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EXPERIMENTAL KNEE-RELATED PAIN ENHANCES ATTENTIONAL INTERFERENCE ON POSTURAL CONTROL

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Abstract

Purpose: To quantify how postural stability is modified during experimental pain while performing different cognitively demanding tasks.

Methods: Sixteen healthy young adults participated in the experiment. Pain was induced by intramuscular injection of hypertonic saline solution (1mL, 6%) in both vastus medialis and vastus lateralis muscles (0.9% isotonic saline was used as control). The participants stood barefoot in tandem position for one minute on a force plate. Center of pressure (CoP) was recorded before and immediately after injections, while performing two cognitive tasks: (i) counting forwards by adding one; (ii) counting backwards by subtracting three. CoP variables – total area of displacement, velocity in anterior-posterior (AP-velocity) and medial-lateral (ML-velocity) directions, and CoP sample entropy in anterior-posterior and medial-lateral directions were displayed as the difference between the values obtained after and before each injection and compared between tasks and injections.

Results: CoP total area (-84.5 ± 145.5 vs. 28.9 ± 78.5 cm²) and ML-velocity (-1.71 ± 2.61 vs. 0.98 ± 1.93 cm/s) decreased after the painful injection vs. Control injection while counting forward ($P < 0.05$). CoP total area (112.8 ± 53.9 vs. -84.5 ± 145.5 cm²), ML-velocity (-0.34 ± 1.92 vs. -1.71 ± 2.61 cm/s) and AP-velocity (1.07 ± 2.35 vs. -0.39 ± 1.82 cm/s) increased while counting backwards vs. forwards after the painful injection ($P < 0.05$).

Conclusion: Pain interfered with postural stability according to the type of cognitive task performed, suggesting that pain may occupy cognitive resources, potentially resulting in poorer balance performance.

Keywords: postural stability, center of pressure, attention, distraction, pain

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List of abbreviations

ANOVA	Analysis of variance
au	Arbitrary units
CoP	Center of pressure
SaEn	Sample entropy
SD	Standard deviation
VAS	Visual analogue scale
VM	Vastus medialis
VL	Vastus lateralis

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1. Introduction

Controlling of upright posture requires a significant amount of attention to ~~constantly~~ gather information from the body and the environment and to generate adapted and accurate muscle activation for postural control (Morasso and Sanguineti 2002). Although the majority of postural control is regulated via automatic neural processes (Bronstein and Buckwell 1997), higher cortical centers are significantly involved in processing sensory information to plan and execute the best motor strategy for postural control (Winter 1995). In daily life, postural control is challenging as several tasks simultaneously compete for the cognitive resources available (Woollacott and Shumway-Cook 2002), limited by the capacity of higher centers to process sensory information (Kahneman 1973). Therefore, sharing attentional resources may cause impairments in the performance of daily living activities (Brauer et al. 2004). ~~Evidence suggests that~~ ~~For example,~~ competition for cognitive resources during tasks involving postural stability results in body stability being prioritized over secondary tasks (Liston et al. 2014).

Dual tasks paradigms, where subjects perform an additional task during ~~quiet~~ standing, are employed to quantify the extent to which attention is associated with postural control. Decreases in postural sway while performing a secondary task compared with control conditions have been reported (Andersson et al. 2002; Pellecchia 2003) whereby focusing the attention on standing as still as possible increased postural sway compared with conditions without similar instructions (Vuillerme and Nafati 2007). Altogether, these results suggest that postural control demands attention (Woollacott and Shumway-Cook 2002) and that simultaneous cognitive loading plays an important role in balance stability (Swan et al. 2007).

Although detrimental effects of cognitive loading on postural sway during unperturbed standing are more commonly reported for older adults and patients, studies using dual-task approaches in young ~~and~~ ~~control~~ subjects show controversial results (Huxhold et al. 2006; Fraizer and Mitra 2008). Young healthy subjects have probably more ability to allocate the attentional resources ~~during upright standing~~ without

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87 8 sacrificing postural stability, showing that a system without impairments prioritizes postural stability when
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88 10 dealing with dual-cognitive tasks (Siu and Woollacott 2007).

89 11 ~~Evidence suggests that S~~ subjects with pain demonstrate increased postural sway compared with
90 12 controls (Hirata et al. 2011). ~~Among several A potential possible~~ explanations for this finding, ~~one hypothesis~~
91 13 ~~is~~ that the increased postural sway may relate to a disrupting effect of nociceptive stimuli on attention to
92 14
93 15 other simultaneous non-nociceptive tasks (Eccleston et al. 1999), ~~underlining that processing of nociceptive~~
94 16
95 17 stimuli is cognitively demanding (Veldhuijzen et al. 2006). Thus, the execution of cognitive tasks during pain
96 18
97 19 might interfere with postural control. Although previous studies have shown that patients with pain present
98 20
99 21 impaired balance while performing a secondary cognitive task in comparison to health subjects (Van Daele
100 22
101 23 et al. 2010; Larivière et al. 2013; Mazaheri et al. 2014; Sherafat et al. 2014; Etemadi et al. 2016; Levinger et
102 24
103 25 al. 2016), it is not clear yet the isolate effect of pain ~~in these conditions and comparisons, since in clinical~~
104 26
105 27 ~~pain populations, besides pain, other factors like~~ reduced muscle strength, reduced flexibility and
106 28
107 29 degenerative changes at the affected segment also cause both stiffness and instability ~~in patients suffering~~
108 30
109 31 ~~from chronic pain~~ (Knoop et al. 2012). Therefore, further investigation of the interaction between pain,
110 32
111 33 cognition and postural stability is warranted. This investigation is of particular interest for clinical practice
112 34
113 35 since there are evidences that attention can be directed away from pain using some specific strategies (Van
114 36
115 37 Ryckeghem et al. 2018). If selective attention could be directed away from the painful stimulus and modify
116 38
117 39 the deleterious effect of muscle pain on postural control, these results could have important implications
118 40
119 41 for clinical settings. Likewise, if the execution of cognitive tasks impairs postural control in the presence of
120 42
121 43 pain, this should also be taken into account in rehabilitation context.

122 44
123 45 Considering that posture can be defined as the dynamic stability of a continuous moving body
124 46
125 47 (Harbourne and Stergiou 2003; Madeleine et al. 2011), nonlinear analysis of the dynamic structure of the
126 48
127 49 center of pressure (CoP) time series would contribute to understand the physiological complexity of posture
128 50
129 51 by accessing motor patterns that would be implicit in the CoP variability. Sample entropy (SaEn) measures

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111 variations in the system output along time, ~~which is independent of the signal magnitude (Slifkin and Newell~~
112 ~~1999; Richman and Moorman 2000).~~ Therefore, measures of physiological complexity of the postural sway
113 during quiet standing may relate to the system functionality as they are defined as the capacity of generating
114 adaptive answers to an ever-changing environment such as controlling posture (Manor et al. 2010). SaEn
115 provides a measure of “orderly structure” within the time series since it tests if there are any repeated
116 patterns of various lengths, including the ones that are not repeated at regular intervals (Duarte and Sternad
117 2008). So, the lower the SaEn values are, the higher the similarity and lesser the complexity in the temporal
118 series is (Richman and Moorman 2000). ~~SaEn has been used to measure the structure of the CoP variability~~
119 ~~(Roerdink et al. 2006; Donker et al. 2007; Duarte and Sternad 2008; Stins et al. 2009) and thus address the~~
120 ~~complexity of the signal.~~

121 ~~Most definitions of complexity are driven by operational considerations on the number of system~~
122 ~~elements and their functional interactions. Therefore, eComplexity depends on the number of structural~~
123 components of the system, the existing coupling among these components and how this interaction is
124 influenced by the intrinsic dynamic properties of the system and the motor task demands (Vaillancourt and
125 Newell 2002). Thus, if the presence of pain and the execution of a cognitive task are both concurring with
126 the attentional resources used in postural control, then the coupling between the components of the system
127 responsible for balance may be affected and, consequently, the complexity of the postural sway is affected.
128 ~~The literature shows that the eExecution of a concurrent cognitive task during standing increases the~~
129 complexity of the postural sway, and this increase has been attributed to a more automatized postural sway,
130 when less attention is directed to the balance control (Donker et al. 2007; Stins et al. 2009; Kuczyński et al.
131 2011). On the other hand, there is some evidence that the complexity of postural control decreases with
132 pain. ~~Søndergaard et al. (2010) found a decrease SaEn of CoP displacement~~ during sitting with increased
133 perceived discomfort in healthy young subjects (Søndergaard et al. 2010). ~~The same~~ Similar finding was
134 reported in young subjects with transient acute episode of low back pain during two continuous hours of

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standing, but without history of low back pain (Fewster et al. 2017), showing a relation between the occurrence of pain and the decrease in CoP complexity. Therefore, examining the complexity of postural sway in a dual task context and the effect of experimental pain in this condition may improve the understanding of the decrease in postural stability (Levinger et al. 2016) and complexity (Fewster et al. 2017) that may exist as a result of pain in an otherwise healthy system.

The aim of this study was to quantify how postural stability, *i.e.*, ~~CoP sway~~ [(CoP sway velocity and area of displacement) and ~~CoP~~ complexity (CoP SaEn)], is modified during experimental pain while performing a cognitive task. It was hypothesized that (i) the kind of cognitive task (more or less demanding) in a non-painful condition will not interfere with CoP sway or CoP complexity, since the system would have enough cognitive resources to overcome it; (ii) experimental pain will increase CoP sway and decrease CoP complexity, regardless the type of cognitive task performed; (iii) the presence of experimental pain while performing a difficult cognitive task will overload the cognitive resources and impair postural stability, increasing CoP sway and decreasing CoP complexity.

2. Methods

2.1. Subjects

Sixteen young adults, all university students, (to control for the effect of education level on multitasking performance (Voos et al. 2015)), participated in the experiment – 8 males (mean \pm SD: age = 26.9 ± 2.8 years; body mass = 74.9 ± 13.8 kg; height = 1.76 ± 0.08 m) and 8 females (mean \pm SD: age = 27.1 ± 4.0 years; body mass = 68.8 ± 5.2 kg; height = 1.68 ± 0.06 m). The exclusion criteria were body mass index above 25 kg/m^2 , pregnancy, drug addiction, previous neurologic, musculoskeletal or mental illness, lack of ability to cooperate, current use of medications (e.g. analgesics, anti-inflammatory medicine), consumption of alcohol, caffeine, nicotine or painkillers 8 hours prior to the data collection, recent history of acute pain affecting the upper-lower limb and/or trunk, past history of chronic pain conditions, participation in other pain trials throughout the study period. All procedures performed in studies involving human participants

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were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the local Ethics Committee (N-20120077). This sample size was calculated to detect a minimum difference of 40% in the CoP area assuming type error 1 as 5% and power of 80% between the conditions before and after the induction of experimental pain. All participants gave signed informed consents prior to inclusion in the study.

