or injury, any history of seizure or concussion, pacemaker/pump holder, change of medication in the 2 weeks preceding enrollment, medication affecting cortical excitability, metallic implants in skull or jaw. The informed written consent of all participants and the experimental procedures were approved by the local research ethics boards, in accordance with the Declaration of the World Medical Association (www.wma.net).

2.2. Study design

The study was conducted over 3 weeks (Fig. 1) with participants attending 4 sessions (one per week). At the first session (S1), TMS, APA and pain data were collected before the exercise (pre-S1) and each participant learnt and practiced the allocation group exercise (ISOM or GLOB) under the supervision of an expert physical therapist. At sessions 2 and 3, the participant practiced the exercise under supervision and, whenever possible, the difficulty was increased (see Section 2.7). Participants had to perform their exercise twice daily and compliance was reported in an exercise log. At session 4 (S4), the exercise was practiced and APA and pain data were collected after the exercise (post-S4). TMS data were collected before (pre-S4) and after the exercise (post-S4). At all time points (S1, pre- and post-S4), TMS was always tested before APA and, at S4, TMS and APA outcomes were collected before training in the lab and immediately after.

2.3. Surface electromyography (EMG)

Parallel-bar surface EMG sensors were positioned bilaterally to record the activity of superficial MF (MF-S), lower transversus abdominis and internal oblique (TrA/IO), external oblique (EO), semitendinosus (ST) and anterior deltoid (AD) muscles (16-Channel Bagnoli EMG System, Delsys Inc., Boston, MA). After careful skin

preparation, electrodes were placed following SENIAM recommendations for MF, AD and ST [29] and according to Marshall & Murphy's for TrA/IO and EO [30]. A common ground electrode was positioned on the iliac crest. EMG signals were bandpass-filtered (10–450 Hz), amplified before digitization (2 kHz), and stored for online display and offline analysis (PowerLab Acquisition System, LabChart-ADInstruments, Colorado Springs, CO).

2.4. Postural tasks

Two rapid limb movement tasks were used to study APA latency of MF, TrA/IO and EO muscles. For bilateral shoulder flexion, the participant, initially in quiet standing with the arms aligned with thighs and both hands at shoulder width apart handling a rigid stick, had to flex the shoulders (raise the stick) to 90° as fast as possible in response to an auditory tone (see Fig. 2, upper left scheme for final position). Ten trials were recorded, each separated by a break. For unilateral hip extension in prone, the participant had to extend one hip to the neutral position, from ~10° of flexion (pillow under the pelvis) as fast as possible in response to an auditory tone (see Fig. 2, lower left scheme for final position). Three trials were recorded on each side (see [31] for details of protocol).

2.5. TMS testing of MF muscle

The participants were seated on a chair without arm support and the feet flat on the floor [15,16,32]. TMS testing of MF-S is challenging at rest [33] and M1 function worth being tested with tonic activity of the muscle for increasing M1 excitability and stabilizing motoneuronal excitability and spinal cord output [34]. Thus, participants had to lean the trunk forward and maintain the lumbar spine in lordosis: maintenance of this posture with minimal pain or discomfort required tonic activation of MF-S. This activity was monitored at 15% of maximum voluntary contraction as follows (MVC was measured in resisted back extension while sitting): the mean rectified MF EMG activity associated with the posture was displayed as a line on an oscilloscope screen for real-time visual feedback (2 Hz low-pass filtered) and participants had to superimpose their activity on the 15% MVC target line displayed on the same screen. Trials in which EMG fell outside the acceptance window were rejected and recorded again.

TMS of M1 was applied over the hemisphere contralateral to the most painful side. Magnetic stimuli were applied using a double-cone coil (7-cm outer diameter each wing; Magstim Company Limited, Whitland, UK) optimal for the activation of MF M1 cells [15,35,36]. The TMS coil was positioned over MF M1 area that was first approximated at 2 cm lateral to the vertex using 10-20 EEG system [15]. The position was adjusted slightly to determine the 'hot spot', namely the M1 location eliciting the largest amplitudes of MF MEP at a given intensity. Scalp locations were marked using a surgical marker to ensure reliable positioning and orientation of the coil. The active motor threshold (AMT) was defined as TMS intensity eliciting at least 5 measurable MEP in the preactivated MF out of 10 trials.

Double TMS paradigms (coil connected to two Magstim 200^2 monophasic stimulators) were used to test the intracortical circuits of M1 function. The short-interval intracortical inhibition (SICI) was probed by the combination of a subthreshold conditioning TMS (70% AMT) and a suprathreshold test TMS at 120% AMT; two inter-stimulus intervals were tested with the conditioning TMS delivered 2 ms then 3 ms before the test [37,38]. The long-interval intracortical inhibition (LICI) was tested using a conditioning TMS at 120% AMT followed 100 ms later by a test TMS at 120% AMT [39]. The long-interval intracortical facilitation (LICF) was tested with a subthreshold conditioning TMS (80% AMT) followed 15 ms later by a test MEP at 120% AMT. The short-interval intracortical facilitation (SICF) was probed by a subthreshold conditioning TMS (90% AMT) delivered 1 ms after a test TMS at 100% AMT [40,41]. In each paradigm, eight to ten unconditioned (test) MEP and 8–10 conditioned MEP were elicited. Inhibition or facilitation (as appropriate per paradigm) corresponded to the decrease or increase, respectively, of the conditioned MEP amplitude as compared to its test MEP. The amplitudes of the conditioned MEP were expressed in percent of the mean test MEP amplitude. For each participant, the amplitude of the test MEP was matched between S1, pre-S4 and post-S4 time points (adjustment of test TMS intensity) to ensure valid comparisons of conditioned MEP amplitudes. Rest periods were allowed between TMS trials to avoid fatigue and pain.

