

Original article

Bilateral sensory and motor as well as cognitive differences between persons with and without musculoskeletal disorders of the wrist and hand.

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ABSTRACT

Background: Sensory and motor disturbances are characteristic of musculoskeletal injuries and conditions. Rehabilitation interventions aimed at remediating these disturbances are traditionally exclusively targeted to the affected area. However, there is some evidence of bilateral changes in sensory and motor function associated with unilateral injuries and conditions suggesting central changes. Deficits on specific cognitive tasks have also been documented in persons with chronic pain.

Purpose: The purpose of the present study was to determine if participants with unilateral pain arising from heterogeneous wrist/hand injuries and conditions demonstrate bilateral changes in sensory and motor functions as well as cognitive deficits.

Design/methods: Sensory (Pressure Pain Thresholds, Two Point Orientation Discrimination), Motor (grip strength and Purdue Pegboard), and Cognitive function (Stroop test and mental rotation task) were measured in 30 participants with wrist/hand pain and 30 healthy control participants in an observational cross-sectional study.

Results: Participants with unilateral wrist/hand pain demonstrated differences in cognitive function measured with the Stroop test ($p = 0.03$). They also demonstrated bilateral sensorimotor differences in pressure pain thresholds ($p = 0.03$), grip strength ($p = 0.00$) and Purdue pegboard test ($p = 0.03$) results compared to healthy control participants.

Conclusion: Cognitive as well as bilateral alterations in sensory and motor function in participants with musculoskeletal injuries and conditions suggest central changes are involved in their pathophysiology. These findings in persons with heterogeneous injuries/conditions suggest that these changes are not specific to an injury/condition. Bilateral sensorimotor changes have important implications with regards to the pathophysiology of musculoskeletal disorders of the wrist/hand, for rehabilitative interventions and research.

1. Introduction

Sensory and motor disturbances are characteristic of musculoskeletal disorders (MSD) including those of the wrist and hand (Smeulders et al., 2002; Forget et al., 2008; Fernandez-de-Las-Penas, Perez-de-Heredia-Torres et al., 2009a,b; Chiarotto, Fernandez-de-las-Peñas et al.,

2013a,b). Rehabilitation efforts are usually directed at restoring normal sensory and motor function to the affected area. However, there is evidence of both bilateral changes in sensory and motor functions as well as central changes in cognitive function and sensorimotor integration.

Animal studies have demonstrated contralateral structural and

Abbreviations: Dash, Disability of the Arm, Shoulder and Hand; LRJT, Left Right Judgement Task; MSD, Musculoskeletal Disorders; PPG, Purdue Pegboard; PPT, Pressure Pain Threshold; TPOD, Two-Point Orientation Discrimination; VAS, Visual Analog Scale

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functional peripheral changes including immunohistochemical and morphological changes in association with unilateral injury in homologous structures on the uninjured side (Koltzenburg et al., 1999; Lowrie, 1999; Shenker et al., 2003; Kelly et al., 2007; Andersson et al., 2011). These findings are believed to be mediated by neurophysiological processes and may cause altered sensory and motor function (Shenker et al., 2003; Koltzenburg et al., 1999). Bilateral sensory, proprioceptive and motor changes have been demonstrated in some studies with humans experiencing upper extremity disorders including lateral epicondylitis (Pienimäki et al., 1997; Bisset et al. 2006, 2009; Fernandez-Carnero et al., 2009; Ruiz-Ruiz et al., 2011; Coombes et al. 2012a, 2012b; Heales et al., 2013), de Quervain's tenosynovitis (Forget et al., 2008), carpal tunnel syndrome (Bagatur and Zorer, 2001; Fernandez-de-las-Penas, de la Llave-Rincon, et al. 2009a,b; de la Llave-Rincón et al., 2011) and in participants with chronic wrist and hand pain (Smeulders et al., 2002). The majority of these studies have investigated changes in the nociceptive system (changes in mechanical and thermal pain thresholds, hyperalgesia and allodynia) (Fernandez-Carnero et al., 2009; Fernandez-de-las-Penas, de la Llave-Rincon, et al. 2009; Heales et al., 2013). Fewer studies have assessed other sensory functions such as tactile acuity, proprioception (Wikstrom et al., 2010; Heales et al., 2013), and motor processes (changes in strength, reaction time, speed and fluency of movements, and range of motion) (Smeulders et al., 2002; Forget et al., 2008; Heales et al., 2013).

There is evidence of central deficits associated with chronic MSD. Altered cognitive function including selective attention deficits have been found in persons with chronic pain associated with MSD (Moriarty et al., 2011). There is also evidence of changes in sensorimotor integration. The Left Right Judgement Task (LRJT) is a complex mental task that involves determining if images of body parts are of the left or right side as quickly and accurately as possible. There is evidence of altered performance on the LRJT in persons with MSD (Breckenridge et al., 2019; Ravat et al., 2019). It is believed to be a measure of sensory and proprioceptive integration used to formulate an online representation of the body in peri-personal space which in turn is tightly coupled with motor processes (Moseley, 2012; Breckenridge et al., 2019). The LRJT is associated with extensive neural activation suggesting that several cortical processes may be associated with altered performance in the task and therefore provides information regarding both cognitive function and sensorimotor integration (Parsons et al., 1995; Decety, 1996; Kosslyn et al., 1998; Hetu et al., 2013; Tomasino and Gremese, 2015).

The purpose of the present study was to extend past research by testing a comprehensive battery of sensory and motor functions bilaterally, as well as central deficits related to sensorimotor integration and cognitive function. Secondly, to determine if the sensory, motor and central deficits are condition-specific or whether they are present in a heterogeneous sample. We hypothesized that participants with heterogeneous MSD of the wrist/hand would demonstrate decreased motor and sensory performance bilaterally as well as altered sensorimotor integration and cognitive function compared to healthy control participants. The presence of bilateral signs and symptoms as well as central changes within a heterogeneous sample provides important information in regard to the pathophysiology of these conditions with implications both clinically and in research.