2.2. Experimental protocol

Since in healthy individuals approximately 70% of the information used for controlling posture originates from proprioceptive systems (Peterka 2003), we controlled the effect of different footwear on postural control by asking the subjects to stand barefoot during the experiment. The participants stood on a triangular force plate that measures vertical forces (Good Balance System, Metitur, Jyväskylä, Finland; dimensions: equilateral triangle – 800-mm; sampling frequency: 50-Hz as suggested by the International Society for Posture and Gait Research Standardization Committee (Scoppa et al. 2013)). This is a valid and reliable system for postural sway measurements (Era et al. 2006; Ha et al. 2014) with accuracy better than 1-mm for the CoP position measurement (Good Balance System User Manual). The CoP position was calculated via the Good Balance Software (Metitur, Jyväskylä, Finland) which uses the weighted arithmetic mean between the vertical force measured by four sensors and their corresponding position: one in each corner of the force-plate and the last one in the centroid of the force-plate (Fig. 1). The rationale for using the tandem position for the feet was based in previous studies showing that greater pain effects are presented when posture is challenged (Hirata et al. 2013). This was important to ensure that postural stability adaptations due to pain could be observed. Therefore, subjects were asked to stand in tandem position, to increase postural challenge during the tasks, with the right leg behind (Fig. 1), arms hanging relaxed alongside the body, and were instructed to maintain balance while looking forward. Tape markers were placed on the force plate to ensure that the same foot position was maintained through all conditions. During

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183 the assessment of postural control, subjects were instructed to look forward at a target positioned at eye-
184 level approximately 45-cm from the subjects to minimize the influence of the target distance on postural
185 sway (Kapoula and Lê 2006). CoP records were made under eight experimental conditions, depending on the
186 type of injection (control or painful), the dual-task (counting forward or counting backward as the less and
187 more challenging tasks, respectively), before (pre-injection) and immediately after the injection. The
188 counting forward task consisted of adding one and the counting backward was performed by subtracting
189 three, beginning from a random number. The total number of answers and the number of correct answers
190 during each trial were recorded. The order of the injections and the order of the tasks were randomized,
191 with the same number of subjects receiving the hypertonic or isotonic injections first.

192 The experiment always followed the same order for all participants: (i) CoP measurement while
193 performing the first randomly assigned task (cognitive task 1 or 2) over 60-s (pre-injection 1); (ii) 1-min rest;
194 (iii) CoP measurement over 60-s while performing the second randomly assigned task (cognitive task 1 or 2)
195 over 60-s (pre-injection 2); (iv) injections of the first saline solution (painful or control) into vastus medialis
196 (VM) and vastus lateralis (VL) muscles; (v) assessment of pain intensity by visual analogue scale (VAS); (vi)
197 CoP measurement over 60-s while performing task A; (vii) collecting VAS scores of the pain intensity and 1-
198 min rest; (viii) CoP measurement over 60-s while performing task B; (ix) collecting VAS scores of the pain
199 intensity. After the final step, the pain VAS scores were taken each minute until the pain had subsided which
200 was followed by a 5-min break. Following the break, all steps of the experiment were performed again with
201 the injection of the other saline solution, including new pre-injection CoP recordings. Before each CoP
202 measurement, all subjects confirmed that no tiredness or other problems were presented. The duration of
203 the CoP measurements were performed according to guidelines proposed by the International Society for
204 Posture and Gait Research (Scoppa et al. 2013). Fig. 2 summarizes the study procedures along time.

205 3.3. Experimental muscle pain

206 Before the experiment all subjects were instructed about the nature and effects of the injections,

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207 and that one type of injection would be painful while the other would be a non-painful stimulus, although
208 they would not know which kind of injection they would be receiving. Pain was induced through
209 intramuscular injection of 1-mL of 6% sterile hypertonic saline solution or as a control condition 1-mL of
210 isotonic (0.9%) saline solution (Graven-Nielsen et al. 1997; Farina 2003; Schulte et al. 2004; Falla et al. 2006).

211 The injections were performed with a 2-mL syringe with a disposable needle (27G, 40-mm) into right VM
212 muscle and right VL muscle. Both injections locations were marked to ensure that they were applied
213 approximately in the same location. The VM muscle injection was performed 5-cm proximal and 5-cm medial
214 to the medial corner of the patella (Shiozawa et al. 2013), and in the VL muscle, injections were performed
215 at two thirds of the distance from the anterior spina iliaca to the lateral side of the patella (Fig. 3). The depth
216 of the injection was determined by an ultrasound scanner (LOGIQ™ S7, General Electric, USA). This pain
217 model has been successfully used previously to mimic knee-related pain during quiet standing tasks
218 providing moderate pain intensities for approximately five minutes (Hirata et al. 2011). Hypertonic saline
219 injections have been shown to activate nociceptors around the injected site (Mense 1993) whereas the 0.9%
220 isotonic saline injections have induced little or no pain during postural control tasks similar to the one used
221 in the present study (Hirata et al. 2010, 2011, 2013).

222 2.4. *Assessment of pain intensity*

223 The subjects were asked to rate the pain intensity using a 10-cm VAS from 0-cm to 10-cm (0-cm
224 means “no pain” and 10-cm means “maximum pain”) immediately after the injections and after each balance
225 measurement. Therefore, three VAS scores were obtained for each set of experiments (balance
226 measurements after isotonic injection and balance measurements after hypertonic injection, respectively;
227 Fig. 2), and the mean values of the three VAS scores were considered as the pain intensity after each injection
228 paradigm. Additionally, following each set of experiments subjects were asked to indicate the overall pain
229 areas during the trials on a body chart and to respond the McGill Pain Questionnaire (Melzack 1975). The
230 area of pain was extracted from the body charts with VistaMetrix 1.38 software. The pain rating index based

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on the rank values of the words chosen within each category (sensory, affective, evaluative and miscellaneous) from McGill Pain Questionnaire were obtained and the score for each category, as well as the total pain rating index were determined as the sum of the ranked values of the words (Melzack 1975).

2.5. Data analysis

All variables for postural sway were calculated based on 50-s of the standing tasks, with the first and last 5-s from the original 60-s time series being excluded. The analyses were performed with Matlab R2016a software (Mathworks, Massachusetts, USA). The area fitted to 95% confidence interval of the CoP displacement was calculated as representative of the total CoP area displacement (95% confidence interval ellipse), along with the CoP velocity in both directions (anterior-posterior and medial-lateral). The structural variability of the CoP was calculated by means of SaEn with the embedding dimension (m) and the tolerance distance (r) set to $m=2$ and $r=0.2 \times \text{SD}$ (Vaillancourt and Newell 2000). All CoP variables are displayed as the difference between the values obtained immediately after the injection and the correspondent pre-injection condition. Negative values show that the CoP variable decreased after the injection of the saline solution compared to its respective pre-injection condition. Likewise, positive values show that the CoP variable increased after the injection compared to its respective pre-injection condition.

2.6. Statistical analysis

Pain outcomes were compared between injection types (isotonic or hypertonic injections) with paired T-tests when normal distribution was present (VAS scores and pain area data) and with the Wilcoxon Signed Rank Test when the data distribution was non-normal (McGill scores). The task measures (number of answers, number of correct answers) were evaluated with a 3-way RM-ANOVA with *injection* (isotonic vs hypertonic), *time* (pre-injection vs after injection) and *task* (counting forward vs backwards) as main factors. The CoP parameters were compared with a 2-Way RM-ANOVA with *task* and *injection* as main factors, and the p-values are shown in the table 3. Bonferroni post-hoc correction for multiple comparisons was applied and p-values are shown in the results texts. The alfa-value (α) for statistical significance was set to 0.05.

Results

3.1. Experimental muscle pain and cognitive task performance

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3.1. Area and amplitude of perceived pain'

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Fig. 4 shows the reported pain areas following both isotonic and hypertonic injections. Pain was present in the anterior and lateral portions of the thigh after both isotonic and hypertonic injections, being more concentrated in the lower half of the thigh after the isotonic injections. The hypertonic saline injections induced higher pain area (mean area ± SD: isotonic = 518.6 ± 690.6 au; hypertonic = 1659.3 ± 1574.0 au; P=0.003) and higher VAS scores (mean score ± SD: isotonic = 0.9 ± 1.1 cm; hypertonic = 4.7 ± 1.7 cm; P<0.001) than isotonic saline injections. Table 1 shows the scores for each class of words from McGill Pain Questionnaire and the pain rating index. Subjects presented a higher total pain rating index and scored higher in all the categories, with the exception of the affective class, after the hypertonic injections (P<0.05).

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3.2. Cognitive task performance

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Only for the analysis of the cognitive task performance, one subject was not included due to problems in the answers recording. The total number of answers and the number of correct answers decreased during backwards counting conditions compared with forwards counting despite the injection effect (significant main effect for task factor; Table 2).

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Effect of experimental pain in CoP variables

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There were no statistical differences between the different conditions for the factor injection on any of the CoP variables (Table 3).

Effect of cognitive task in CoP variables

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8 A main effect of *task* was found for the CoP AP-velocity ($F=5.82$; $P=0.028$), showing that there was an
9 increased AP-velocity during the counting backwards task compared to the counting forwards task,
10
11 regardless the type of injection (Table 3).
12

13 *Effect of the interaction between experimental pain and cognitive task in CoP variables*

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15 An interaction effect was found between *injection* and *task* factors for CoP total area and CoP ML-
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17 velocity (CoP total $F=7.78$, $P=0.049$; CoP ML $F=4.69$, $P=0.021$) (Table 3). Post-hoc comparisons showed that
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19 both variables decreased after the hypertonic injection in comparison to the condition with isotonic injection
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21 when subjects were counting forward (Bonferroni: $P = 0.010$ for total area; $P = 0.015$ for ML-velocity). After
22
23 the hypertonic injection, CoP total area increased when subjects were counting backwards in comparison to
24
25 when they were counting forwards (Bonferroni: $P = 0.019$). ML-velocity showed differences between the
26
27 different cognitive tasks also after the injection of hypertonic solution, with a smaller decrease of ML-velocity
28
29 while counting backwards (Bonferroni: $P = 0.049$).
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31 **4. Discussion**

32 The present study aimed at quantifying how postural stability, represented by CoP sway (velocity and
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34 area of displacement) and CoP complexity (CoP SaEn), is modified during experimental pain while performing
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36 a cognitive task. The main results showed that the kind of cognitive task did not interfere with postural
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38 stability in the absence of pain. Experimental pain around the knee joint reduced CoP sway but did not affect
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40 CoP complexity during the performance of an easier cognitive task. During experimentally induced pain, the
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42 performance of a difficult cognitive task increased CoP sway but did not change CoP complexity.

43 *Pain intensity and counting performance*

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45 The subjects showed higher pain intensity for the hypertonic saline injection and a larger pain area
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47 compared with the isotonic saline injection, as expected, indicating that experimental pain occurred (Hirata
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49 et al. 2011). The McGill pain questionnaire indicated that hypertonic saline was perceived more impairing
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than the isotonic injection in all subscales except for the affective one. It is important to note that during isotonic injections subjects rated pain around 1/10, which cannot be classified as a totally pain free condition. Counting performance requires the use of cognitive process which relies on the working memory of the subject (Lemaire 1996), impairing motor output performance when executed simultaneously with a motor task (Vuillerme and Nafati 2007). Seminowicz and Davis (2007) showed that subjects are able to maintain performance of difficult cognitive task while experiencing different levels of pain. In this study, the painful condition did not affect the counting performance while performing a motor task (standing still) indicating that healthy subjects are able to engage multiple tasks (motor and cognitive) during pain without compromising performance. This suggests that sufficient cognitive resources were available to manage the cognitive process of counting forwards or backwards despite the interpretation of painful stimuli and the postural control task (Eccleston et al. 1999). Finally, education level is associate with both motor and perceptual performance, where higher education level is associated with better performance (Voos et al. 2015). -Since our subjects were all university students, we believe that bias due to education level did not affect the present results.

Effect of cognitive tasks on postural stability

Our first initial hypothesis, that (i) the kind of cognitive task (more or less demanding) in a non-painful condition would not interfere with CoP sway or CoP complexity, was confirmed. The factor task affected the CoP anterior-posterior velocity, indicating an increased velocity during the execution of the more difficult task (counting backwards) in comparison to the easier task (counting ~~backwards~~forward). Nevertheless, the CoP SaEn was not affected by the kind of the performed cognitive task. These results indicate that enough cognitive resources were available to overcome the demands of both cognitive and postural tasks, which was expected since they were young individuals without any sensory-motor alterations.