2.6. Questionnaires (pain, function, kinesiophobia)

At S1, the Global Physical Activity Questionaire (GPAQ) rated the level of physical activity and a body diagram was used to determine the more painful side [42]. The following scales and questionnaires were administrated at S1 and post-S4 (i.e. 3 weeks apart): a visual analogue scale [42] was used to assess the intensity of LBP in a sitting position at time of testing (spontaneous pain) and the intensity of the mean pain over the last week (week pain); the Oswestry disability index (ODI) [43] and the Patient-specific functional scale (PSFS) [44] assessed the functional disability of the participants; the Tampa Scale of Kinesiophobia (TSK) [45] measured the fear of movement or of (re)injury. In addition, ODI and TSK were further administrated at 2 follow-ups (2 weeks and 1 month after S4). The psychometric properties of these scales and questionnaires in CLBP, such as validity, test-retest reliability and responsiveness are reported elsewhere [46].

2.7. Training at ISOM and GLOB

Each participant received detailed information on the low back anatomy and the rationale of paravertebral muscles exercises in LBP management.

The ISOM group performed isometric contraction of the lumbar MF, with particular attention to contracting the deep MF (dMF) with minimal activation of MF-S and adjacent ES [47]. The physical therapist supervising training used different strategies to ease dMF contraction and ensure its quality: real-time ultrasound imaging (Terason t3200 MSK series 15L4, Burlington, MA, USA), palpation, verbal cues and virtual motor imagery (e.g. stretching a rope between the thorax and pelvis, bringing closer two points of each side of the lumbar spine, and progressively and softly harden muscles palpated). When a participant succeeded in MF volitional activation for three consecutive sets while in prone, the difficulty of the exercise was progressed from the lying posture to standing then to sitting [47].

The GLOB group performed exercises in a four-point kneeling position, with the hip and knee maintained in extension on alternance between the right and left sides. The therapist first taught how to brace the trunk muscles. Bracing is defined as a low-intensity contraction of the abdominal wall. We asked participants to stiffen the abdomen as if they had to resist a punch in the belly [48].

During the exercise, the participants had to focus on keeping the pelvis parallel to the therapeutic table while maintaining lumbar lordosis and bracing trunk muscles. Different approaches were used to facilitate the exercise, including palpation, verbal cues, and balancing a ball or a bottle on the lumbar lordosis. When the participant correctly completed three consecutive sets, the exercise was progressed: flexion of the contralateral shoulder was added, then the lumbar lordosis should be maintained during dynamic hip extension and opposite shoulder flexion [48]. This exercise

targeted the global activation of paravertebral muscles (MF and erector spinae – ES) [49].

For each training program (ISOM, GLOB), a trial/repetition lasted 10 s without holding breath. At each laboratory session (S1 to S4), 3 sets of 10 repetitions were one-on-one supervised and the difficulty was progressed whenever possible. At home, participants were asked to perform 3 sets of 10 repetitions twice a day.

2.8. Data reduction and statistical analysis

All data were codified to blind measures extraction to individual, group and time points until completion of analyses.

Postural tasks outcomes. The onsets of MF-S, TrA/IO, EO and ST activation were expressed in ms relative to AD (for shoulder flexion) or ST activation time (for hip extension). These latencies of MF-S, TrA/IO and EO APA corresponded to the first increase (after the auditory tone) of EMG activity above background and that lasted for at least 50 ms [50]. EMG background was measured by averaging the 500-ms epoch preceding the auditory tone. In addition to visual inspection, one standard deviation over background during at least 50 ms was used to detect onset of muscle activation.

In the bilateral shoulder flexion task a mixed design analysis of variance (ANOVA) with repeated measures, using Group (ISOM vs. GLOB) as between-factor, Time (S1 vs. post-S4) and Side (more vs. less painful) as within-factors, was applied on MF-S, TrA/IO, EO and ST onsets. In the prone hip extension MF-S and EO onsets were tested by a mixed design ANOVA with repeated measures using Group as between-factor and Time × Hip Extension (more vs. less painful side) × Side of effect (contralateral vs. ipsilateral to hip extension) as within-factors TrA/IO onsets contralateral and ipsilateral to the hip extension were tested as independent factors with ANOVA applied separately given that some participants did not present any ipsilateral TrA/IO onset.