2. Methods

An observational cross-sectional study was performed with participants experiencing unilateral wrist/hand pain. Participants were recruited when attending the hand clinic for consultation with plastic surgeons specializing in wrist and hand disorders at the CIUSSS du Centre-Sud-de-l'Île-de-Montréal Notre Dame Hospital between June 2017 and June 2018. Eligibility required participants in the experimental group (PAIN) to have pain associated with unilateral MSD of the wrist/hand and stated that their injury or condition impacted their

activities of daily living. Participants in the control group (CONTROL) were a sample of convenience with no history of MSD of the wrist/hand. All participants were required to be right-handed, 18 years and older, able to follow instructions and answer questionnaires in English or French, suffered from no known neurological condition impacting cognitive function, no radicular or neurological symptoms, and no MSD of the lower extremities. The protocol and procedures conformed to the Declaration of Helsinki. Ethical approval was granted by institutional review board (CER CHUM 16.372). Verbal and written informed consents were obtained prior to participation. Demographic and descriptive information including gender, age, diagnosis, symptom duration, and areas of pain were documented. Handedness was verified utilizing the Edinburgh Handedness Inventory (Oldfield, 1971).

2.1. Sensory measures

Tactile acuity was assessed with the Two-Point Orientation Discrimination (TPOD) task utilizing a hand-held caliper (Fowler, Model # 54-101-150-2, Newton, MA, USA) (Dellon et al., 1987; Catley et al., 2013). Participants were blindfolded and rested their supinated arms on their thighs. Two vertical and horizontal trials were performed in ascending and descending order with separations between 4 and 14 mm in both hands over the hypothenar and thenar eminences. When participants stated that they perceived two points of contact, they were required to state if they were oriented vertically or horizontally (Tong et al., 2013). The caliper was held at its end allowing for only the weight of the caliper head to apply pressure. The distance at which the participant consistently had $\geq 3/4$ correct responses for the thenar and hypothenar eminences were recorded (Tong et al., 2013).

Pressure Pain Threshold (PPT) was determined using a digital pressure algometry (Wagner Instruments, Greenwich, CT, USA, model# Wagner FPX25). PPT was measured bilaterally on the palmar aspect of the first carpometacarpal joint and the hypothenar eminence medial to the pisiform. The average of three trials was recorded (Nussbaum and Downes, 1998; Chiarotto, Fernandez-de-las-Peñas et al., 2013a,b). Order of site of assessment was randomized across subjects. The two PPT values were summed giving a single value for each hand.

2.2. Motor performance measures

Motor performance was assessed by grip strength utilizing a hand-held Jamar dynamometer (Sammons Preston Rolyan, Bolingbrook, IL, USA) following recommended protocols (Mathiowetz et al., 1984). Participants were asked to squeeze the handle as hard as possible and were provided with verbal encouragement. Three trials were performed on each side, alternating from side to side. The maximum value was recorded. The reliability and validity of this task has previously been documented (Mathiowetz et al., 1984).

Fine and gross motor function was assessed with the Purdue Pegboard Test (PPG) (Lafayette Instruments, Lafayette IN, USA, Model #32020A). The PPG test is a manual dexterity test with documented reliability and validity (Tiffin and Asher, 1948; Buddenberg and Davis, 2000). The PPG involves five scores per participant. Three scores are related to placing pins in holes with the right hand only, the left hand only, and with both hands during 30-s epochs. A single total score for each participant consists of the aggregate of these three measures (scores for the right hand, left hand, and both hands). For the fifth score, participants are asked to perform assemblies involving placing the pins in the holes and adding washers and collars in a 1-min epoch.

2.3. Disability and pain measures

Disability of Shoulder, Arm and Hand questionnaire (DASH) was utilized to assess both symptoms and functional status in persons with upper extremity MSD. It is a self-rated assessment with documented construct validity and reliability (Hudak et al., 1996; Gummesson et al.,

Table 1
Demographic and Descriptive information.

\	Participants with unilateral musculoskeletal disorders of the wrist and hand (PAIN) (N = 30)	Healthy participants (CONTROL) (N = 30)
Gender		
Female	16 (53%)	18 (60%)
Male	14 (47%)	12 (40%)
Average age (years) (Mean \pm SD)	58.8 \pm 15.0	56.7 \pm 12.6
Visual Analog Scale Pain (\bar{x} \pm SD) (max 10)	6.7 \pm 2.6	
Disability of Arm, Shoulder and Hand (\bar{x} \pm SD) (max 100)	47.9 \pm 19.7	

2003). Participants in the PAIN group were also asked to indicate their average pain level for the previous 48 h prior on a visual analog scale anchored at 0 indicating no pain and 10 as the worst imaginable pain (Jensen et al., 1989).

2.4. Sensory integration/mental rotation task

The LRJT consisted in determining if images of hands and feet were of the left or right side utilizing the Recognise™ (Neuro-orthopedic Institute, Adelaide, South Australia) software (Wallwork et al., 2013; Linder et al., 2016; Breckenridge et al., 2017). The LRJT involved a block of 40 images of hands and of 40 images of feet (control condition) presented on a plain (vanilla) background, with a maximum duration per image of 5 s, on an 8-inch computer tablet. Participants were instructed not to move their hands or feet to assist in determining laterality and to answer, “as quickly and accurately as possible” by depressing the left or right button on the tablet screen that matches the laterality of the image presented with their left or right index finger. Participants were given the chance to practice on 10 images before proceeding with the actual tasks. The order of the block of images of hands and feet was randomized across participants. Accuracy (percentage of correct responses) and reaction times (seconds) were recorded.

2.5. Cognitive function

Cognitive function was evaluated utilizing a modified Stroop test (Stroop, 1935) with the Encephalapp application installed on an 8-inch computer tablet (Bajaj et al., 2015). The task involved the words red, green, blue or a neutral stimulus (number signs - ###) randomly presented and written in red, green or blue colors. Participants indicated as quickly and as accurately as possible the color in which the word or neutral stimulus was presented by depressing the keys at the bottom of the screen (Red, Green, Blue). The time taken to perform 2 successful trials of 10 images without making an error was recorded. The Stroop test is considered a measure of selective attention and processing speed ability (Lamers et al., 2010). The validity, reliability and sensitivity of the Stroop test have been documented (see (Homack and Riccio, 2004)).

2.6. Statistical analysis

Statistical analysis was performed using GraphPad Prism 7 (GraphPad Software Inc., La Jolla, CA, USA) and SPSS 24 (IBM Corporation, Armonk, New York, USA) statistical software. Normality of the data was assessed by visual inspection of the data and by the D'Agostino Pearson normality test. Equality of variance was evaluated with Levene's test. Sample size was calculated for differences in group means utilizing previously published means and standard deviations for sensory and motor tests (PPT, grip strength and PPG) performed in this study. A sample size of 30 was adequate to detect a difference in means between the groups for these measures ($\beta = 0.80$, $p = 0.95$).