Effect of experimental knee-related pain on postural stability

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8 Our second initial hypothesis, that (ii) experimental pain would increase CoP sway and decrease CoP
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10 complexity was not confirmed since the type of saline solution injected did not affect the CoP variables.
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12 However, even though the factor *injection* did not show statistical differences between the different
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14 conditions for any of the studied CoP variables, there was a difference between total area and ML-velocity
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16 between the control and the painful condition when the subjects were counting forwards, i.e., in conditions
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18 where the kind of cognitive task performed was the same. Interestingly, during the counting forward, the
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20 type of injection resulted significant changes in postural sway (total area and ML-velocity) in opposite
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22 directions: positive values of the difference between pre-injection and after injection of the isotonic solution,
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24 whereas after the injection of the hypertonic solution both variables showed negative values. Additionally,
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26 no significant changes were observed in the structural variability of the CoP signal. This is contrary to the
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28 initial hypothesis, where an increase in postural sway and a decrease in structural variability during painful
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30 conditions were expected. It is also in contrast with previous findings (Mazaheri et al. 2013) but may relate
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32 to the different position of the feet used in this study, which affects the postural sway (Day et al. 1993). The
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34 tandem feet position adopted allows less displacement of the CoP due to the limited base of support
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36 compared to side-by-side feet position, since if the subjects increase the CoP amplitude they may fall (Day
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38 et al. 1993). This also may reflect a voluntary strategy, requiring a greater amount of cognitive resources and
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40 attention (Morasso and Sanguineti 2002), attempting to avoid large excursions of the body and consequent
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42 loss of balance. For the current study, this might indicate that the subjects prioritized the balance task over
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44 the other tasks, also known as *posture first strategy* (Vuillerme and Nafati 2007). The subjects were able to
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46 reduce the postural sway without compromising the counting performance during the easy cognitive task,
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48 suggesting that the available cognitive resource was sufficient to perform the less challenging cognitive task
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50 without compromising postural stability. Therefore, these results indicate that healthy subjects have the
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52 capacity to perform easy cognitive tasks while ensuring postural stability (Siu and Woollacott 2007).
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54 Reducing postural sway might reflect a motor strategy available for healthy subjects to avoid excessive
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8 translation of the body, which could lead to balance loss (Winter 1995). This strategy was also observed
9 during the control injection while counting backwards, probably indicating that a high cognitive load seems
10 to be interpreted as a treat to postural stability. An alternative explanation for the contrast between the
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12 present study and the previous studies with pain patients showing larger postural sway (Schulte et al. 2004;
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14 Levinger et al. 2016) might be the pain model used that is not a complete proxy to the impaired pain patients'
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16 sensory-motor system.
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19 Interactions between pain and cognitive load on postural stability

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21 Our initial third hypothesis, that (iii) the presence of experimental pain would increase CoP sway and
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23 decrease CoP complexity only when performing a difficult cognitive task was partially confirmed since CoP
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25 sway increased during pain under a difficult cognitive task, but the CoP complexity did not change. ANOVA
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27 results showed an interaction between the task and injection factors for total area and ML-velocity. After
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29 the hypertonic injection CoP total area increased and CoP ML-velocity decreased less while counting
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31 backwards in comparison to counting forwards condition, corroborating our hypothesis. ANOVA results also
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33 showed an effect of the task factor on AP-velocity with post-hoc comparisons showing a difference only
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35 during the hypertonic injection condition: while counting backwards AP-velocity also increased. Altogether
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37 these results show that CoP sway increases when performing a more demanding cognitive task in the
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39 presence of experimental pain. This might reflect an interference with the information-processing capacity
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41 and an attention disruption from both postural control and cognitive task (Eccleston et al. 1999). Previous
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43 studies suggest that disruptions of sensory information lead to worsening of proprioception in the affected
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45 area (Matre et al. 2002), further impairing postural sway (Hirata et al. 2010, 2011). The results indicate that
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47 the posture first strategy (Vuillerme and Nafati 2007) found during the easy cognitive task during pain is no
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49 longer feasible when a difficult cognitive task is performed during painful conditions. The increased cognitive
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51 load in painful conditions seems to impair the motor performance maybe due to insufficient cognitive
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53 resource to simultaneously maintain postural stability (which requires significant amount of attention
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(Morasso and Sanguineti 2002)) and execute a difficult cognitive task. These results might have important new implications in understanding the mechanisms related to fall accidents. Postural stability in daily life activities is usually performed in combination with additional tasks, for example, walking in a busy slippery sidewalk. These daily life activities involves simultaneously competition for the cognitive resources available (Woollacott and Shumway-Cook 2002) to evaluate the environment constrains in order to promote the best motor strategy (Winter 1995). Our present results indicate that, if the subject performs a challenging postural task in pain, his/her capacity for maintain balance while exposed to a difficult cognitive task is suboptimal, which could increase the likelihood of losing balance.

The complexity of postural sway did not show any differences between the experimental conditions. This result is contrary to the literature finding that young healthy subjects present a more regular and less automatic postural sway (decreased CoP SaEn) when the motor task is more difficult (e. g. standing with eyes closed) and more irregular postural sway and more automatic postural sway (increased CoP SaEn) when a cognitive task is added (Donker et al. 2007; Stins et al. 2009). The fact that the cognitive task did not interfere with CoP complexity may be due to the nature of both motor (standing in tandem position) and cognitive (subtraction calculus) tasks used in the experimental setup that did not interfere with the automaticity of postural control. Besides that, pain also did not affect CoP complexity, showing that experimental knee-related pain did not compromise the coupling between the components of the system responsible for balance in the current experimental setup. Future studies should investigate the interaction between pain, cognition and on CoP complexity with different motor and cognitive demands, in addition to different populations.

Despite interesting results regarding the effects of cognitive tasks in postural control during pain, the relevance of the findings for clinical populations should be interpreted with care. The experimental pain model used here is convenient to assess the effect of pain without the interference of potential structural or pathologies. However, extrapolating the current findings to an older population can only be done to some

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8 degree. Additionally, chronic pain patients may also suffer from depressive symptoms (Bair et al. 2003) or
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10 anxiety (McWilliams et al. 2003), which might increase cognitive load (Nebes et al. 2001). Furthermore,
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12 cognitive impairments are often found in chronic pain patients, decreasing the possibility to maintain
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14 performance of two or more concurrent tasks (Brauer et al. 2004), as opposed to what was observed in this
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16 study where young healthy subjects were recruited. Also, there was no recording of postural sway without
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18 any cognitive task. This would have allowed comparisons with a condition where neither pain nor cognitive
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20 tasks were influencing postural sway, and could have reduced type 2 errors given that multiple CoP variables
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22 were analyzed in the study. Thus, it can be considered a limitation to our interpretations.

23 **5. Conclusions**

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25 Pain and cognitive task interfered on postural stability, changing its patterns. During the performance
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27 of a simple cognitive task, pain, reduced postural sway, while during the performance of a more demanding
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29 cognitive task, postural sway was increased in young healthy subjects. Since our subjects were young healthy
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31 subjects, the direct translation of the present results to patients suffering from pain should be done with
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33 caution. However, these results may suggest that rehabilitation approaches should take into account that
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35 pain not only affects directly the motor system, but may occupy cognitive resources, potentially resulting in
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37 poorer performance when performing rehabilitation exercises. Additionally, rehabilitation strategies using
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39 both motor and cognitive resources need further investigation to outline the effect of interaction between
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41 pain and cognition on the performance during activities of daily life in patients.

42 **Compliance with ethical standards**

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51 **Conflict of Interest:** The authors declare that they have no conflict of interest.

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419 **REFERENCES**

420 Andersson G, Hagman J, Talianzadeh R, et al (2002) Effect of cognitive load on postural control. *Brain Res*
421 10 Bull 58:135–9
422 Bair MJ, Robinson RL, Katon W, Kroenke K (2003) Depression and Pain Comorbidity. *Arch Intern Med*
423 12 163:2433. doi: 10.1001/archinte.163.20.2433
424 Brauer SG, Broome A, Stone C, et al (2004) Simplest tasks have greatest dual task interference with balance
425 15 in brain injured adults. *Hum Mov Sci* 23:489–502. doi: 10.1016/j.humov.2004.08.020
426 Bronstein AM, Buckwell D (1997) Automatic control of postural sway by visual motion parallax. *Exp Brain*
427 17 Res 113:243–248. doi: 10.1007/BF02450322
428 Day BYBL, Steiger MJ, Thompson PD, Marsden CD (1993) Human Body Motion When Standing :
429 20 Implications for. *J Physiol* 469:479–499
430 Donker SF, Roerdink M, Greven AJ, Beek PJ (2007) Regularity of center-of-pressure trajectories depends on
431 22 the amount of attention invested in postural control. *Exp Brain Res* 181:1–11. doi: 10.1007/s00221-
432 23 007-0905-4
433 Duarte M, Sternad D (2008) Complexity of human postural control in young and older adults during
434 25 prolonged standing. *Exp Brain Res* 191:265–276. doi: 10.1007/s00221-008-1521-7
435 Eccleston C, Baeyens F, Helen P, et al (1999) Pain Demands Attention : A Cognitive-Affective Model of the
436 28 Interruptive Function of Pain. 125:356–366
437 Era P, Sainio P, Koskinen S, et al (2006) Postural balance in a random sample of 7,979 subjects aged 30
438 30 years and over. *Gerontology* 52:204–213. doi: 10.1159/000093652
439 Etemadi Y, Salavati M, Arab AM, Ghanavati T (2016) Balance recovery reactions in individuals with
440 32 recurrent nonspecific low back pain: Effect of attention. *Gait Posture* 44:123–127. doi:
441 33 10.1016/j.gaitpost.2015.11.017
442 Falla D, Farina D, Dahl MK, Graven-Nielsen T (2006) Muscle pain induces task-dependent changes in
443 36 cervical agonist/antagonist activity. *J Appl Physiol* 102:601–609. doi: 10.1152/jappphysiol.00602.2006
444 Farina D (2003) Effect of Experimental Muscle Pain on Motor Unit Firing Rate and Conduction Velocity. *J*
445 38 *Neurophysiol* 91:1250–1259. doi: 10.1152/jn.00620.2003
446 Fewster KM, Gallagher KM, Howarth SH, Callaghan JP (2017) Low back pain development differentially
447 40 influences centre of pressure regularity following prolonged standing. *Gait Posture*. doi:
448 41 10.1016/j.gaitpost.2017.06.005
449 Fraizer E V., Mitra S (2008) Methodological and interpretive issues in posture-cognition dual-tasking in
450 44 upright stance. *Gait Posture* 27:271–279. doi: 10.1016/j.gaitpost.2007.04.002
451 Graven-Nielsen T, Arendt-Nielsen L, Svensson P, Jensen TS (1997) Quantification of local and referred
452 46 muscle pain in humans after sequential i.m. injections of hypertonic saline. *Pain* 69:111–7
453 Ha H, Cho K, Lee W (2014) Reliability of the Good Balance System® for Postural Sway Measurement in
454 48 Poststroke Patients. *J Phys Ther Sci* 26:121–124. doi: 10.1589/jpts.26.121
455 Harbourne RT, Stergiou N (2003) Nonlinear analysis of the development of sitting postural control. *Dev*
456 51 *Psychobiol* 42:368–377. doi: 10.1002/dev.10110
457 Hirata RP, Arendt-Nielsen L, Graven-Nielsen T (2010) Experimental calf muscle pain attenuates the postural