TMS outcomes. Seven TMS outcomes associated with MF-S were acquired for each participant: AMT (% maximum stimulator outcome, MSO) reflected the basic M1 excitability during tonic MF-S activity; peak-to-peak amplitude of test MEP (μV) reflected the volume of M1 cells synchronized by TMS and the synchronicity of descending volleys onto motoneurons; peak-to-peak amplitudes of the four different conditioned MEP (% test MEP) informed on the levels of SICI (ISI: 2 and 3 ms), LICI, LICF and SICF; normalized duration of the EMG silent period (SP) following the MEP in EMG recordings (SP in % test MEP amplitude). The normalization of SP by MEP amplitude was used because MEP amplitude affects SP duration [51] and training could have affected MEP amplitude. Thus, the normalization reduced the impact on the absolute length of SP. A two-way ANOVA with factors Group (ISOM vs. GLOB) × Time (S1, pre-S4, post-S4) with repeated measures on Time was applied to all outcomes.

Questionnaires outcomes. A mixed ANOVA model with factor Group × Time (S1 vs. post-S4) was applied on pain, ODI, PSFS and TSK scores. An ANOVA with factor Group × Time (S1, 2 weeks follow-up, 1 month follow-up) was additionally applied on ODI and TSK scores.

TMS outcomes and questionnaires scores were first tested with Time (S1 vs. post-S4) to allow for direct comparison with APA and pain. Post hoc tests analyses were performed using Sidak correction for multiple comparisons to test where differences lie in case of interactions detected by ANOVA. Shapiro–Wilk's test was performed to determine the normality of the distribution. If the target outcome was not normally distributed, it was transformed with a natural log function (Ln). Mauchly's test verified the sphericity i.e. if the variances of the differences between all combinations of related groups were equal. If the target outcome failed the sphericity assumption, a Greenhouse–Geisser correction was applied on the ANOVA results. Significance level was set at $p < 0.05$.

3. Results

Group characteristics were comparable at baseline for age, body mass index, height, weight, level of physical activity, pain, disability and kinesiophobia (Table 1). Two participants stopped the 3-week training due to compromised availability thus 22 participants ($n = 11$ per group) completed the protocol. No adverse effect was reported. Most of the data were normally distributed except MEP amplitude elicited at 120% AMT that was thus Ln-transformed. The AMT data failed the sphericity assumption and the ANOVA result was modified with a Greenhouse–Geisser correction. The main ANOVA results (F-value, DF effect, error, p-value, power) are reported in Table 2 for the postural tasks outcomes and in Table 3 for the TMS outcomes.

3.1. Postural tasks outcomes

One participant in GLOB group was withdrawn due to technical issue, thus bringing to $n = 21$ the number of subjects for postural tasks ($n = 11$ in ISOM group; $n = 10$ in GLOB group).

In bilateral shoulder flexion task, the ANOVA detected a Group × Time interaction close to significance for MF-S onset. In ISOM group, there was significant effect of Time ($F_{(1, 10)} = 12.34$, $p = 0.006$) which means an earlier MF-S onset at post-S4 than at S1 (change between time points: -5.6 ± 5.3 ms; $F_{(1, 19)} = 6.64$, $p = 0.02$) and not changed in GLOB group (change between time points: $+0.8 \pm 8.8$ ms; $F_{(1, 19)} = 0.13$, $p = 0.73$; Fig. 2A). No difference was found between group means at S1 and post-S4. ANOVA also detected a main effect of Time for TrA/IO onset ($F_{(1, 19)} = 7.75$, $p = 0.01$; Fig. 2B).

In the prone hip extension task, the ANOVA detected a Group × Time interaction for MF onset. In ISOM group, a main effect of Time was detected ($F_{(1, 9)} = 5.74$, $p = 0.04$) with MF-S onset earlier at post-S4 than at S1 (changes between time points: -7.1 ± 18.2 ms). Fig. 2C and E shows these changes for the hip extension on most-painful side and on the less painful side respectively with the details of MF contralateral and ipsilateral to hip extension in each case.

No difference was detected in the GLOB group. ANOVA also showed that in both groups and for both time points (S1, post-S4) the onset of ipsilateral MF occurred earlier than the contralateral (main effect: $F_{(1, 19)} = 19.72$, $p < 0.001$). No change was detected in TrA/IO for hip extension (Fig. 2D and F show the equivalent details as Fig. 2C and E for MF) and none at all for both tasks in EO and ST (not represented).

3.2. TMS outcomes

Changes were detected for AMT, MEP amplitude and normalized SP duration (Tables 3 and 4). No change was detected in any TMS outcome between pre-S4 and S1. One participant in ISOM group was withdrawn for TMS analysis due to the absence of MEP, thus bringing to $N = 21$ the number of participants ($n = 10$ ISOM; $n = 11$ GLOB).

AMT. The corrected ANOVA detected a main effect of Time for AMT with a significant decrease in both groups at post-S4 (48.6 ± 11.7% MSO) compared to pre-S4 (51.1 ± 11.4% MSO). There was no between-group difference. Individual data present that AMT decreased from pre- to post-training at S4 in most participants (Fig. 3).

Ln-transform MEP amplitude. Due to contamination of EMG traces by TMS artefact, one other participant was withdrawn at S1 ($n = 20$, $n = 10$ ISOM, $n = 10$ GLOB) and two at pre-S4 ($n = 19$, $n = 9$ ISOM, $n = 10$ GLOB). The ANOVA detected a main effect of Time, a main effect of Group and a Group × Time interaction. Post hoc tests detected that, in ISOM group only, MF Ln-transform MEP amplitude

Table 2
ANOVA results for postural tasks on Time and Group effects only.