Several variables did not have a normal distribution and/or the equality of variance was not present between the groups violating the

assumptions for parametric tests. For these variables non-parametric Mann Whitney U tests were performed to determine if there were differences PAIN and CONTROL groups for gender, age, Stroop test time and LRJT results. Adjustments for multiple comparisons were made when necessary using the False Discovery Rate Benjamini-Hochberg procedure with an $\alpha < 0.05$ (Benjamini and Hochberg, 1995; Verhoeven et al., 2005). To determine if there was a speed accuracy trade-off between LRJT performance accuracy and reaction time, non-parametric Spearman rank correlations were determined between LRJT performance accuracy and reaction time.

For within group differences for the PPG and Grip Strength paired T-tests were performed. For the results of PPT, TPOD, PPG and grip strength Multivariate ANOVA were performed. Included in the MANOVA are univariate ANOVA results.

3. Results

3.1. Demographic and descriptive information

Demographic and descriptive information are found in Table 1. There were no differences between groups for age ($p = 0.50$, $U = 404$) or gender ($p = 0.79$, $U = 420$). Average symptom duration for participants in the PAIN group was 38.8 months (median: 34 months, range: 1–120 months). Diagnoses included amputation (3), fractures (6), tendinitis/tenosynovitis (3), first carpometacarpal osteoarthritis (10), carpal tunnel syndrome (1), sprains (3), and other (4).

3.2. Sensory measures

PPT values for the CONTROL group were comparable to previously published normative data (Torgén and Swerup, 2002). Pillai's trace in MANOVA demonstrated a significant difference between groups for the PPT. Both right hand and left hand PPT values were significantly different between groups (see Tables 2 and 3, Fig. 1).

TPOD discrimination results were similar to previously published data (Cately et al., 2013). There was no difference between groups for TPOD (Tables 2 and 3, Fig. 1). The TPOD of the right (affected) hand in the PAIN group was significantly different from the CONTROL group and the left (non-affected) hand in the PAIN group was not statistically different (Tables 2 and 3). Collectively, there were significant differences between groups for measures of sensory function which were bilateral for PPT.

3.3. Motor measures

Purdue pegboard test and grip strength values for the CONTROL group were within previously published normative values (Agnew et al., 1988; Larson and Ye, 2017). Using Pillai's trace in MANOVA there was a difference between groups for both grip strength and the PPG. For grip strength, both right hand and left-hand values were significantly different between groups (see Table 2, Fig. 1). Within group differences for grip strength were found in the PAIN group between right and left hands ($p < 0.001$, $t = 4.871$, $df = 29$) where the right (affected hand)

Table 2
Results for sensory, motor and cognitive variables.

	Participants with unilateral musculoskeletal disorders of the wrist and hand (PAIN) Mean (standard deviation)	Healthy (CONTROL) participants Mean (standard deviation)
Two Point Orientation Discrimination (mm)		
Right	23,7 (4,2)	20,8 (4,8)
Left	23,0 (4,9)	20,8 (4,7)
Pressure Pain Threshold (kg)		
Right ^a	6,2 (4,0)	11,3 (4,4)
Left	7,6 (4,6)	11,8 (5,1)
Purdue Pegboard Test		
Right ^a	11,4 (3,7)	14,2 (2,6)
Left	12,6 (2,3)	14,0 (2,1)
Both	9,2 (3,7)	11,5 (1,9)
Total	32,8 (9,6)	39,7 (5,9)
Assemblies	19,7 (8,1)	24,1 (5,9)
Grip Strength - maximum (kg)		
Right ^a	20,8 (11,1)	40,8 (12,9)
Left	30,2 (14,7)	37,9 (11,5)
Laterality Recognition Task		
Accuracy (%)		
Right Hand ^a	75,5 (12,61)	79,5 (15,4)
Left Hand	72,7 (18,27)	76 (12,5)
Right Foot	82,0 (17,39)	85,3 (15,4)
Left Foot	81,5 (18,62)	83,5 (18,3)
Reaction Time (seconds)		
Right Hand ^a	2,3 (0,74)	1,98 (0,5)
Left Hand	2,1 (0,46)	1,98 (0,5)
Right Foot	1,9 (0,52)	1,7 (0,5)
Left Foot	1,9 (0,53)	1,7 (0,5)
Stroop test (sec)	40,2 (8,0)	36,3 (11,7)

^a affected hand in the pain group.

Table 3
Multivariate Analysis of Variance results for sensory and motor variables between groups. TPOD: Two Point Orientation Discrimination; PPT: Pressure Pain Threshold.

Sensory	MANOVA		Univariate		
	F values	P value		F values	P value
TPOD	F _{2,57} = 3.02	0.057	Right Hand	F _{1,58} = 6.05	0.017
			Left Hand	F _{1,58} = 3.36	0.072
PPT	F _{2,57} = 57.00	0.000	Right Hand	F _{1,58} = 21.88	0.000
			Left Hand	F _{1,58} = 11.35	0.001
Motor					
Purdue Pegboard	F _{5,54} = 2.67	0.032	Right Hand	F _{1,58} = 11.76	0.001
			Left Hand	F _{1,58} = 5.79	0.023
			Both	F _{1,58} = 9.52	0.003
			Total	F _{1,58} = 11.49	0.001
			Assemblies	F _{1,58} = 5.77	0.020
Grip Strength	F _{2,57} = 33.30	0.000	Right Hand	F _{1,58} = 41.39	0.000
			Left Hand	F _{1,58} = 5.15	0.027

was weaker (see Table 2). A within group difference was also found in the CONTROL group ($p < 0.001$, $t = 4.90$, $df = 29$) for grip strength where the right hand was found to be stronger (see Table 2). For the PPG values, all measures were significantly different between groups (Table 3, Fig. 1). Within group differences were found in the PAIN group between right and left hands ($p = 0.031$, $t = 2.27$, $df = 29$) but not the CONTROL group ($p = 0.519$, $t = 0.65$, $df = 29$) in the PPG test.

Therefore, participants in the PAIN group had decreased performance on all the measures of motor function in both hands compared to the CONTROL group. There was a difference in PPG performance between hands in the PAIN group only and in grip strength between right and left hands where the PAIN group was weaker in their right (affected) hand whereas the right hand was stronger in the CONTROL group.