- 1
2
3
4
5
6
7
8 stability during quiet stance and perturbation. *Clin Biomech* 25:931–937. doi:
9 10.1016/j.clinbiomech.2010.06.001
- 10 Hirata RP, Ervilha UF, Arendt-Nielsen L, Graven-Nielsen T (2011) Experimental muscle pain challenges the
11 postural stability during quiet stance and unexpected posture perturbation. *J Pain* 12:911–919. doi:
12 10.1016/j.jpain.2011.02.356
- 13 Hirata RP, Jørgensen TS, Rosager S, et al (2013) Altered Visual and Feet Proprioceptive Feedbacks during
14 Quiet Standing Increase Postural Sway in Patients with Severe Knee Osteoarthritis. *PLoS One* 8:1–8.
15 doi: 10.1371/journal.pone.0071253
- 16
17 Huxhold O, Li SC, Schmiedek F, Lindenberger U (2006) Dual-tasking postural control: Aging and the effects
18 of cognitive demand in conjunction with focus of attention. *Brain Res Bull* 69:294–305. doi:
19 10.1016/j.brainresbull.2006.01.002
- 20 Kahneman D (1973) *Attention and effort*. Prentice-Hall
- 21
22 Kapoula Z, Lê TT (2006) Effects of distance and gaze position on postural stability in young and old subjects.
23 *Exp Brain Res* 173:438–445. doi: 10.1007/s00221-006-0382-1
- 24 Knoop J, Van Der Leeden M, Van Der Esch M, et al (2012) Association of lower muscle strength with self-
25 reported knee instability in osteoarthritis of the knee: Results from the Amsterdam Osteoarthritis
26 Cohort. *Arthritis Care Res* 64:38–45. doi: 10.1002/acr.20597
- 27 Kuczyński M, Szymańska M, Bieć E (2011) Dual-task effect on postural control in high-level competitive
28 dancers. *J Sports Sci* 29:539–545. doi: 10.1080/02640414.2010.544046
- 29
30 Larivière C, Butler H, Sullivan MJL, Fung J (2013) An exploratory study on the effect of pain interference and
31 attentional interference on neuromuscular responses during rapid arm flexion movements. *Clin J Pain*
32 29:265–275. doi: 10.1097/AJP.0b013e318250ed6f
- 33 Lemaire P (1996) The Role of Working Memory Resources in Simple Cognitive Arithmetic. *Eur J Cogn*
34 *Psychol* 8:73–104. doi: 10.1080/095414496383211
- 35
36 Levinger P, Nagano H, Downie C, et al (2016) Biomechanical balance response during induced falls under
37 dual task conditions in people with knee osteoarthritis. *Gait Posture* 48:106–112. doi:
38 10.1016/j.gaitpost.2016.04.031
- 39
40 Liston MB, Bergmann JH, Keating N, et al (2014) Postural prioritization is differentially altered in healthy
41 older compared to younger adults during visual and auditory coded spatial multitasking. *Gait Posture*
42 39:198–204. doi: 10.1016/j.gaitpost.2013.07.004
- 43
44 Madeleine P, Nielsen M, Arendt-Nielsen L (2011) Characterization of postural control deficit in whiplash
45 patients by means of linear and nonlinear analyses - A pilot study. *J Electromyogr Kinesiol* 21:291–297.
46 doi: 10.1016/j.jelekin.2010.05.006
- 47
48 Manor B, Costa MD, Hu K, et al (2010) Physiological complexity and system adaptability: evidence from
49 postural control dynamics of older adults. *J Appl Physiol* 109:1786–1791. doi:
50 10.1152/jappphysiol.00390.2010
- 51
52 Matre D, Arendt-Nielsen L, Knardahl S (2002) Effects of localization and intensity of experimental muscle
53 pain on ankle joint proprioception. *Eur J Pain* 6:245–260. doi: 10.1053/eujp.2002.0332
- 54
55 Mazaheri M, Coenen P, Parnianpour M, et al (2013) Low back pain and postural sway during quiet standing
56 with and without sensory manipulation: A systematic review. *Gait Posture* 37:12–22. doi:
57
58
59
60
61
62
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- 1
2
3
4
5
6
7
8 10.1016/j.gaitpost.2012.06.013
- 498 9
10 Mazaheri M, Heidari E, Mostamand J, et al (2014) Competing effects of pain and fear of pain on postural
11 control in low back pain? *Spine (Phila Pa 1976)* 39:E1518–E1523. doi:
12 10.1097/BRS.0000000000000605
- 13
14 McWilliams LA, Cox BJ, Enns MW (2003) Mood and anxiety disorders associated with chronic pain: an
15 examination in a nationally representative sample. *Pain* 106:127–33
- 16
17 Melzack R (1975) The McGill Pain Questionnaire: major properties and scoring methods. *Pain* 1:277–99
- 18
19 Mense S (1993) Nociception from skeletal muscle in relation to clinical muscle pain. *Pain* 54:241–89
- 20
21 Morasso PGP, Sanguineti V (2002) Ankle muscle stiffness alone cannot stabilize balance during quiet
22 standing. *J Neurophysiol* 88:2157–2162. doi: 10.1152/jn.00719.2001
- 23
24 Nebes RD, Butters MA, Houck PR, et al (2001) Dual-task performance in depressed geriatric patients.
25 *Psychiatry Res* 102:139–151. doi: 10.1016/S0165-1781(01)00244-X
- 26
27 Pellecchia GL (2003) Postural sway increases with attentional demands of concurrent cognitive task. *Gait
28 Posture* 18:29–34. doi: 10.1016/S0966-6362(02)00138-8
- 29
30 Peterka RJ (2003) Dynamic Regulation of Sensorimotor Integration in Human Postural Control. *J
31 Neurophysiol* 91:410–423. doi: 10.1152/jn.00516.2003
- 32
33 Richman JS, Moorman JR (2000) Physiological time-series analysis using approximate entropy and sample
34 entropy. *Physiological time-series analysis using approximate entropy and sample entropy. Am Physiol
35 Soc*
- 36
37 ~~Roerdink M, De Haart M, Daffertshofer A, et al (2006) Dynamical structure of center-of-pressure
38 trajectories in patients recovering from stroke. *Exp Brain Res* 174:256–269. doi: 10.1007/s00221-006-
39 0441-7~~
- 40
41 Schulte E, Ciubotariu A, Arendt-Nielsen L, et al (2004) Experimental muscle pain increases trapezius muscle
42 activity during sustained isometric contractions of arm muscles. *Clin Neurophysiol* 115:1767–1778.
43 doi: 10.1016/j.clinph.2004.03.005
- 44
45 Scoppa F, Capra R, Gallamini M, Shiffer R (2013) Clinical stabilometry standardization. Basic definitions -
46 Acquisition interval - Sampling frequency. *Gait Posture* 37:290–292. doi:
47 10.1016/j.gaitpost.2012.07.009
- 48
49 Seminowicz DA, Davis KD (2007) Interactions of pain intensity and cognitive load: The brain stays on task.
50 *Cereb Cortex* 17:1412–1422. doi: 10.1093/cercor/bhl052
- 51
52 Sherafat S, Salavati M, Takamjani IE, et al (2014) Effect of dual-tasking on dynamic postural control in
53 individuals with and without nonspecific low back pain. *J Manipulative Physiol Ther* 37:170–179. doi:
54 10.1016/j.jmpt.2014.02.003
- 55
56 Shiozawa S, Hirata RP, Graven-Nielsen T (2013) Reorganised anticipatory postural adjustments due to
57 experimental lower extremity muscle pain. *Hum Mov Sci* 32:1239–1252. doi:
58 10.1016/j.humov.2013.01.009
- 59
60 Siu KC, Woollacott MH (2007) Attentional demands of postural control: The ability to selectively allocate
61 information-processing resources. *Gait Posture* 25:121–126. doi: 10.1016/j.gaitpost.2006.02.002
- 62
63 Slifkin AB, Newell KM (1999) Noise, information transmission, and force variability. *J Exp Psychol Hum
64*
- 65

- 1
2
3
4
5
6
7
8 Percept Perform 25:837–851. doi: 10.1037//0096-1523.25.3.837
- 9
10 Søndergaard KHE, Olesen CG, Søndergaard EK, et al (2010) The variability and complexity of sitting postural
11 control are associated with discomfort. *J Biomech* 43:1997–2001. doi:
12 10.1016/j.jbiomech.2010.03.009
- 13
14 Stins JF, Michielsen ME, Roerdink M, Beek PJ (2009) Sway regularity reflects attentional involvement in
15 postural control: Effects of expertise, vision and cognition. *Gait Posture* 30:106–109. doi:
16 10.1016/j.gaitpost.2009.04.001
- 17
18 Swan L, Otani H, Loubert P V. (2007) Reducing postural sway by manipulating the difficulty levels of a
19 cognitive task and a balance task. *Gait Posture* 26:470–474. doi: 10.1016/j.gaitpost.2006.11.201
- 20
21 Vaillancourt DE, Newell KM (2002) Changing complexity in human behavior and physiology through aging
22 and disease. *Neurobiol Aging* 23:1–11. doi: 10.1016/S0197-4580(02)00052-0
- 23
24 Vaillancourt DE, Newell KM (2000) The dynamics of resting and postural tremor in Parkinson’s disease. *Clin*
25 *Neurophysiol* 111:2046–2056. doi: 10.1016/S1388-2457(00)00467-3
- 26
27 Van Daele U, Hagman F, Truijen S, et al (2010) Decrease in postural sway and trunk stiffness during
28 cognitive dual-task in nonspecific chronic low back pain patients, performance compared to healthy
29 control subjects. *Spine (Phila Pa 1976)* 35:583–589. doi: 10.1097/BRS.0b013e3181b4fe4d
- 30
31 Van Ryckeghem DM, Van Damme S, Eccleston C, Crombez G (2018) The efficacy of attentional distraction
32 and sensory monitoring in chronic pain patients: A meta-analysis. *Clin Psychol Rev* 59:16–29. doi:
33 10.1016/j.cpr.2017.10.008
- 34
35 Veldhuijzen DS, Kenemans JL, De Bruin CM, et al (2006) Pain and attention: Attentional disruption or
36 distraction? *J Pain* 7:11–20. doi: 10.1016/j.jpain.2005.06.003
- 37
38 Yoos MC, Piemonte MEP, Castelli LZ, et al (2015) Association between Educational Status and Dual-Task
39 Performance in Young Adults. *Percept Mot Skills* 120:416–437. doi: 10.2466/22.PMS.120v18x8
- 40
41 Vuillerme N, Nafati G (2007) How attentional focus on body sway affects postural control during quiet
42 standing. *Psychol Res* 71:192–200. doi: 10.1007/s00426-005-0018-2
- 43
44 Winter DA (1995) A. B. C. (Anatomy, Biomechanics, Control) of Balance During Standing and Walking.
45 Waterloo Biomechanics, Ontario
- 46
47 Woollacott M, Shumway-Cook A (2002) Attention and the control of posture and gait: A review of an
48 emerging area of research. *Gait Posture* 16:1–14. doi: 10.1016/S0966-6362(01)00156-4
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Figure captions

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Fig 1 Schematic drawing representing the force platform size, sensor locations, and the tandem position of the subjects during the experiment

Fig 2 Study design overview: pain assessments were performed immediately after each injection and each balance measurement; the order of the saline injections was randomized in a balanced way

Fig 3 Injections sites for vastus lateralis muscle, performed at two thirds of the distance from the anterior spina iliaca (a) to the lateral side of the patella (b); and for the vastus medialis muscle, performed 5 cm proximal and 5 cm medial to the medial corner of the patella (c),

Fig 4 Representation of the experimental pain distribution reported areas after isotonic (top, blue in the online version) and hypertonic (bottom, red in the online version saline injections (A); the individual distributions are superimposed in the anatomical drawings

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585 **8 EXPERIMENTAL KNEE-RELATED PAIN ENHANCES ATTENTIONAL INTERFERENCE ON POSTURAL CONTROL**

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Abstract

Purpose: To quantify how postural stability is modified during experimental pain while performing different cognitively demanding tasks.

Methods: Sixteen healthy young adults participated in the experiment. Pain was induced by intramuscular injection of hypertonic saline solution (1mL, 6%) in both vastus medialis and vastus lateralis muscles (0.9% isotonic saline was used as control). The participants stood barefoot in tandem position for one minute on a force plate. Center of pressure (CoP) was recorded before and immediately after injections, while performing two cognitive tasks: (i) counting forwards by adding one; (ii) counting backwards by subtracting three. CoP variables – total area of displacement, velocity in anterior-posterior (AP-velocity) and medial-lateral (ML-velocity) directions, and CoP sample entropy in anterior-posterior and medial-lateral directions were displayed as the difference between the values obtained after and before each injection and compared between tasks and injections.