APA	Effect	*F*-value	DF effect: error	*p*-value	Power
Shoulder flexion					
MF-S	Time	2.31	1: 19	0.15	0.30
	Time × Group	4.14	1: 19	0.056	0.49
TrA/IO	Time	8.14	1: 19	*0.01*	0.77
	Time × Group	0.55	1: 19	0.47	0.11
Hip extension					
MF-S	Time	3.09	1: 19	0.10	0.39
	Time × Group	4.62	1: 19	*0.045*	0.53
TrA/IO contralateral	Time	2.59	1: 19	0.12	0.33
	Time × Group	0.79	1: 19	0.46	0.10
TrA/IO ipsilateral	Time	0.85	1: 14	0.37	0.14
	Time × Group	2.52	1: 14	0.14	0.32

APA: anticipatory postural adjustment; MF-S: superficial multifidus; TrA/IO: transversus abdominis/internal oblique; DF: degree of freedom; Group = global vs. isometric exercise; Time = first session (pre-training) vs. fourth session (post-training); italics: $p < 0.05$.

was significantly decreased over time ($F_{(2, 18)} = 8.57, p = 0.002$). Pairwise comparisons detected a decrease between S1 and post-S4 ($p = 0.006$), and between pre-S4 and post-S4 ($p = 0.015$; Fig. 4A). A close-to-significance between-group difference was present at post-S4 ($p = 0.059$). No change was present in GLOB group ($p > 0.05$).

Normalized SP duration. Due to their insufficient EMG background for proper SP analysis, six other participants were withdrawn ($n = 15$, $n = 8$ ISOM, $n = 7$ GLOB). ANOVA detected a Time × Group interaction. In ISOM group, there was a significant effect of Time for SP duration ($F_{(2, 12)} = 5.05$, $p = 0.03$) However,