3.4. Sensory integration

There were no differences in the LRJT performance between groups

for both accuracy and reaction time for the hands ($p = 0.11$ – 0.58) or the feet ($p = 0.11$ – 0.55), with a trend for the reaction time in both hands to be greater in the PAIN group compared to the CONTROL group ($p = 0.03$) (Fig. 2). Spearman correlations in the CONTROL group for the right ($r_s = -0.17$) and left hands ($r_s = -0.35$) between reaction time and accuracy were negative, indicating that better performance accuracy was associated with a decreased reaction time in this group. These correlations were positive in the right ($r_s = 0.19$) and left ($r_s = 0.23$) hands in participants with unilateral MSD in the PAIN group, suggesting that improved accuracy was associated with increased reaction time.

3.5. Cognitive function

There is a significant difference ($p = 0.032$, $U = 282$) between the PAIN ($\bar{x} = 40.2 \pm 8.0$ s, Median = 39.8 s) and CONTROL groups ($\bar{x} = 36.3 \pm 1.7$ s, Median = 34.7 s) for the Stroop test time (Table 2, Fig. 1).

4. Discussion

The purpose of this experiment was to determine if participants with unilateral heterogeneous MSD of the wrist/hand pain had bilateral sensory and motor deficits as well as changes in cognitive function compared to healthy control participants. As was hypothesized, participants with unilateral wrist/hand pain had poorer cognitive function and demonstrated bilateral altered sensory and motor function compared to healthy participants. The importance of these findings are the suggestion that peripheral and centrally mediated mechanisms are involved in the pathogenesis of MSD of the wrist/hand that are not injury/condition specific (Barr et al., 2004; Andersson et al., 2011).

4.1. Bilateral changes in sensorimotor function

Sensory and motor disturbances are characteristic of MSD and are the focus of research and rehabilitation efforts of the affected side. There has been less investigation into the changes in sensory and motor

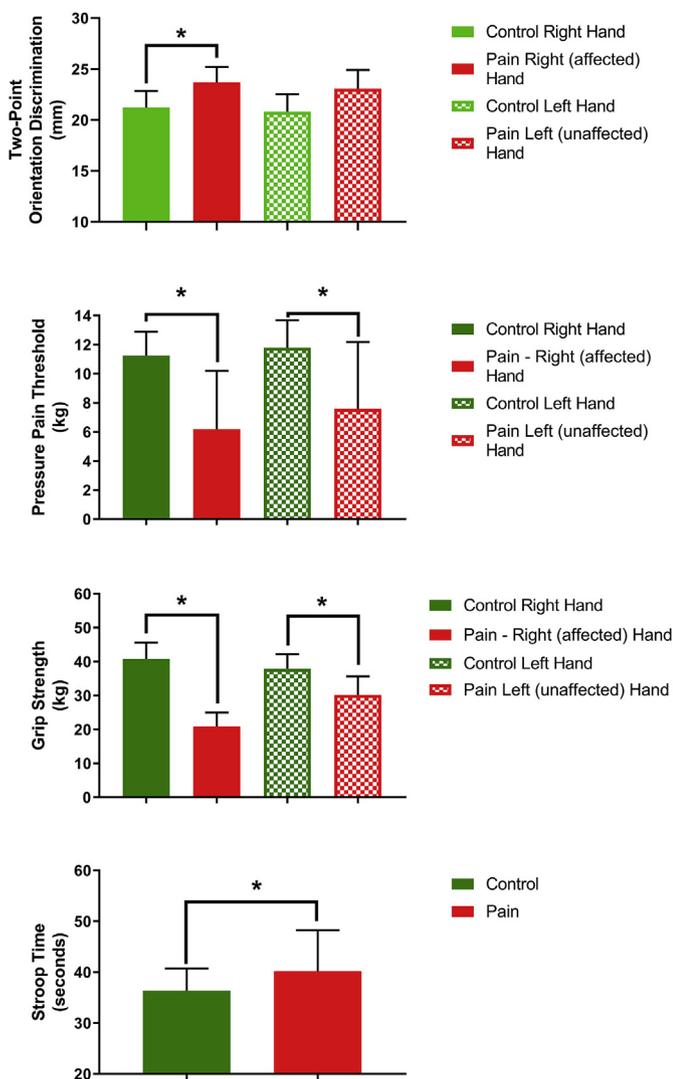


Fig. 1. Comparisons of sensory, motor and cognitive variables. Mean ± 95% Confidence Intervals. * denotes p < 0.05.

function of the unaffected limb associated with unilateral MSD. There is a body of literature that demonstrates contralateral functional and structural changes in response to unilateral insult in animal models (Koltzenburg et al., 1999; Shenker et al., 2003). Animal models of unilateral overuse tendon injuries result in inflammatory and morphological responses in the contralateral homonymous structures (Barbe et al., 2003; Andersson et al., 2011). Levels of macrophages and cytokines are elevated in the contralateral homonymous tendon in a rat model of repetitive reach and grasp overuse tendon injury (Barbe et al., 2003). Bilateral pathological changes including hypervascularization and increased tenocytes in the Achilles tendon have been found in unilateral exercise induced overuse injury in a rabbit model (Andersson et al., 2011). These contralateral effects are believed to be mediated by neurological mechanisms via spinal cord interneurons and influence the presence of pro-inflammatory neuropeptides such as substance P and calcitonin gene-related peptide in the contralateral homonymous structures (Shenker et al., 2003). The presence of these bilateral structural and histochemical changes may be responsible for the bilateral changes in sensory and motor function found within the present study.

Bilateral sensory (PPT) and motor deficits (grip strength and PPG) were found bilaterally in the PAIN group. Sensory changes have been previously demonstrated in the contralateral limb in studies with human participants with MSD of the upper extremity. Bilateral sensory