Results: CoP total area (-84.5 ± 145.5 vs. 28.9 ± 78.5 cm²) and ML-velocity (-1.71 ± 2.61 vs. 0.98 ± 1.93 cm/s) decreased after the painful injection vs. Control injection while counting forward ($P < 0.05$). CoP total area (12.8 ± 53.9 vs. -84.5 ± 145.5 cm²), ML-velocity (-0.34 ± 1.92 vs. -1.71 ± 2.61 cm/s) and AP-velocity (1.07 ± 2.35 vs. -0.39 ± 1.82 cm/s) increased while counting backwards vs. forwards after the painful injection ($P < 0.05$).

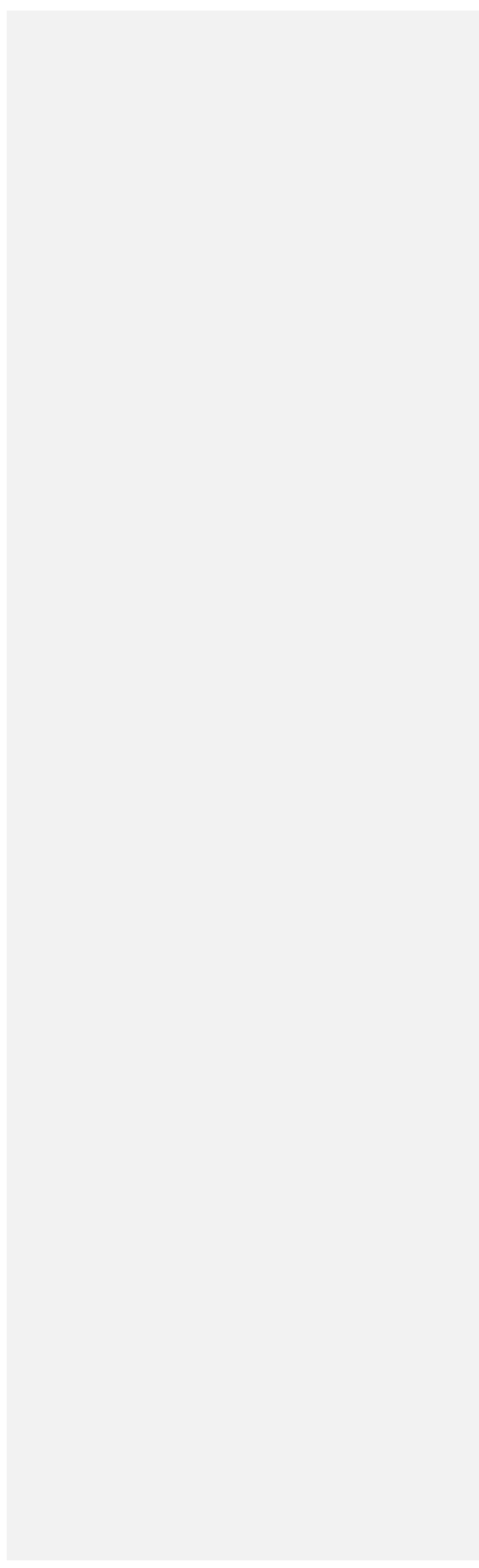
Conclusion: Pain interfered with postural stability according to the type of cognitive task performed, suggesting that pain may occupy cognitive resources, potentially resulting in poorer balance performance.

Keywords: postural stability, center of pressure, attention, distraction, pain

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637 **List of abbreviations**

638		
639	ANOVA	Analysis of variance
640	au	Arbitrary units
641	CoP	Center of pressure
642	SaEn	Sample entropy
643	SD	Standard deviation
644	VAS	Visual analogue scale
645	VM	Vastus medialis
646	VL	Vastus lateralis



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1. Introduction

Controlling of upright posture requires a significant amount of attention to gather information from the body and the environment and to generate adapted and accurate muscle activation for postural control (Morasso and Sanguineti 2002). Although the majority of postural control is regulated via automatic neural processes (Bronstein and Buckwell 1997), higher cortical centers are significantly involved in processing sensory information to plan and execute the best motor strategy for postural control (Winter 1995). In daily life, postural control is challenging as several tasks simultaneously compete for the cognitive resources available (Woollacott and Shumway-Cook 2002), limited by the capacity of higher centers to process sensory information (Kahneman 1973). Therefore, sharing attentional resources may cause impairments in the performance of daily living activities (Brauer et al. 2004). For example, competition for cognitive resources during tasks involving postural stability results in body stability being prioritized over secondary tasks (Liston et al. 2014).

Dual tasks paradigms, where subjects perform an additional task during standing, are employed to quantify the extent to which attention is associated with postural control. Decreases in postural sway while performing a secondary task compared with control conditions have been reported (Andersson et al. 2002; Pellecchia 2003) whereby focusing the attention on standing as still as possible increased postural sway compared with conditions without similar instructions (Vuillerme and Nafati 2007). Altogether, these results suggest that postural control demands attention (Woollacott and Shumway-Cook 2002) and that simultaneous cognitive loading plays an important role in balance stability (Swan et al. 2007).

Although detrimental effects of cognitive loading on postural sway during unperturbed standing are more commonly reported for older adults and patients, studies using dual-task approaches in young subjects show controversial results (Huxhold et al. 2006; Fraizer and Mitra 2008). Young healthy subjects have probably more ability to allocate the attentional resources without sacrificing postural stability, showing that

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671 a system without impairments prioritizes postural stability when dealing with dual-cognitive tasks (Siu and
672 Woollacott 2007).

673 11 Subjects with pain demonstrate increased postural sway compared with controls (Hirata et al. 2011).

674 13 A possible explanation for this finding is that the increased postural sway may relate to a disrupting effect of
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675 15 nociceptive stimuli on attention to other simultaneous non-nociceptive tasks (Eccleston et al. 1999),
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676 17 underlining that processing of nociceptive stimuli is cognitively demanding (Veldhuijzen et al. 2006). Thus,
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677 19 the execution of cognitive tasks during pain might interfere with postural control. Although previous studies
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678 21 have shown that patients with pain present impaired balance while performing a secondary cognitive task
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679 23 in comparison to health subjects (Van Daele et al. 2010; Larivière et al. 2013; Mazaheri et al. 2014; Sherafat
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680 25 et al. 2014; Etemadi et al. 2016; Levinger et al. 2016), it is not clear yet the isolate effect of pain since reduced
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681 27 muscle strength, reduced flexibility and degenerative changes at the affected segment also cause both
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682 29 stiffness and instability in patients suffering from chronic pain (Knoop et al. 2012). Therefore, further
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683 31 investigation of the interaction between pain, cognition and postural stability is warranted. This investigation
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684 33 is of particular interest for clinical practice since there are evidences that attention can be directed away
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685 35 from pain using some specific strategies (Van Ryckeghem et al. 2018). If selective attention could be directed
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686 37 away from the painful stimulus and modify the deleterious effect of muscle pain on postural control, these
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687 39 results could have important implications for clinical settings. Likewise, if the execution of cognitive tasks
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688 41 impairs postural control in the presence of pain, this should also be taken into account in rehabilitation
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689 43 context.

690 44 Considering that posture can be defined as the dynamic stability of a continuous moving body
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691 46 (Harbourne and Stergiou 2003; Madeleine et al. 2011), nonlinear analysis of the dynamic structure of the
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692 48 center of pressure (CoP) time series would contribute to understand the physiological complexity of posture
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693 50 by accessing motor patterns that would be implicit in the CoP variability. Sample entropy (SaEn) measures
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694 52 variations in the system output along time. Therefore, measures of physiological complexity of the postural
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695 sway during quiet standing may relate to the system functionality as they are defined as the capacity of
696 generating adaptive answers to an ever-changing environment such as controlling posture (Manor et al.
697 2010). SaEn provides a measure of “orderly structure” within the time series since it tests if there are any
698 repeated patterns of various lengths, including the ones that are not repeated at regular intervals (Duarte
699 and Sternad 2008). So, the lower the SaEn values are, the higher the similarity and lesser the complexity in
700 the temporal series is (Richman and Moorman 2000).

701 Complexity depends on the number of structural components of the system, the existing coupling
702 among these components and how this interaction is influenced by the intrinsic dynamic properties of the
703 system and the motor task demands (Vaillancourt and Newell 2002). Thus, if the presence of pain and the
704 execution of a cognitive task are both concurring with the attentional resources used in postural control,
705 then the coupling between the components of the system responsible for balance may be affected and,
706 consequently, the complexity of the postural sway is affected. Execution of a concurrent cognitive task
707 during standing increases the complexity of the postural sway, and this increase has been attributed to a
708 more automatized postural sway, when less attention is directed to the balance control (Donker et al. 2007;
709 Stins et al. 2009; Kuczyński et al. 2011). On the other hand, there is some evidence that the complexity of
710 postural control decreases with pain during sitting with increased perceived discomfort in healthy young
711 subjects (Søndergaard et al. 2010). Similar finding was reported in young subjects with transient acute
712 episode of low back pain during two continuous hours of standing, but without history of low back pain
713 (Fewster et al. 2017), showing a relation between the occurrence of pain and the decrease in CoP complexity.
714 Therefore, examining the complexity of postural sway in a dual task context and the effect of experimental
715 pain in this condition may improve the understanding of the decrease in postural stability (Levinger et al.
716 2016) and complexity (Fewster et al. 2017) that may exist as a result of pain in an otherwise healthy system.

717 The aim of this study was to quantify how postural stability [CoP sway velocity and area of
718 displacement and complexity (CoP SaEn)], is modified during experimental pain while performing a cognitive

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task. It was hypothesized that (i) the kind of cognitive task (more or less demanding) in a non-painful condition will not interfere with CoP sway or CoP complexity, since the system would have enough cognitive resources to overcome it; (ii) experimental pain will increase CoP sway and decrease CoP complexity, regardless the type of cognitive task performed; (iii) the presence of experimental pain while performing a difficult cognitive task will overload the cognitive resources and impair postural stability, increasing CoP sway and decreasing CoP complexity.

2. Methods

2.1. Subjects

Sixteen young adults, all university students, (to control for the effect of education level on multitasking performance (Voos et al. 2015)), participated in the experiment – 8 males (mean \pm SD: age = 26.9 \pm 2.8 years; body mass = 74.9 \pm 13.8 kg; height = 1.76 \pm 0.08 m) and 8 females (mean \pm SD: age = 27.1 \pm 2.0 years; body mass = 68.8 \pm 5.2 kg; height = 1.68 \pm 0.06 m). The exclusion criteria were body mass index above 25 kg/m², pregnancy, drug addiction, previous neurologic, musculoskeletal or mental illness, lack of ability to cooperate, current use of medications (e.g. analgesics, anti-inflammatory medicine), consumption of alcohol, caffeine, nicotine or painkillers 8 hours prior to the data collection, recent history of acute pain affecting the lower limb and/or trunk, past history of chronic pain conditions, participation in other pain trials throughout the study period. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the local Ethics Committee (N-20120077). This sample size was calculated to detect a minimum difference of 40% in the CoP area assuming type error 1 as 5% and power of 80% between the conditions before and after the induction of experimental pain. All participants gave signed informed consents prior to inclusion in the study.