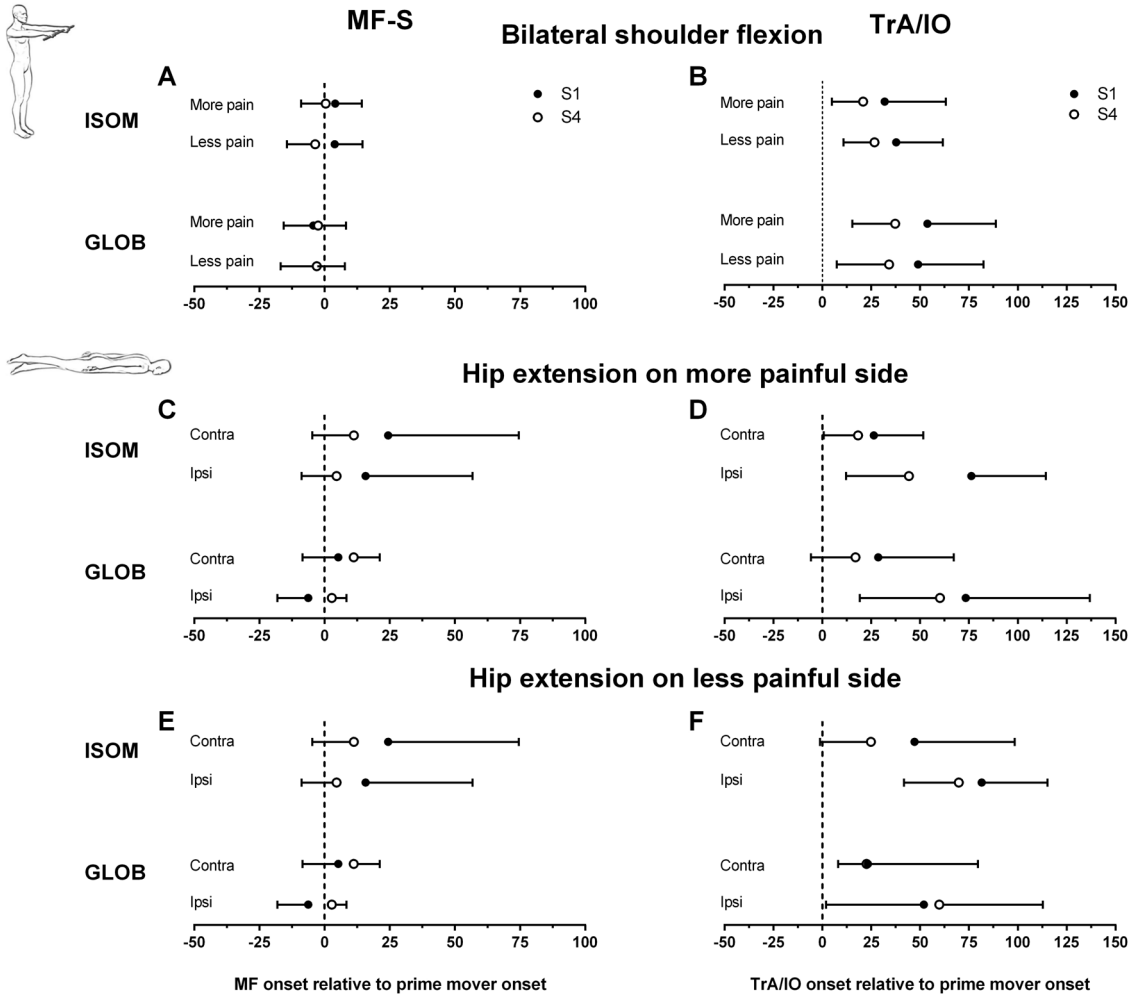

Fig. 2. Anticipatory postural adjustments (APA) of MF-S (left column) and TrA/IO (right column) in bilateral shoulder flexion (A and B), unilateral prone hip extension on the more painful side (C and D) and the less painful side (E and F) in ISOM and GLOB groups at first (S1) and last (S4) training sessions. In (A) and (B), APA are reported for MF-S and TrA/IO on the most and less painful sides. In (C) to (E), APA are reported for MF-S and TrA/IO contralateral and ipsilateral to the movement. MF-S: superficial multifidus; TrA/IO: transversus abdominis and internal oblique; GLOB: global exercise; ISOM: isometric exercise.

Table 3
ANOVA results for TMS outcomes on Time and Group effects only.

	Effect	*F*-value	DF effect: error	*p*-value	Power
AMT (%MSO)	Time	4.77	1.32: 25.06	*0.01*	0.76
	Group	0.05	1: 19	0.84	0.05
	Time × Group	0.34	1.32: 25.06	0.91	0.05
MEP amplitude (Ln-μV)	Time	5.70	2: 34	*0.01*	0.83
	Group	4.63	1: 17	*0.046*	0.52
	Time × Group	4.10	2: 34	*0.03*	0.68
SP/MEP (%)	Time	0.91	2: 24	0.42	0.19
	Group	1.20	1: 12	0.30	0.17
	Time × Group	3.88	2: 24	*0.04*	0.65

AMT: active motor threshold; MEP: motor evoked potential; Ln: natural logarithmic transformation; SP: silent period duration; DF: degree of freedom; Group = global vs. isometric exercise; Time = first session (pre-training) vs. fourth session (pre/post-training); italics: $p < 0.05$.

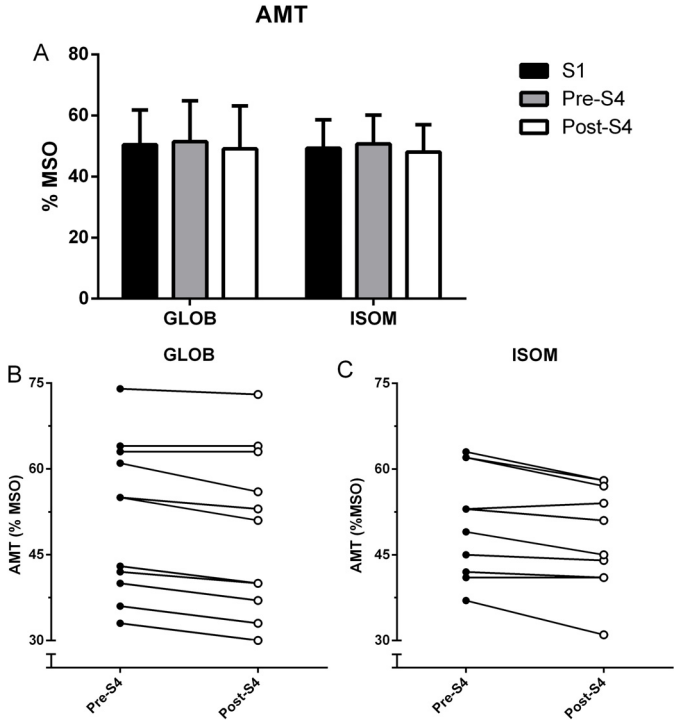

Fig. 3. Active motor threshold (AMT) in both groups. (A) Means at the three time points. (B) Individual data before and after training at session 4. A main effect of Time was detected between pre-S4 and post-S4. MSO: maximal stimulator output; GLOB: global exercise; ISOM: isometric exercise; S1: first session; S4: fourth session; pre, post: before, after training.

pairwise comparisons did fail to show a difference between time points (S1 vs. pre-S4: $p = 0.08$; pre- vs. post-S4: $p = 0.14$). A significant between-group difference was present at post-S4 where ISOM group showed higher normalized SP duration compared to GLOB

Table 4
TMS outcomes.