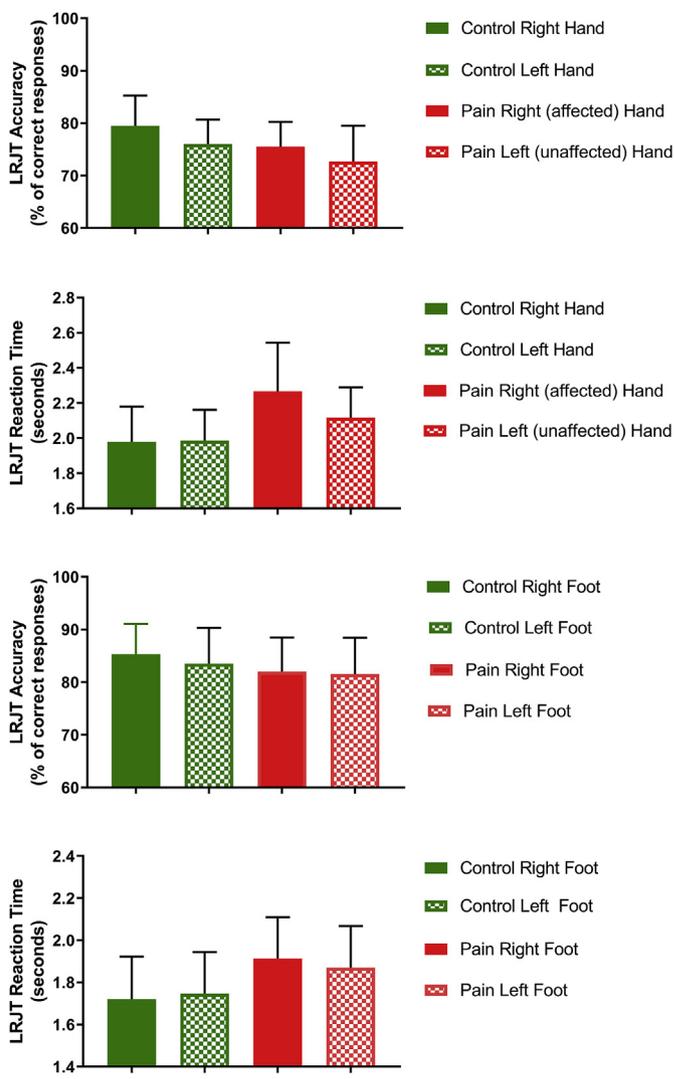


Fig. 2. Left Right Judgement Task results. Mean ± 95% Confidence Intervals. LRJT: Left, Right Judgement Task.

findings in participants with MSD include bilateral decreased PPT (Fernandez-de-Las-Penas, Perez-de-Heredia-Torres et al., 2009a,b; de la Llave-Rincón et al., 2009; Heales et al., 2013) and widespread hyperalgesia (Chiarotto, Fernandez-de-las-Peñas et al., 2013a,b) suggestive of central sensitization. Motor deficits have previously been found contralaterally with unilateral MSD of the upper extremity. These bilateral motor deficits include increased reaction time and slower speed of movement (Heales et al., 2013), bilateral differences in grip and pinch strength (Fernandez-de-Las-Penas, Perez-de-Heredia-Torres et al., 2009a,b; Heales et al., 2013), isometric strength (Forget et al., 2008), PPG results (Fernandez-de-Las-Penas, Perez-de-Heredia-Torres et al., 2009a,b) and movement fluency (Smeulders et al., 2002). The present results further suggest that these sensorimotor changes occur in persons with heterogeneous MSD of the wrist/hand.

Although the mechanisms responsible for the decrease in motor function on the unaffected side are poorly understood they may be the result of the structural and functional (i.e. presence of pro-inflammatory mediators) changes in contralateral homologous structures in the unaffected limb in animal models described above (Shenker et al., 2003). Another possibility for the presence of bilateral findings associated with unilateral MSD stem from supraspinal processes. Areas of sensory and proprioceptive integration occur within the secondary somatosensory cortex and the posterior parietal areas. In primates the neurons in these areas often demonstrate bilateral receptor fields

(Iwamura et al., 1994; Dijkerman and de Haan, 2007; Makin et al., 2008) and have reciprocal connections with premotor areas (Kalaska, 1996). Representational changes have been found in the primary somatosensory cortex (Flor et al., 1997; Dhond et al., 2012; Di Pietro et al., 2013) and sensory integrative areas in persons with MSD and may therefore be associated with bilateral perceptual and motor changes (Hotz-Boendermaker et al., 2016). Collectively the findings of bilateral sensorimotor changes in function suggest centrally mediated changes associated with unilateral MSD.

4.2. Left/Right Judgement Task

The lack of difference between groups in LRJT performance was a surprising finding given that the LRJT is believed to be a measure of sensory and proprioceptive integration (Moseley, 2012; Breckenridge et al., 2019) and has been associated with sensory (Stanton et al., 2013) and motor performance (Pelletier et al., 2018a,b). Although a recent meta-analysis of the LRJT in persons with chronic pain associated with MSD found that persons with upper extremity MSD demonstrate increased reaction times and decreased accuracy compared to healthy controls, there was significant heterogeneity in study results (Breckenridge et al., 2019). The absence of a significant difference in LRJT performance may have been affected in the PAIN group by slowing the response time to improve accuracy as evidenced by the difference in correlation between accuracy and response times between groups. The differences in results between studies are often attributed to differences in methodology, pain mechanisms, and study populations (Linder et al., 2016) and possible differences in concentration and motor imagery ability which are often not measured (Reinersmann et al., 2010; Pelletier et al., 2018a,b). The extensive neural activation in cortical areas involved in perception and sensory integration, sensory motor transformations, movement planning and execution, and cortical areas involved in short-term working memory associated with the LRJT may all contribute to altered performance (Parsons et al., 1995; Decety, 1996; Kosslyn et al., 1998; Hetu et al., 2013; Tomasino and Gremese, 2015). No difference in LRJT performance between groups may have been the result of the heterogeneous injuries/conditions of those in the PAIN group, although previous research has documented LRJT difference in a heterogeneous population (Pelletier et al., 2018a,b). Alternatively, the difference in correlations of reaction time with accuracy between the PAIN and CONTROL groups suggest that participants in the PAIN group may have decreased their speed in an attempt to improve accuracy.

4.3. Changes in cognitive function

The participants with unilateral MSD of the wrist/hand had decreased cognitive function as assessed with Stroop test. Several studies have previously demonstrated that participants with chronic pain demonstrate decreased cognitive function with a battery of tests including the Stroop test (Moriarty et al., 2011). These studies include participants with low back pain, arthritis and peripheral neuropathies (Moriarty et al., 2011) but to our knowledge has not been demonstrated in persons with MSD of the upper extremity. The Stroop test, a test to measure selective attention, involves activation of the medial and anterior frontal structures including the anterior cingulate cortex, dorsolateral prefrontal cortex, insula and the posterior parietal cortices (Bench et al., 1993; Leung et al., 2000). The Stroop test therefore activates areas involved in working memory, executive function, decision-making and error monitoring (Milham et al., 2003). It remains unclear if changes in cognitive function in persons with pain are related to the changes in structure and function in forebrain areas and/or the mobilization of attentional resources directly attributed to the pain experience (Moriarty et al., 2011).