2.2. Experimental protocol

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743 Since in healthy individuals approximately 70% of the information used for controlling posture
744 originates from proprioceptive systems (Peterka 2003), we controlled the effect of different footwear on
745 postural control by asking the subjects to stand barefoot during the experiment. The participants stood on
746 a triangular force plate that measures vertical forces (Good Balance System, Metitur, Jyväskylä, Finland;
747 dimensions: equilateral triangle – 800-mm; sampling frequency: 50-Hz as suggested by the International
748 Society for Posture and Gait Research Standardization Committee (Scoppa et al. 2013)). This is a valid and
749 reliable system for postural sway measurements (Era et al. 2006; Ha et al. 2014) with accuracy better than
750 11-mm for the CoP position measurement (Good Balance System User Manual). The CoP position was
751 calculated via the Good Balance Software (Metitur, Jyväskylä, Finland) which uses the weighted arithmetic
752 mean between the vertical force measured by four sensors and their corresponding position: one in each
753 corner of the force-plate and the last one in the centroid of the force-plate (Fig. 1). The rationale for using the
754 tandem position for the feet was based in previous studies showing that greater pain effects are presented
755 when posture is challenged (Hirata et al. 2013). This was important to ensure that postural stability
756 adaptations due to pain could be observed. Therefore, subjects were asked to stand in tandem position, to
757 increase postural challenge during the tasks, with the right leg behind (Fig. 1), arms hanging relaxed
758 alongside the body, and were instructed to maintain balance while looking forward. Tape markers were
759 placed on the force plate to ensure that the same foot position was maintained through all conditions. During
760 the assessment of postural control, subjects were instructed to look forward at a target positioned at eye-
761 level approximately 45-cm from the subjects to minimize the influence of the target distance on postural
762 sway (Kapoula and Lê 2006). CoP records were made under eight experimental conditions, depending on the
763 type of injection (control or painful), the dual-task (counting forward or counting backward as the less and
764 more challenging tasks, respectively), before (pre-injection) and immediately after the injection. The
765 counting forward task consisted of adding one and the counting backward was performed by subtracting
766 three, beginning from a random number. The total number of answers and the number of correct answers

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8 during each trial were recorded. The order of the injections and the order of the tasks were randomized,
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10 with the same number of subjects receiving the hypertonic or isotonic injections first.

11 The experiment always followed the same order for all participants: (i) CoP measurement while
12 performing the first randomly assigned task (cognitive task 1 or 2) over 60-s (pre-injection 1); (ii) 1-min rest;
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14 (iii) CoP measurement over 60-s while performing the second randomly assigned task (cognitive task 1 or 2)
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16 over 60-s (pre-injection 2); (iv) injections of the first saline solution (painful or control) into vastus medialis
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18 (VM) and vastus lateralis (VL) muscles; (v) assessment of pain intensity by visual analogue scale (VAS); (vi)
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20 CoP measurement over 60-s while performing task A; (vii) collecting VAS scores of the pain intensity and 1-
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22 min rest; (viii) CoP measurement over 60-s while performing task B; (ix) collecting VAS scores of the pain
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24 intensity. After the final step, the pain VAS scores were taken each minute until the pain had subsided which
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26 was followed by a 5-min break. Following the break, all steps of the experiment were performed again with
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28 the injection of the other saline solution, including new pre-injection CoP recordings. Before each CoP
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30 measurement, all subjects confirmed that no tiredness or other problems were presented. The duration of
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32 the CoP measurements were performed according to guidelines proposed by the International Society for
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34 Posture and Gait Research (Scoppa et al. 2013). Fig. 2 summarizes the study procedures along time.

35 36 2.3. Experimental muscle pain

37 Before the experiment all subjects were instructed about the nature and effects of the injections,
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39 and that one type of injection would be painful while the other would be a non-painful stimulus, although
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41 they would not know which kind of injection they would be receiving. Pain was induced through
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43 intramuscular injection of 1-mL of 6% sterile hypertonic saline solution or as a control condition 1-mL of
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45 isotonic (0.9%) saline solution (Graven-Nielsen et al. 1997; Farina 2003; Schulte et al. 2004; Falla et al. 2006).
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47 The injections were performed with a 2-mL syringe with a disposable needle (27G, 40-mm) into right VM
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49 muscle and right VL muscle. Both injections locations were marked to ensure that they were applied
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51 approximately in the same location. The VM muscle injection was performed 5-cm proximal and 5-cm medial

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791 8o the medial corner of the patella (Shiozawa et al. 2013), and in the VL muscle, injections were performed
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792 10 at two thirds of the distance from the anterior spina iliaca to the lateral side of the patella (Fig. 3). The depth
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793 12 of the injection was determined by an ultrasound scanner (LOGIQ™ S7, General Electric, USA). This pain
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794 14 model has been successfully used previously to mimic knee-related pain during quiet standing tasks
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795 16 providing moderate pain intensities for approximately five minutes (Hirata et al. 2011). Hypertonic saline
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796 18 injections have been shown to activate nociceptors around the injected site (Mense 1993) whereas the 0.9%
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797 20 isotonic saline injections have induced little or no pain during postural control tasks similar to the one used
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798 22 in the present study (Hirata et al. 2010, 2011, 2013).

799 23 2.4. Assessment of pain intensity

800 24 The subjects were asked to rate the pain intensity using a 10-cm VAS from 0-cm to 10-cm (0-cm
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801 26 means “no pain” and 10-cm means “maximum pain”) immediately after the injections and after each balance
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802 28 measurement. Therefore, three VAS scores were obtained for each set of experiments (balance
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803 30 measurements after isotonic injection and balance measurements after hypertonic injection, respectively;
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804 32 Fig. 2), and the mean values of the three VAS scores were considered as the pain intensity after each injection
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805 34 paradigm. Additionally, following each set of experiments subjects were asked to indicate the overall pain
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806 36 areas during the trials on a body chart and to respond the McGill Pain Questionnaire (Melzack 1975). The
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807 38 area of pain was extracted from the body charts with VistaMetrix 1.38 software. The pain rating index based
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808 40 on the rank values of the words chosen within each category (sensory, affective, evaluative and
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809 42 miscellaneous) from McGill Pain Questionnaire were obtained and the score for each category, as well as
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810 44 the total pain rating index were determined as the sum of the ranked values of the words (Melzack 1975).

811 45 2.5. Data analysis

812 46 All variables for postural sway were calculated based on 50-s of the standing tasks, with the first and
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813 48 last 5-s from the original 60-s time series being excluded. The analyses were performed with Matlab R2016a
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814 50 software (Mathworks, Massachusetts, USA). The area fitted to 95% confidence interval of the CoP
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8 displacement was calculated as representative of the total CoP area displacement (95% confidence interval
9 ellipse), along with the CoP velocity in both directions (anterior-posterior and medial-lateral). The structural
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11 variability of the CoP was calculated by means of SaEn with the embedding dimension (m) and the tolerance
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13 distance (r) set to $m=2$ and $r=0.2 \times \text{SD}$ (Vaillancourt and Newell 2000). All CoP variables are displayed as the
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15 difference between the values obtained immediately after the injection and the correspondent pre-injection
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17 condition. Negative values show that the CoP variable decreased after the injection of the saline solution
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19 compared to its respective pre-injection condition. Likewise, positive values show that the CoP variable
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21 increased after the injection compared to its respective pre-injection condition.

22 3.6. Statistical analysis

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24 Pain outcomes were compared between injection types (isotonic or hypertonic injections) with
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26 paired T-tests when normal distribution was present (VAS scores and pain area data) and with the Wilcoxon
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28 Signed Rank Test when the data distribution was non-normal (McGill scores). The task measures (number of
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30 answers, number of correct answers) were evaluated with a 3-way RM-ANOVA with *injection* (isotonic vs
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32 hypertonic), *time* (pre-injection vs after injection) and *task* (counting forward vs backwards) as main factors.
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34 The CoP parameters were compared with a 2-Way RM-ANOVA with *task* and *injection* as main factors, and
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36 the p-values are shown in the table 3. Bonferroni post-hoc correction for multiple comparisons was applied
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38 and p-values are shown in the results texts. The alfa-value (α) for statistical significance was set to 0.05.

39 3. Results

40 3.1 Area and amplitude of perceived pain'

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42 Fig. 4 shows the reported pain areas following both isotonic and hypertonic injections. Pain was
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44 present in the anterior and lateral portions of the thigh after both isotonic and hypertonic injections, being
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46 more concentrated in the lower half of the thigh after the isotonic injections. The hypertonic saline injections
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48 induced higher pain area (mean area \pm SD: isotonic = 518.6 ± 690.6 au; hypertonic = 1659.3 ± 1574.0 au;
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50 $P=0.003$) and higher VAS scores (mean score \pm SD: isotonic = 0.9 ± 1.1 cm; hypertonic = 4.7 ± 1.7 cm; $P<0.001$)
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8 than isotonic saline injections. Table 1 shows the scores for each class of words from McGill Pain
9 Questionnaire and the pain rating index. Subjects presented a higher total pain rating index and scored
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11 higher in all the categories, with the exception of the affective class, after the hypertonic injections ($P < 0.05$).
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13 3.2 Cognitive task performance

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15 Only for the analysis of the cognitive task performance, one subject was not included due to problems
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17 in the answers recording. The total number of answers and the number of correct answers decreased during
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19 backwards counting conditions compared with forwards counting despite the injection effect (significant
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21 main effect for *task factor*; Table 2).
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23 3.3 Center of pressure

24 Effect of experimental pain in CoP variables

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26 There were no statistical differences between the different conditions for the factor *injection* on any
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28 of the CoP variables (Table 3).
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30 Effect of cognitive task in CoP variables

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32 A main effect of *task* was found for the CoP AP-velocity ($F = 5.82$; $P = 0.028$), showing that there was an
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34 increased AP-velocity during the counting backwards task compared to the counting forwards task,
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36 regardless the type of injection (Table 3).
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38 Effect of the interaction between experimental pain and cognitive task in CoP variables

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40 An interaction effect was found between *injection* and *task* factors for CoP total area and CoP ML-
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42 velocity (CoP total $F = 7.78$, $P = 0.049$; CoP ML $F = 4.69$, $P = 0.021$) (Table 3). Post-hoc comparisons showed that
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44 both variables decreased after the hypertonic injection in comparison to the condition with isotonic injection
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46 when subjects were counting forward (Bonferroni: $P = 0.010$ for total area; $P = 0.015$ for ML-velocity). After
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48 the hypertonic injection, CoP total area increased when subjects were counting backwards in comparison to
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50 when they were counting forwards (Bonferroni: $P = 0.019$). ML-velocity showed differences between the
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862 different cognitive tasks also after the injection of hypertonic solution, with a smaller decrease of ML-velocity
863 while counting backwards (Bonferroni: $P = 0.049$).

864 **4. Discussion**

865 The present study aimed at quantifying how postural stability, represented by CoP sway (velocity and
866 area of displacement) and CoP complexity (CoP SaEn), is modified during experimental pain while performing
867 a cognitive task. The main results showed that the kind of cognitive task did not interfere with postural
868 stability in the absence of pain. Experimental pain around the knee joint reduced CoP sway but did not affect
869 CoP complexity during the performance of an easier cognitive task. During experimentally induced pain, the
870 performance of a difficult cognitive task increased CoP sway but did not change CoP complexity.

871 Pain intensity and counting performance

872 The subjects showed higher pain intensity for the hypertonic saline injection and a larger pain area
873 compared with the isotonic saline injection, as expected, indicating that experimental pain occurred (Hirata
874 et al. 2011). The McGill pain questionnaire indicated that hypertonic saline was perceived more impairing
875 than the isotonic injection in all subscales except for the affective one. It is important to note that during
876 isotonic injections subjects rated pain around 1/10, which cannot be classified as a totally pain free condition.