	S1	Pre-S4	Post-S4
GLOB group			
AMT (%MSO)	50.5 ± 11.4	51.5 ± 13.4	49.1 ± 14.1
MEP amplitude (Ln-μV)	2.02 ± 0.23	2.01 ± 0.22	1.99 ± 0.25
SP/MEP (%)	40.2 ± 23.86	38.9 ± 24.2	36.0 ± 14.3
SICI – 2 ms (% test)	77.5 ± 21.7	93.7 ± 19.0	79.5 ± 23.8
SICI – 3 ms (% test)	83.6 ± 24.7	103.1 ± 26.7	85.0 ± 17.4
LICI (% test)	68.2 ± 26.9	73.7 ± 32.3	74.7 ± 24.9
SICF (% test)	177.7 ± 48.7	174.3 ± 54.0	196.8 ± 103.0
LICF (% test)	101.1 ± 28.1	98.2 ± 31.5	82.3 ± 9.8
ISOM group			
AMT (%MSO)	49.3 ± 9.3	50.7 ± 9.5	48.0 ± 9.1
MEP amplitude (Ln-μV)	1.96 ± 0.25	1.92 ± 0.24	1.78 ± 0.23*,×
SP/MEP (%)	58.9 ± 40.8	43.3 ± 18.6	74.2 ± 42.4
SICI – 2 ms (% test)	84.6 ± 19.9	96.8 ± 31.8	84.8 ± 21.8
SICI – 3 ms (% test)	85.6 ± 24.4	74.7 ± 26.4	91.7 ± 25.0
LICI (% test)	71.3 ± 11.5	79.7 ± 23.0	75.7 ± 29.2
SICF (% test)	160.9 ± 52.8	206.7 ± 137.0	195.4 ± 67.0
LICF (% test)	114.5 ± 19.2	120.3 ± 43.8	108.8 ± 44.7

AMT: active motor threshold; MEP: motor evoked potential; SP: silent period; S/LICI: short/long-interval intracortical inhibition; S/LICF: short/long-interval intracortical facilitation; S1: first session; S4: fourth session; pre, post: before, after training; GLOB: global exercise; ISOM: isometric exercise.
* Significant difference between S1 and post-S4.
× Significant difference between pre and post-S4.

($F_{(1, 13)} = 5.88$, $p = 0.03$; Fig. 4B). ANOVA did not detect any other difference for TMS outcomes (Table 4).

3.3. Questionnaires

Post-S4 vs. S1. A main effect of Time was detected by the two-way ANOVA for the mean pain level in the last week (week pain), ODI and PSFS (week pain: $F_{(1, 20)} = 20.47$, $p < 0.001$; ODI: $F_{(1, 20)} = 5.38$, $p = 0.03$; PSFS: $F_{(1, 20)} = 16.25$, $p = 0.001$; see Table 5). ANOVA applied to TSK score (kinesiophobia) detected a Group × Time interaction

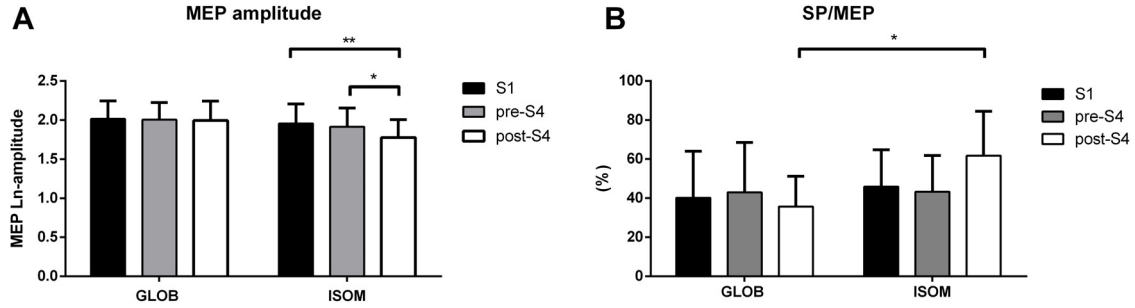

Fig. 4. Corticospinal excitability. Means of MEP amplitude (A) and silent period duration (B) at the three time points in both groups. Note the specific influence of ISOM training on both outcomes. MEP: motor evoked potential; SP: silent period; GLOB: global exercise; ISOM: isometric exercise; S1: first session; S4: fourth session; pre, post: before, after training. $^{*}p < 0.05$; $^{**}p < 0.01$.

Table 5
Questionnaire scores.

	S1	S4	2 w post-S4	1 mo post-S4
GLOB				
Spontaneous pain[a] (/10)	18.7 ± 20.3	13.1 ± 13.0		
Week pain[b] (/10)	41.1 ± 22.5	26.1 ± 18.0		
ODI (%)	21.1 ± 9.4	19.3 ± 9.6	18.7 ± 11.4	17.4 ± 12.6
PSFS (/30)	14.3 ± 4.9	18.3 ± 4.2		
TSK (/68)	38.2 ± 8.3	38.2 ± 7.4	36.3 ± 6.6	34.6 ± 7.7
ISOM				
Spontaneous pain[a] (/10)	20.4 ± 22.2	16.6 ± 20.0		
Week pain[b] (/10)	42.1 ± 21.4	17.5 ± 13.5		
ODI (%)	23.6 ± 14.1	17.4 ± 14.2	16.2 ± 13.0	16.1 ± 14.0
PSFS (/30)	12.2 ± 5.3	17.1 ± 7.0		
TSK (/68)	43.7 ± 8.3	37.6 ± 10.4[*]	37.0 ± 9.9[×]	37.2 ± 8.8[†]

ODI: Oswestry disability index; PSFS: patient specific functional scale; TSK: Tampa Scale of Kinesiophobia; w: week; mo: month; S1: first session; S4: fourth session; 2 w, 1 mo: 2 weeks, 1 month; post-S4: time elapsed after S4; GLOB: global exercise; ISOM: isometric exercise.

[a] Measured in sitting.
[b] Mean pain level of the last week.
[*] Significant difference between S1 and S4.
[×] Significant difference between S1 and 2 weeks post-S4.
[†] Significant difference between S1 and 1 month post-S4.