4.4. Limitations

There are several limitations that should be noted when interpreting the results from the study. Participants in the PAIN group were recruited from a single setting. The TPOD requires further study for reliability and therefore should be interpreted with caution. TPOD measurements were not made directly on the area of injury. The TPOD results were close to statistical significance and may be influenced by the fact that they were not made directly over the site of injury/pain. Participants were experiencing pain unilaterally, but some may have had subclinical bilateral changes as subjects with osteoarthritis of the thumb often demonstrate bilateral changes on x-rays. Finally, assessors were not blinded to group allocation.

5. Conclusion

Bilateral sensorimotor changes and cognitive deficits associated with unilateral disorders suggest that there are central and/or systemic changes involved in the pathophysiology associated with unilateral MSD of the wrist/hand. These results have important clinical and research implications. Clinically, the generalized use as the unaffected side for comparison during assessment by physicians and rehabilitation specialists should be utilized with caution. Comparisons made to an unaffected limb may falsely mitigate the importance of the sensory and motor deficits present in the affected area. Secondly, it may be necessary to target the unaffected limb as well as the affected limb when performing rehabilitation exercises. Literature demonstrates that for several unilateral MSD there is an increased risk of contralateral injury (Bagatur and Zorer, 2001; Årøen et al., 2004; Swärd et al., 2010; Ewald, 2011). In regard to research it is imperative that sensory, proprioceptive and motor function be compared to a healthy control group. The presence of cognitive deficits associated with MSD also suggests that tasks requiring attentional resources may demonstrate deficits not because of altered motor and/or sensory processes alone and should be considered in the interpretation of test results both clinically and in research. Further elucidation of these central and systemic changes should help to develop more effective treatment interventions.

Conflict of interests

None.

Ethical approval

Ethical approval was granted from the institutional review board (CÉR-CHUM 16.372) - Centre Hospitalier de l'Université de Montréal, Notre Dame hospital.

References

- Agnew, J., Bolla-Wilson, K., Kawas, C.H., Bleecker, M.L., 1988. Purdue pegboard age and sex norms for people 40 years old and older. *Dev. Neuropsychol.* 4, 29–35.
- Andersson, G., Forsgren, S., Scott, A., Gaida, J.E., Stjernfeldt, J.E., Lorentzon, R., Alfredson, H., Backman, C., Danielson, P., 2011. Tenocyte hypercellularity and vascular proliferation in a rabbit model of tendinopathy: contralateral effects suggest the involvement of central neuronal mechanisms. *Br. J. Sports Med.* 45, 399–406.
- Årøen, A., Helgø, D., Granlund, O.G., Bahr, R., 2004. Contralateral tendon rupture risk is increased in individuals with a previous Achilles tendon rupture. *Scand. J. Med. Sci. Sport.* 14, 30–33.
- Bagatur, A.E., Zorer, G., 2001. The carpal tunnel syndrome is a bilateral disorder. *J. Bone Jt. Surg.* 83-B, 655–658.
- Bajaj, J.S., Heuman, D.M., Sterling, R.K., Sanyal, A.J., Siddiqui, M., Matherly, S., Luketic, V., Stravitz, R.T., Fuchs, M., Thacker, L.R., Gilles, H., White, M.B., Unser, A., Hovermale, J., Gavis, E., Noble, N.A., Wade, J.B., 2015. Validation of EncephalApp, smartphone-based stroop test, for the diagnosis of covert hepatic encephalopathy. *Clin. Gastroenterol. Hepatol.* 13, 1828–18235 e1.
- Barbe, M.F., Barr, A.E., Gorzelany, I., Amin, M., Gaughan, J.P., Safadi, F.F., 2003. Chronic repetitive reaching and grasping results in decreased motor performance and widespread tissue responses in a rat model of MSD. *J. Orthop. Res.* 21, 167–176.
- Barr, A.E., Barbe, M.F., Clark, B.D., 2004. Systemic inflammatory mediators contribute to