877 Counting performance requires the use of cognitive process which relies on the working memory of
878 the subject (Lemaire 1996), impairing motor output performance when executed simultaneously with a
879 motor task (Vuillerme and Nafati 2007). Seminowicz and Davis (2007) showed that subjects are able to
880 maintain performance of difficult cognitive task while experiencing different levels of pain. In this study, the
881 painful condition did not affect the counting performance while performing a motor task (standing still)
882 indicating that healthy subjects are able to engage multiple tasks (motor and cognitive) during pain without
883 compromising performance. This suggests that sufficient cognitive resources were available to manage the
884 cognitive process of counting forwards or backwards despite the interpretation of painful stimuli and the
885 postural control task (Eccleston et al. 1999). Finally, education level is associate with both motor and

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886 perceptual performance, where higher education level is associated with better performance (Voos et al.
887 2015). Since our subjects were all university students, we believe that bias due to education level did not
888 affect the present results.

889 Effect of cognitive tasks on postural stability

890 Our first initial hypothesis, that (i) the kind of cognitive task (more or less demanding) in a non-painful
891 condition would not interfere with CoP sway or CoP complexity, was confirmed. The factor task affected the
892 CoP anterior-posterior velocity, indicating an increased velocity during the execution of the more difficult
893 task (counting backwards) in comparison to the easier task (counting forward). Nevertheless, the CoP SaEn
894 was not affected by the kind of the performed cognitive task. These results indicate that enough cognitive
895 resources were available to overcome the demands of both cognitive and postural tasks, which was expected
896 since they were young individuals without any sensory-motor alterations.

897 Effect of experimental knee-related pain on postural stability

898 Our second initial hypothesis, that (ii) experimental pain would increase CoP sway and decrease CoP
899 complexity was not confirmed since the type of saline solution injected did not affect the CoP variables.
900 However, even though the factor *injection* did not show statistical differences between the different
901 conditions for any of the studied CoP variables, there was a difference between total area and ML-velocity
902 between the control and the painful condition when the subjects were counting forwards, i.e., in conditions
903 where the kind of cognitive task performed was the same. Interestingly, during the counting forward, the
904 type of injection resulted significant changes in postural sway (total area and ML-velocity) in opposite
905 directions: positive values of the difference between pre-injection and after injection of the isotonic solution,
906 whereas after the injection of the hypertonic solution both variables showed negative values. Additionally,
907 no significant changes were observed in the structural variability of the CoP signal. This is contrary to the
908 initial hypothesis, where an increase in postural sway and a decrease in structural variability during painful
909 conditions were expected. It is also in contrast with previous findings (Mazaheri et al. 2013) but may relate

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8 to the different position of the feet used in this study, which affects the postural sway (Day et al. 1993). The
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10 tandem feet position adopted allows less displacement of the CoP due to the limited base of support
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12 compared to side-by-side feet position, since if the subjects increase the CoP amplitude they may fall (Day
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14 et al. 1993). This also may reflect a voluntary strategy, requiring a greater amount of cognitive resources and
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16 attention (Morasso and Sanguineti 2002), attempting to avoid large excursions of the body and consequent
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18 loss of balance. For the current study, this might indicate that the subjects prioritized the balance task over
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20 the other tasks, also known as *posture first strategy* (Vuillerme and Nafati 2007). The subjects were able to
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22 reduce the postural sway without compromising the counting performance during the easy cognitive task,
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24 suggesting that the available cognitive resource was sufficient to perform the less challenging cognitive task
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26 without compromising postural stability. Therefore, these results indicate that healthy subjects have the
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28 capacity to perform easy cognitive tasks while ensuring postural stability (Siu and Woollacott 2007).
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30 Reducing postural sway might reflect a motor strategy available for healthy subjects to avoid excessive
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32 translation of the body, which could lead to balance loss (Winter 1995). This strategy was also observed
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34 during the control injection while counting backwards, probably indicating that a high cognitive load seems
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36 to be interpreted as a threat to postural stability. An alternative explanation for the contrast between the
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38 present study and the previous studies with pain patients showing larger postural sway (Schulte et al. 2004;
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40 Levinger et al. 2016) might be the pain model used that is not a complete proxy to the impaired pain patients'
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42 sensory-motor system.

43 Interactions between pain and cognitive load on postural stability

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45 Our initial third hypothesis, that (iii) the presence of experimental pain would increase CoP sway and
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47 decrease CoP complexity only when performing a difficult cognitive task was partially confirmed since CoP
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49 sway increased during pain under a difficult cognitive task, but the CoP complexity did not change. ANOVA
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51 results showed an interaction between the task and injection factors for total area and ML-velocity. After
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53 the hypertonic injection CoP total area increased and CoP ML-velocity decreased less while counting
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934 8 backwards in comparison to counting forwards condition, corroborating our hypothesis. ANOVA results also
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935 10 showed an effect of the task factor on AP-velocity with post-hoc comparisons showing a difference only
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936 12 during the hypertonic injection condition: while counting backwards AP-velocity also increased. Altogether
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937 14 these results show that CoP sway increases when performing a more demanding cognitive task in the
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938 16 presence of experimental pain. This might reflect an interference with the information-processing capacity
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939 18 and an attention disruption from both postural control and cognitive task (Eccleston et al. 1999). Previous
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940 20 studies suggest that disruptions of sensory information lead to worsening of proprioception in the affected
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941 22 area (Matre et al. 2002), further impairing postural sway (Hirata et al. 2010, 2011). The results indicate that
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942 24 the posture first strategy (Vuillerme and Nafati 2007) found during the easy cognitive task during pain is no
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943 26 longer feasible when a difficult cognitive task is performed during painful conditions. The increased cognitive
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944 28 load in painful conditions seems to impair the motor performance maybe due to insufficient cognitive
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945 30 resource to simultaneously maintain postural stability (which requires significant amount of attention
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946 32 (Morasso and Sanguineti 2002)) and execute a difficult cognitive task. These results might have important
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947 34 new implications in understanding the mechanisms related to fall accidents. Postural stability in daily life
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948 36 activities is usually performed in combination with additional tasks, for example, walking in a busy slippery
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949 38 sidewalk. These daily life activities involves simultaneously competition for the cognitive resources available
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950 40 (Woollacott and Shumway-Cook 2002) to evaluate the environment constrains in order to promote the best
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951 42 motor strategy (Winter 1995). Our present results indicate that, if the subject performs a challenging
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952 44 postural task in pain, his/her capacity for maintain balance while exposed to a difficult cognitive task is
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953 46 suboptimal, which could increase the likelihood of losing balance.

954 47 The complexity of postural sway did not show any differences between the experimental conditions.
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955 49 This result is contrary to the literature finding that young healthy subjects present a more regular and less
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956 51 automatic postural sway (decreased CoP SaEn) when the motor task is more difficult (e. g. standing with eyes
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957 53 closed) and more irregular postural sway and more automatic postural sway (increased CoP SaEn) when a
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cognitive task is added (Donker et al. 2007; Stins et al. 2009). The fact that the cognitive task did not interfere with CoP complexity may be due to the nature of both motor (standing in tandem position) and cognitive (subtraction calculus) tasks used in the experimental setup that did not interfere with the automaticity of postural control. Besides that, pain also did not affect CoP complexity, showing that experimental knee-related pain did not compromise the coupling between the components of the system responsible for balance in the current experimental setup. Future studies should investigate the interaction between pain, cognition and on CoP complexity with different motor and cognitive demands, in addition to different populations.

Despite interesting results regarding the effects of cognitive tasks in postural control during pain, the relevance of the findings for clinical populations should be interpreted with care. The experimental pain model used here is convenient to assess the effect of pain without the interference of potential structural or pathologies. However, extrapolating the current findings to an older population can only be done to some degree. Additionally, chronic pain patients may also suffer from depressive symptoms (Bair et al. 2003) or anxiety (McWilliams et al. 2003), which might increase cognitive load (Nebes et al. 2001). Furthermore, cognitive impairments are often found in chronic pain patients, decreasing the possibility to maintain performance of two or more concurrent tasks (Brauer et al. 2004), as opposed to what was observed in this study where young healthy subjects were recruited. Also, there was no recording of postural sway without any cognitive task. This would have allowed comparisons with a condition where neither pain nor cognitive tasks were influencing postural sway, and could have reduced type 2 errors given that multiple CoP variables were analyzed in the study. Thus, it can be considered a limitation to our interpretations.

5. Conclusions

Pain and cognitive task interfered on postural stability, changing its patterns. During the performance of a simple cognitive task, pain reduced postural sway, while during the performance of a more demanding cognitive task, postural sway was increased in young healthy subjects. Since our subjects were young healthy

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8 subjects, the direct translation of the present results to patients suffering from pain should be done with
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10 caution. However, these results may suggest that rehabilitation approaches should take into account that
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12 pain not only affects directly the motor system, but may occupy cognitive resources, potentially resulting in
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14 poorer performance when performing rehabilitation exercises. Additionally, rehabilitation strategies using
15
16 both motor and cognitive resources need further investigation to outline the effect of interaction between
17
18 pain and cognition on the performance during activities of daily life in patients.
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20 **Compliance with ethical standards**

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30 **REFERENCES**

- 31
32 Andersson G, Hagman J, Talianzadeh R, et al (2002) Effect of cognitive load on postural control. *Brain Res*
33 *Bull* 58:135–9
34
35 Bair MJ, Robinson RL, Katon W, Kroenke K (2003) Depression and Pain Comorbidity. *Arch Intern Med*
36 163:2433. doi: 10.1001/archinte.163.20.2433
37
38 Brauer SG, Broome A, Stone C, et al (2004) Simplest tasks have greatest dual task interference with balance
39 in brain injured adults. *Hum Mov Sci* 23:489–502. doi: 10.1016/j.humov.2004.08.020
40
41 Bronstein AM, Buckwell D (1997) Automatic control of postural sway by visual motion parallax. *Exp Brain*
42 *Res* 113:243–248. doi: 10.1007/BF02450322
43
44 Day BYBL, Steiger MJ, Thompson PD, Marsden CD (1993) Human Body Motion When Standing :
45 Implications for. *J Physiol* 469:479–499
46
47 Donker SF, Roerdink M, Grevén AJ, Beek PJ (2007) Regularity of center-of-pressure trajectories depends on
48 the amount of attention invested in postural control. *Exp Brain Res* 181:1–11. doi: 10.1007/s00221-
49 007-0905-4
50
51 Duarte M, Sternad D (2008) Complexity of human postural control in young and older adults during
52 prolonged standing. *Exp Brain Res* 191:265–276. doi: 10.1007/s00221-008-1521-7
53
54 Eccleston C, Baeyens F, Helen P, et al (1999) Pain Demands Attention : A Cognitive-Affective Model of the
55 Interruptive Function of Pain. 125:356–366
56
57 Era P, Sainio P, Koskinen S, et al (2006) Postural balance in a random sample of 7,979 subjects aged 30
58 years and over. *Gerontology* 52:204–213. doi: 10.1159/000093652
59
60
61
62
63
64
65