($F_{(1, 20)} = 6.70$, $p = 0.02$) with a decrease at post-S4 in ISOM group only ($F_{(1, 10)} = 10.73$, $p = 0.008$).

Follow-ups vs. S1. ODI and TSK scores were missing at 2 weeks (questionnaires not returned) for three participants ($n = 1$ ISOM; $n = 2$ GLOB) and two participants ($n = 1$ ISOM; $n = 1$ GLOB), respectively. At 1 month, only one participant did not return the questionnaires. A main effect of Time was detected with a decrease of ODI (2 weeks: $F_{(1, 17)} = 7.25$, $p = 0.02$; 1 month: $F_{(1, 19)} = 9.64$, $p = 0.006$) and TSK scores (2 weeks: $F_{(1, 18)} = 12.24$, $p = 0.003$; 1 month: $F_{(1, 19)} = 9.41$, $p = 0.006$).

4. Discussion

This original experimental-designed study testing in CLBP the different influence of two exercises on APA and M1 function related to the control of MF muscle only partially confirmed the working hypothesis. ISOM training influenced brain function and fastened MF APA but likely only in an acute manner after the exercise session at S4. Our result did not support long-term plasticity in M1 since no change was reported at pre-S4 for brain function and for GLOB exercise.

4.1. Long-term M1 plasticity following exercises (S1 vs. pre-S4)

Our study did not detect any change of MF MEP amplitudes before ISOM training for the last session (pre-S4) as compared to pre-S1 (baseline) but only a decrease immediately after training (post-S4). The absence of M1 changes at pre-S4 could be first related to the fact that participants recruited were still able to activate MF muscles or to perform GLOB exercise, thus the exercises may have failed the assumptions of complexity, high-level attention and cognitive demand needed to influence M1 plasticity [27,52–54]. Also, testing paravertebral M1 area with TMS is very challenging, thus experimental procedures chosen could have masked any M1 change, such as TMS intensity (120% AMT) and MF EMG electrodes placement (L5 level), given that M1 'smudging' was better detected by surface electrodes positioned at L3 as compared to L5 [55] and that significant differences in trunk muscles MEP after induction of experimental low back pain were detected only at higher TMS intensities [56]. The absence of significant TMS changes between S1 and pre-S4 time points could also be the result of motor practice over 3 weeks and where acute plastic changes in M1 circuits had returned to baseline over time between training sessions [52]. However, the lack of TMS outcomes changes after one ISOM session and after one week of training does not support this last hypothesis (unpublished data). Given that acute changes of MEP amplitude and SP duration were present at S4 after ISOM exercise, it is questioned whether three weeks at least of this specific type of exercise is required to influence M1 plasticity. Further studies should test this ancillary hypothesis.

4.2. Immediate M1 plasticity following ISOM exercises (pre-S4 vs. pre-S4)

Conversely to previous studies, the amplitude of the MEP was decreased at post-S4. Indeed, a MEP increase is usually depicted after skilled motor training and is referred to as long-term potentiation (LTP)-like phenomenon [27,52,57]. The explanation may relate to the differential after-effects of ISOM exercise on the deep vs. the superficial MF and the methods used for detecting these after-effects, i.e. surface EMG recordings. ISOM monitored by ultrasound imaging consisted of contracting deep MF (dMF) without MF-S or adjacent ES muscles [47]. Thus, ISOM that reinforced dMF synaptic efficacy may have reduced the excitability of MF-S M1 area and altered the descending volleys synchronicity onto MF-S motoneurons (lower strength of corticospinal projections) [58,59]. This is in line with MEP amplitude decrease (reduced corticospinal excitability of MF-S) and SP lengthening, i.e. an increase of type-B GABAergic inhibition in M1 [59] that modified the maps and decreased MF-S pathways efficacy [60]. This assumption is supported by the fact that M1 representations of muscles that should not be recruited (e.g. MF-S) in a task are inhibited whereas M1 area of muscles involved in the task (e.g. dMF) are released from inhibition, i.e. up-regulated, to favour LTP-like plasticity and learning [27,61]. Also, a recent series of study showed that skilled training of the upper trapezius muscle produced an increase of MEP amplitude in pain-free controls [62] but surprisingly, a decrease of MEP amplitude was present in a chronic neck pain group after one exercise session [63]. These differences can be partly explained by the theory of homeostatic metaplasticity, i.e. low neural excitability will favour LTP (facilitation) whereas high excitability will favour LTD (long-term depression) in order to monitor homeostasis [64]. Thus, in people with CLBP presenting a different level of M1 excitability [16,65], i.e. increased or decreased, the effects of exercise could be different as those obtained commonly. Of note, changes of MEP amplitude, that inform on a variation of corticomotoneuronal excitability, can reflect a modulation of motor cortical excitability but also the modification of spinal excitability by peripheral changes. However, in our study, MEP were superimposed on same rate of tonic MF activation between sessions and this may have

reduced the influence of peripheral changes on MEP amplitude [14,31].