- widespread effects in work-related musculoskeletal disorders. *Exerc. Sport Sci. Rev.* 32, 135–142.
- Bench, C.I.J., Frith, C.D., Grasby, P.M., Friston, K.J., Paulesu, E., Frackowiak, R.S.J., Dolan, R.J., 1993. Investigations of the functional anatomy of attention using the Stroop test. *Neuropsychologia* 31, 907–922.
- Benjamini, Y., Hochberg, Y., 1995. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J. R. Stat. Soc. Ser. B* 289–300.
- Bisset, L.M., Coppieters, M.W., Vicenzino, B., 2009. Sensorimotor deficits remain despite resolution of symptoms using conservative treatment in patients with tennis elbow: a randomized controlled trial. *Arch. Phys. Med. Rehabil.* 90, 1–8.
- Bisset, L.M., Russel, T., Bradley, S., Ha, B., Vincenzino, B.T., 2006. Bilateral sensorimotor abnormalities in unilateral epicondylagia. *Arch. Phys. Med. Rehabil.* 87, 490–495.
- Breckenridge, J.D., Ginn, K.A., Wallwork, S.B., McAuley, J.H., 2019. Do people with chronic musculoskeletal pain have impaired motor imagery? A meta-analytical systematic review of the left/right judgement task. *J. Pain* 20 (2), 119–132.
- Breckenridge, J.D., McAuley, J.H., Butler, D.S., Stewart, H., Moseley, G.L., Ginn, K.A., 2017. The development of a shoulder specific left/right judgement task: validity & reliability. *Musculoskelet Sci Pract* 28, 39–45.
- Buddenberg, L.A., Davis, C., 2000. Test Re-test reliability of the Purdue pegboard test'. *Am J Occupational Ther* 54, 555–558.
- Catley, M.J., Tabor, A., Wand, B.M., Moseley, G.L., 2013. Assessing tactile acuity in rheumatology and musculoskeletal medicine—how reliable are two-point discrimination tests at the neck, hand, back and foot? *Rheumatology* 52, 1454–1461.
- Chiarotto, A., Fernandez-de-Las-Penas, C., Castaldo, M., Negrini, S., Villafane, J.H., 2013a. Widespread pressure pain hypersensitivity in elderly subjects with unilateral thumb carpometacarpal osteoarthritis. *Hand* 8, 422–429.
- Chiarotto, A., Fernandez-de-las-Peñas, C., Castaldo, M., Villafañe, J.H., 2013b. Bilateral pressure pain hypersensitivity over the hand as potential sign of sensitization mechanisms in individuals with thumb carpometacarpal osteoarthritis. *Pain Med.* 14, 1585–1592.
- Coombes, B.K., Bisset, L., Vicenzino, B., 2012a. Elbow flexor and extensor muscle weakness in lateral epicondylagia. *Br. J. Sports Med.* 46, 449–453.
- Coombes, B.K., Bisset, L., Vicenzino, B., 2012b. Thermal hyperalgesia distinguishes those with severe pain and disability in unilateral lateral epicondylagia. *Clin. J. Pain* 28, 595–601.
- de la Llave-Rincón, A.I., Fernández-de-las-Peñas, C., Fernández-Carnero, J., Padua, L., Arendt-Nielsen, L., Pareja, J.A., 2009. Bilateral hand/wrist heat and cold hyperalgesia, but not hypoesthesia, in unilateral carpal tunnel syndrome. *Exp. Brain Res.* 198, 455–463.
- de la Llave-Rincón, A.I., et al., 2011. Bilateral deficits in fine motor control and pinch grip force are not associated with electrodiagnostic findings in women with carpal tunnel syndrome. *Am. J. Phys. Med. Rehabil.* 90, 443–451.
- Decety, J., 1996. The neurophysiological basis of motor imagery. *Behav. Brain Res.* 77, 45–52.
- Dellon, A.L., Mackinnon, S.E., Crosby, P.M., 1987. Reliability of two-point discrimination measurements. *J. Hand Surg Am* 12, 693–696.
- Dhond, Rupali P., Ruzich, Emily, Witzel, Thomas, Maeda, Yumi, Malatesta, Cristina, Morse, Leslie R., Joseph, Audette, Hämäläinen, Matti, Kettner, Norman, Napadow, Vitaly, 2012. Spatio-temporal mapping cortical neuroplasticity in carpal tunnel syndrome. *Brain* 135, 3062–3073.
- Di Pietro, F., McAuley, J.H., Parkitny, L., Lotze, M., Wand, B.M., Moseley, G.L., Stanton, T.R., 2013. Primary somatosensory cortex function in complex regional pain syndrome: a systematic review and meta-analysis. *J. Pain* 14, 1001–1018.
- Dijkerman, H.C., de Haan, E.H., 2007. Somatosensory processes subserving perception and action. *Behav. Brain Sci.* 30, 189–201 discussion 01–39.
- Ewald, A., 2011. Adhesive capsulitis: a review. *Am. Fam. Physician* 83, 417–422.
- Fernandez-Carnero, J., Fernandez-de-Las-Penas, C., de la Llave-Rincon, A.I., Ge, H.Y., Arendt-Nielsen, L., 2009. Widespread mechanical pain hypersensitivity as sign of central sensitization in unilateral epicondylagia: a blinded, controlled study. *Clin. J. Pain* 25, 555–561.
- Fernandez-de-las-Penas, C., de la Llave-Rincon, A.I., Fernandez-Carnero, J., Cuadrado, M.L., Arendt-Nielsen, L., Pareja, J.A., 2009a. Bilateral widespread mechanical pain sensitivity in carpal tunnel syndrome: evidence of central processing in unilateral neuropathy. *Brain* 132, 1472–1479.
- Fernandez-de-las-Penas, C., Perez-de-Heredia-Torres, M., Martinez-Piedrola, R., de la Llave-Rincon, A.I., Cleland, J.A., 2009b. Bilateral deficits in fine motor control and pinch grip force in patients with unilateral carpal tunnel syndrome. *Exp. Brain Res.* 194, 29–37.
- Flor, H., Braun, C., Elbert, T., Birbaumer, N., 1997. Extensive reorganization of primary somatosensory cortex in chronic back pain patients. *Neurosci. Lett.* 224, 5–8.
- Forget, N., Pottie, F., Arsenault, J., Harris, P., Bourbonnais, D., 2008. Bilateral thumb's active range of motion and strength in de Quervain's disease: comparison with a normal sample. *J. Hand Ther.* 21, 276–284 quiz 85.
- Gummeson, C., Atroshi, I., Ekdahl, C., 2003. The disabilities of the arm, shoulder and hand (DASH) outcome questionnaire: longitudinal construct validity and measuring self-rated health change after surgery. *BMC Musculoskelet. Disord.* 4, 11.
- Heales, L.J., Lim, E.C.W., Hodges, P.W., Vicenzino, B., 2013. Sensory and motor deficits exist on the non-injured side of patients with unilateral tendon pain and disability—implications for central nervous system involvement: a systematic review with meta-analysis. *Br. J. Sports Med.* 48, 1400–1406.
- Hetu, S., Gregoire, M., Saimpont, A., Coll, M.P., Eugene, F., Michon, P.E., Jackson, P.L., 2013. The neural network of motor imagery: an ALE meta-analysis. *Neurosci. Biobehav. Rev.* 37, 930–949.
- Homack, S., Riccio, C.A., 2004. A meta-analysis of the sensitivity and specificity of the Stroop Color and Word Test with children. *Arch. Clin. Neuropsychol.* 19, 725–743.
- Hotz-Boendermaker, S., Marcar, V.L., Meier, M.L., Boendermaker, B., Humphreys, B.K., 2016. Reorganization in secondary somatosensory cortex in chronic low back pain patients. *Spine* 41, E667–E673.
- Hudak, P.L., Amadio, P.C., Bombardier, C., 1996. Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder and hand) [corrected]. The Upper Extremity Collaborative Group (UECG). *Am. J. Ind. Med.* 29, 602–608.