Both ISOM and GLOB groups presented with a decrease of AMT at post-S4, i.e. an increase of M1 basic excitability. This result seems at odds with MEP data in ISOM group. However, it was already suggested that MEP change without corresponding changes in motor threshold could reveal a modification of corticospinal projection strength [66]. Thus, MEP decrease without concomitant increase of AMT supports further that ISOM markedly reduced the strength of MF-S corticospinal projections. AMT decrease, i.e. up-regulation of M1 transsynaptic activity [38] could have been influenced by inputs from prefrontal-to-motor excitatory networks to comply to the therapist's supervision and perform the task appropriately [67].

4.3. M1 plasticity and APA

Our results on earlier MF APA after 3-week ISOM training are in line with previous studies on changes of MF and TrA APA after one ISOM session [17,18], after one to four week of ISOM training (unpublished data) [19,20] and after one year at least of GLOB training [23]. However, given the design of the present study (at S4, APA were tested only after the practice), it is not possible to tell whether the earlier MF latency in the ISOM group at post-S4 represents long-term changes or changes related to the session. Of note, our group has already shown that APA of TrA/IO or MF was not changed after only one ISOM session but only one week later ([21] and unpublished data). Future studies should thus systematically test APA at pre- and post-practice over several weeks to determine the timing of MF APA changes and whether these changes persist over time. Some studies reported that APA of both MF-S and dMF could be delayed in some people with CLBP during various postural tasks [11,12] and that ISOM improved APA of different MF fascicles [10].

APA improvement after ISOM could have been driven by M1 maps normalization in our CLBP population, as first shown for TrA [19]. Also, an earlier TrA/IO onset was found in the shoulder flexion task for both groups. This result could rely too on M1 plasticity [19] given the complexity of GLOB exercise for controlling pelvis rotation (transverse plane) or bracing, and the implication of abdominal activation to perform an optimal MF ISOM contraction. Of note, and as a result of randomization, MF APA at baseline (S1) were not delayed in GLOB group as compared to ISOM group. Thus, this may have reduced the influence of training on MF APA in GLOB group.

4.4. M1 plasticity and pain

ISOM exercise induced other changes that could have contributed to reduce pain. In CLBP, pain is related to an increased activation of the superficial trunk muscles [8] and ISOM training was shown to reduce this overactivation [17]. Thus, it is legitimate to assume that the decrease of corticospinal drive to MF-S motoneurons, as detected by MEP amplitude decrease, contributed to regulate MF-S overactivation and normalize APA. In other words, earlier MF APA in at least the two postural tasks tested and decreased overactivation of MF-S likely improved the lumbopelvic spine control against daily microtrauma and tissue overload. The decrease of kinesiophobia obtained only in the ISOM group certainly had an effect on pain perception, since both phenomena are interwoven [45]. Therefore, ISOM exercise likely helped the participants being conscious of their ability to activate the muscles of their low back painful area without increasing pain. The GLOB exercise did not yield such effect. Interestingly, it seems that physical exercise could impact on psychological variables, as reported in the present study for kinesiophobia (TSK questionnaire), and, conversely, that cognitive aspects in training could influence pain and motor control. For instance, it was shown that a cognitive-behavioural intervention could improve motor control of the paravertebral muscles [68] and that kinesiophobia, fear-avoidance and anxiety could affect some variables of spine motor control [68–72]. Thus, it is possible that cognitive mechanisms involved in physical practice influenced M1 plasticity, pain and function in our study. Therefore, future studies are warranted to test the influence of cognition on M1 and APA of MF during and after physical practice.

Both ISOM and GLOB exercises however decreased pain scores and improved functional capacity. ISOM improved ODI score over 6 points which is considered the minimum clinically important difference [73] and both ISOM and GLOB improved PSFS more than the minimal detectable changes of 2 points [44]. It is thus likely that statistical power of our study did not suffice to determine which exercise had a greater influence on pain and function. Also, despite no change was detected at S4 for GLOB exercise (TMS and APA), the therapeutic benefits of GLOB are not discount and it is possible that both GLOB and ISOM training could have enhanced endurance [24] and proprioception of paravertebral muscles.

4.5. Methodological considerations

The use of surface EMG recordings could be a main limitation of the study because of cross-talk recording [74]. However, this helped detect for the first time brain plasticity related to MF M1 area after ISOM training and to associate it with MF APA improvement and kinesiophobia reduction. Future studies should use fine-wire electrodes to further document the changes related to motor control of deep fascicles of MF. Also, MEP amplitudes are far smaller in axial muscles than in distal muscles [33], thus potential "floor effects" under preactivated conditions may explain, in part, why M1 inhibition tested by double TMS paradigm was not influenced by ISOM training like SP duration was.

5. Conclusion

This original study showed that different exercise approaches to train MF muscles had a distinct influence on M1 plasticity and APA. ISOM exercise was the most efficient to modulate M1 inhibition and corticospinal excitability, to fasten MF-S APA and decrease kinesiophobia. ISOM could be more suitable to improve posturo-motor control of the trunk by the regulation of M1 inhibitory circuits involved in motor learning, and possibly to decrease overactivation of superficial trunk muscles by down-regulation of the corticospinal drive. Both exercises, however, appear to improve pain and disability and individual patient's evaluation is still warranted before selecting appropriate exercises to manage CLBP.

Disclosures

None.

Conflicts of interest statement

None.

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