- Iwamura, Y., Iriki, A., Tanaka, M., 1994. Bilateral hand representation in the postcentral somatosensory cortex. *Nature* 369, 554–556.
- Jensen, M., Karoly, P., Braver, S., 1989. The measurement of clinical pain intensity: a comparison of six methods. *Pain* 5, 153–159.
- Kalaska, J.F., 1996. Parietal cortex area 5 and visuomotor behavior. *Can. J. Physiol. Pharmacol.* 74, 483–498.
- Kelly, S., Dunham, J.P., Donaldson, L.F., 2007. Sensory nerves have altered function contralateral to a monoarthritis and may contribute to the symmetrical spread of inflammation. *Eur. J. Neurosci.* 26, 935–942.
- Koltzenburg, M., Wall, P.D., McMahon, S.B., 1999. Does the right side know what the left is doing? *Trends Neurosci.* 22, 122–127.
- Kosslyn, S.M., DiGirolamo, G.J., Thompson, W.L., Alpert, N.M., 1998. Mental rotation of objects versus hands: neural mechanisms revealed by positron emission tomography. *Psychophysiology* 35, 151–161.
- Lamers, M.J., Roelofs, A., Rabeling-Keus, I.M., 2010. Selective attention and response set in the Stroop task. *Mem. Cogn.* 38, 893–904.
- Larson, C.C., Ye, Z., 2017. Development of an updated normative data table for hand grip and pinch strength: a pilot study. *Comput. Biol. Med.* 86, 40–46.
- Leung, H.C., Skudlarski, P., Gatenby, J.C., Peterson, B.S., Gore, J.C., 2000. An event-related functional MRI study of the stroop color word interference task. *Cerebr. Cortex* 10, 552–560.
- Linder, M., Michaelson, P., Roijezon, U., 2016. Laterality judgments in people with low back pain—A cross-sectional observational and test-retest reliability study. *Man. Ther.* 21, 128–133.
- Lowrie, M.B., 1999. Contralateral effects of peripheral nerve injury. *TINS (Trends Neurosci.)* 22, 496–497.
- Makin, T.R., Holmes, N.P., Ehrsson, H.H., 2008. On the other hand: dummy hands and peripersonal space. *Behav. Brain Res.* 191, 1–10.
- Mathiowetz, V., Weber, K., Volland, G., Kashman, N., 1984. Reliability and validity of grip and pinch strength evaluations. *Journal of Hand Surgery-American* 9a, 222–226.
- Milham, M.P., Banich, M.T., Claus, E.D., Cohen, N.J., 2003. Practice-related effects demonstrate complementary roles of anterior cingulate and prefrontal cortices in attentional control. *Neuroimage* 18, 483–493.
- Moriarty, O., McGuire, B.E., Finn, D.P., 2011. The effect of pain on cognitive function: a review of clinical and preclinical research. *Prog. Neurobiol.* 93, 385–404.
- Moseley, G.L., 2012. The Graded Motor Imagery Handbook. Noigroup publications.
- Nussbaum, E.L., Downes, L., 1998. Reliability of clinical pressure-pain algometric measurements obtained on consecutive days. *Phys. Ther.* 78, 160–169.
- Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9, 97–113.
- Parsons, L.M., Fox, P.T., Downs, J.H., Glass, T., Hirsch, T.B., Martin, C.C., Jerabek, P.A., Lancaster, J.L., 1995. Use of implicit motor imagery for visual shape discrimination as revealed by PET. *Nature* 375, 54–58.
- Pelletier, R., Bourbonnais, D., Higgins, J., Mireault, M., Danino, M.A., Harris, P.G., 2018a. Left Right Judgement Task and Sensory, Motor, and Cognitive Assessment in Participants with Wrist/Hand Pain. *Rehabilitation Research and Practice* 2018.
- Pelletier, R., Higgins, J., Bourbonnais, D., 2018b. Laterality recognition of images, motor performance, and aspects related to pain in participants with and without wrist/hand disorders: an observational cross-sectional study. *Musculoskelet. Sci. Pract.* 35, 18–24.
- Pienimäki, T.T., Kauranen, K., Vanharanta, H., 1997. Bilaterally decreased motor performance of arms in patients with chronic tennis elbow. *Arch. Phys. Med. Rehabil.* 78, 1092–1095.
- Ravat, S., Olivier, B., Gillion, N., Lewis, F., 2019. Laterality judgment performance between people with chronic pain and pain-free individuals. A systematic review and meta-analysis. *Physiother. Theory Pract.* 1–21.
- Reinersmann, A., Haarmeyer, G.S., Blankenburg, M., Frettlöh, J., Krumova, E.K., Ockelburg, S., Maier, C., 2010. Left is where the L is right. Significantly delayed reaction time in limb laterality recognition in both CRPS and phantom limb pain patients. *Neurosci. Lett.* 486, 240–245.
- Ruiz-Ruiz, B., Fernandez-de-Las-Penas, C., Ortega-Santiago, R., Arendt-Nielsen, L., Madeleine, P., 2011. Topographical pressure and thermal pain sensitivity mapping in patients with unilateral lateral epicondylagia. *J. Pain* 12, 1040–1048.
- Shenker, N., Haigh, R., Roberts, E., Mapp, P., Harris, N., Blake, D., 2003. A review of contralateral responses to a unilateral inflammatory lesion. *Rheumatology* 42, 1279–1286.
- Smeulders, M.J., Kreulen, M., Hage, J.J., Ritt, M.J., Mulder, T., 2002. Motor control impairment of the contralateral wrist in patients with unilateral chronic wrist pain. *Am. J. Phys. Med. Rehabil.* 81, 177–181.
- Stanton, T.R., Lin, C.W.C., Bray, H., Smeets, R.J.E.M., Taylor, D., Law, R.Y.W., Moseley, G.L., 2013. Tactile acuity is disrupted in osteoarthritis but is unrelated to disruptions in motor imagery performance. *Rheumatology* 52, 1509–1519.
- Stroop, J. Ridley, 1935. Studies of interference in serial verbal reactions. *J. Exp. Psychol.* 18, 643.
- Swärd, P., Kostogiannis, I., Roos, H., 2010. Risk factors for a contralateral anterior cruciate ligament injury. *Knee Surg. Sport. Traumatol. Arthrosc.* 18, 277–291.
- Tiffin, J., Asher, E.J., 1948. The Purdue pegboard; norms and studies of reliability and validity. *J. Appl. Psychol.* 32, 234–247.
- Tomasino, B., Gremese, M., 2015. Effects of stimulus type and strategy on mental rotation network: an activation likelihood estimation meta-analysis. *Front. Hum. Neurosci.* 9, 693.

- Tong, J., Mao, O., Goldreich, D., 2013. Two-point orientation discrimination versus the traditional two-point test for tactile spatial acuity assessment'. *Front. Hum. Neurosci.* 7.
- Torgén, M., Swerup, C., 2002. Individual factors and physical work load in relation to sensory thresholds in a middle-aged general population sample. *Eur. J. Appl. Physiol.* 86, 418–427.
- Verhoeven, K.J.F., Simonsen, K.L., McIntyre, L.M., 2005. Implementing false discovery rate control: increasing your power. *Oikos* 108, 643–647.
- Wallwork, S.B., Butler, D.S., Fulton, I., Stewart, H., Darmawan, I., Moseley, G.L., 2013. Left/right neck rotation judgments are affected by age, gender, handedness and image rotation. *Man. Ther.* 18, 225–230.
- Wikstrom, E.A., Naik, S., Lodha, N., Cauraugh, J.H., 2010. Bilateral balance impairments after lateral ankle trauma: a systematic review and meta-analysis. *Gait Posture* 31, 407–414.