- 1
2
3
4
5
6
7
8 Etemadi Y, Salavati M, Arab AM, Ghanavati T (2016) Balance recovery reactions in individuals with
9 recurrent nonspecific low back pain: Effect of attention. *Gait Posture* 44:123–127. doi:
10.1016/j.gaitpost.2015.11.017
- 10
11 Falla D, Farina D, Dahl MK, Graven-Nielsen T (2006) Muscle pain induces task-dependent changes in
12 cervical agonist/antagonist activity. *J Appl Physiol* 102:601–609. doi: 10.1152/jappphysiol.00602.2006
- 13
14 Farina D (2003) Effect of Experimental Muscle Pain on Motor Unit Firing Rate and Conduction Velocity. *J*
15 *Neurophysiol* 91:1250–1259. doi: 10.1152/jn.00620.2003
- 16
17 Fewster KM, Gallagher KM, Howarth SH, Callaghan JP (2017) Low back pain development differentially
18 influences centre of pressure regularity following prolonged standing. *Gait Posture*. doi:
10.1016/j.gaitpost.2017.06.005
- 19
20 Praizer E V., Mitra S (2008) Methodological and interpretive issues in posture-cognition dual-tasking in
21 upright stance. *Gait Posture* 27:271–279. doi: 10.1016/j.gaitpost.2007.04.002
- 22
23 Graven-Nielsen T, Arendt-Nielsen L, Svensson P, Jensen TS (1997) Quantification of local and referred
24 muscle pain in humans after sequential i.m. injections of hypertonic saline. *Pain* 69:111–7
- 25
26 Ha H, Cho K, Lee W (2014) Reliability of the Good Balance System® for Postural Sway Measurement in
27 Poststroke Patients. *J Phys Ther Sci* 26:121–124. doi: 10.1589/jpts.26.121
- 28
29 Harbourne RT, Stergiou N (2003) Nonlinear analysis of the development of sitting postural control. *Dev*
30 *Psychobiol* 42:368–377. doi: 10.1002/dev.10110
- 31
32 Hirata RP, Arendt-Nielsen L, Graven-Nielsen T (2010) Experimental calf muscle pain attenuates the postural
33 stability during quiet stance and perturbation. *Clin Biomech* 25:931–937. doi:
10.1016/j.clinbiomech.2010.06.001
- 34
35 Hirata RP, Ervilha UF, Arendt-Nielsen L, Graven-Nielsen T (2011) Experimental muscle pain challenges the
36 postural stability during quiet stance and unexpected posture perturbation. *J Pain* 12:911–919. doi:
10.1016/j.jpain.2011.02.356
- 37
38 Hirata RP, Jørgensen TS, Rosager S, et al (2013) Altered Visual and Feet Proprioceptive Feedbacks during
39 Quiet Standing Increase Postural Sway in Patients with Severe Knee Osteoarthritis. *PLoS One* 8:1–8.
doi: 10.1371/journal.pone.0071253
- 40
41 Huxhold O, Li SC, Schmiedek F, Lindenberger U (2006) Dual-tasking postural control: Aging and the effects
42 of cognitive demand in conjunction with focus of attention. *Brain Res Bull* 69:294–305. doi:
10.1016/j.brainresbull.2006.01.002
- 43
44 Kahneman D (1973) *Attention and effort*. Prentice-Hall
- 45
46 Kapoula Z, Lê TT (2006) Effects of distance and gaze position on postural stability in young and old subjects.
47 *Exp Brain Res* 173:438–445. doi: 10.1007/s00221-006-0382-1
- 48
49 Knoop J, Van Der Leeden M, Van Der Esch M, et al (2012) Association of lower muscle strength with self-
50 reported knee instability in osteoarthritis of the knee: Results from the Amsterdam Osteoarthritis
51 Cohort. *Arthritis Care Res* 64:38–45. doi: 10.1002/acr.20597
- 52
53 Kuczyński M, Szymańska M, Bieć E (2011) Dual-task effect on postural control in high-level competitive
54 dancers. *J Sports Sci* 29:539–545. doi: 10.1080/02640414.2010.544046
- 55
56 Larivière C, Butler H, Sullivan MJL, Fung J (2013) An exploratory study on the effect of pain interference and
57 attentional interference on neuromuscular responses during rapid arm flexion movements. *Clin J Pain*
58
59
60
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65

- 1
2
3
4
5
6
7
8 29:265–275. doi: 10.1097/AJP.0b013e318250ed6f
- 9
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47
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53
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55
56
57
58
59
60
61
62
63
64
65
- 054 29:265–275. doi: 10.1097/AJP.0b013e318250ed6f
- 055 Lemaire P (1996) The Role of Working Memory Resources in Simple Cognitive Arithmetic. *Eur J Cogn*
056 *Psychol* 8:73–104. doi: 10.1080/095414496383211
- 057 Levinger P, Nagano H, Downie C, et al (2016) Biomechanical balance response during induced falls under
058 dual task conditions in people with knee osteoarthritis. *Gait Posture* 48:106–112. doi:
059 10.1016/j.gaitpost.2016.04.031
- 060 Griston MB, Bergmann JH, Keating N, et al (2014) Postural prioritization is differentially altered in healthy
061 older compared to younger adults during visual and auditory coded spatial multitasking. *Gait Posture*
062 39:198–204. doi: 10.1016/j.gaitpost.2013.07.004
- 063 Madeleine P, Nielsen M, Arendt-Nielsen L (2011) Characterization of postural control deficit in whiplash
064 patients by means of linear and nonlinear analyses - A pilot study. *J Electromyogr Kinesiol* 21:291–297.
065 doi: 10.1016/j.jelekin.2010.05.006
- 066 Manor B, Costa MD, Hu K, et al (2010) Physiological complexity and system adaptability: evidence from
067 postural control dynamics of older adults. *J Appl Physiol* 109:1786–1791. doi:
068 10.1152/jappphysiol.00390.2010
- 069 Matre D, Arendt-Nielsen L, Knardahl S (2002) Effects of localization and intensity of experimental muscle
070 pain on ankle joint proprioception. *Eur J Pain* 6:245–260. doi: 10.1053/eujp.2002.0332
- 071 Mazaheri M, Coenen P, Parnianpour M, et al (2013) Low back pain and postural sway during quiet standing
072 with and without sensory manipulation: A systematic review. *Gait Posture* 37:12–22. doi:
073 10.1016/j.gaitpost.2012.06.013
- 074 Mazaheri M, Heidari E, Mostamand J, et al (2014) Competing effects of pain and fear of pain on postural
075 control in low back pain? *Spine (Phila Pa 1976)* 39:E1518–E1523. doi:
076 10.1097/BRS.0000000000000605
- 077 McWilliams LA, Cox BJ, Enns MW (2003) Mood and anxiety disorders associated with chronic pain: an
078 examination in a nationally representative sample. *Pain* 106:127–33
- 079 Melzack R (1975) The McGill Pain Questionnaire: major properties and scoring methods. *Pain* 1:277–99
- 080 Mense S (1993) Nociception from skeletal muscle in relation to clinical muscle pain. *Pain* 54:241–89
- 081 Morasso PGP, Sanguineti V (2002) Ankle muscle stiffness alone cannot stabilize balance during quiet
082 standing. *J Neurophysiol* 88:2157–2162. doi: 10.1152/jn.00719.2001
- 083 Nebes RD, Butters MA, Houck PR, et al (2001) Dual-task performance in depressed geriatric patients.
084 *Psychiatry Res* 102:139–151. doi: 10.1016/S0165-1781(01)00244-X
- 085 Pellecchia GL (2003) Postural sway increases with attentional demands of concurrent cognitive task. *Gait*
086 *Posture* 18:29–34. doi: 10.1016/S0966-6362(02)00138-8
- 087 Peterka RJ (2003) Dynamic Regulation of Sensorimotor Integration in Human Postural Control. *J*
088 *Neurophysiol* 91:410–423. doi: 10.1152/jn.00516.2003
- 089 Richman JS, Moorman JR (2000) Physiological time-series analysis using approximate entropy and sample
090 entropy Physiological time-series analysis using approximate entropy and sample entropy. *Am Physiol*
091 *Soc*
- 092 Schulte E, Ciubotariu A, Arendt-Nielsen L, et al (2004) Experimental muscle pain increases trapezius muscle

- 1
2
3
4
5
6
7
8 activity during sustained isometric contractions of arm muscles. *Clin Neurophysiol* 115:1767–1778.
9 doi: 10.1016/j.clinph.2004.03.005
- 10
11 Scoppa F, Capra R, Gallamini M, Shiffer R (2013) Clinical stabilometry standardization. Basic definitions -
12 Acquisition interval - Sampling frequency. *Gait Posture* 37:290–292. doi:
13 10.1016/j.gaitpost.2012.07.009
- 14
15 Seminowicz DA, Davis KD (2007) Interactions of pain intensity and cognitive load: The brain stays on task.
16 *Cereb Cortex* 17:1412–1422. doi: 10.1093/cercor/bhl052
- 17
18 Sherafat S, Salavati M, Takamjani IE, et al (2014) Effect of dual-tasking on dynamic postural control in
19 individuals with and without nonspecific low back pain. *J Manipulative Physiol Ther* 37:170–179. doi:
20 10.1016/j.jmpt.2014.02.003
- 21
22 Shiozawa S, Hirata RP, Graven-Nielsen T (2013) Reorganised anticipatory postural adjustments due to
23 experimental lower extremity muscle pain. *Hum Mov Sci* 32:1239–1252. doi:
24 10.1016/j.humov.2013.01.009
- 25
26 Siu KC, Woollacott MH (2007) Attentional demands of postural control: The ability to selectively allocate
27 information-processing resources. *Gait Posture* 25:121–126. doi: 10.1016/j.gaitpost.2006.02.002
- 28
29 Slifkin AB, Newell KM (1999) Noise, information transmission, and force variability. *J Exp Psychol Hum*
30 *Percept Perform* 25:837–851. doi: 10.1037//0096-1523.25.3.837
- 31
32 Søndergaard KHE, Olesen CG, Søndergaard EK, et al (2010) The variability and complexity of sitting postural
33 control are associated with discomfort. *J Biomech* 43:1997–2001. doi:
34 10.1016/j.jbiomech.2010.03.009
- 35
36 Stins JF, Michielsen ME, Roerdink M, Beek PJ (2009) Sway regularity reflects attentional involvement in
37 postural control: Effects of expertise, vision and cognition. *Gait Posture* 30:106–109. doi:
38 10.1016/j.gaitpost.2009.04.001
- 39
40 Swan L, Otani H, Loubert P V. (2007) Reducing postural sway by manipulating the difficulty levels of a
41 cognitive task and a balance task. *Gait Posture* 26:470–474. doi: 10.1016/j.gaitpost.2006.11.201
- 42
43 Vaillancourt DE, Newell KM (2002) Changing complexity in human behavior and physiology through aging
44 and disease. *Neurobiol Aging* 23:1–11. doi: 10.1016/S0197-4580(02)00052-0
- 45
46 Vaillancourt DE, Newell KM (2000) The dynamics of resting and postural tremor in Parkinson's disease. *Clin*
47 *Neurophysiol* 111:2046–2056. doi: 10.1016/S1388-2457(00)00467-3
- 48
49 Van Daele U, Hagman F, Truijten S, et al (2010) Decrease in postural sway and trunk stiffness during
50 cognitive dual-task in nonspecific chronic low back pain patients, performance compared to healthy
51 control subjects. *Spine (Phila Pa 1976)* 35:583–589. doi: 10.1097/BRS.0b013e3181b4fe4d
- 52
53 Van Ryckeghem DM, Van Damme S, Eccleston C, Crombez G (2018) The efficacy of attentional distraction
54 and sensory monitoring in chronic pain patients: A meta-analysis. *Clin Psychol Rev* 59:16–29. doi:
55 10.1016/j.cpr.2017.10.008
- 56
57 Veldhuijzen DS, Kenemans JL, De Bruin CM, et al (2006) Pain and attention: Attentional disruption or
58 distraction? *J Pain* 7:11–20. doi: 10.1016/j.jpain.2005.06.003
- 59
60 Voos MC, Piemonte MEP, Castelli LZ, et al (2015) Association between Educational Status and Dual-Task
61 Performance in Young Adults. *Percept Mot Skills* 120:416–437. doi: 10.2466/22.PMS.120v18x8
- 62
63 Vuillerme N, Nafati G (2007) How attentional focus on body sway affects postural control during quiet
64
65

1
2
3
4
5
6
7
8 standing. Psychol Res 71:192–200. doi: 10.1007/s00426-005-0018-2
9
10 Winter DA (1995) A. B. C. (Anatomy, Biomechanics, Control) of Balance During Standing and Walking.
11 Waterloo Biomechanics, Ontario
12
13 Woollacott M, Shumway-Cook A (2002) Attention and the control of posture and gait: A review of an
14 emerging area of research. Gait Posture 16:1–14. doi: 10.1016/S0966-6362(01)00156-4
15
16
17
18
19
20
21
22
23
24
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Figure captions

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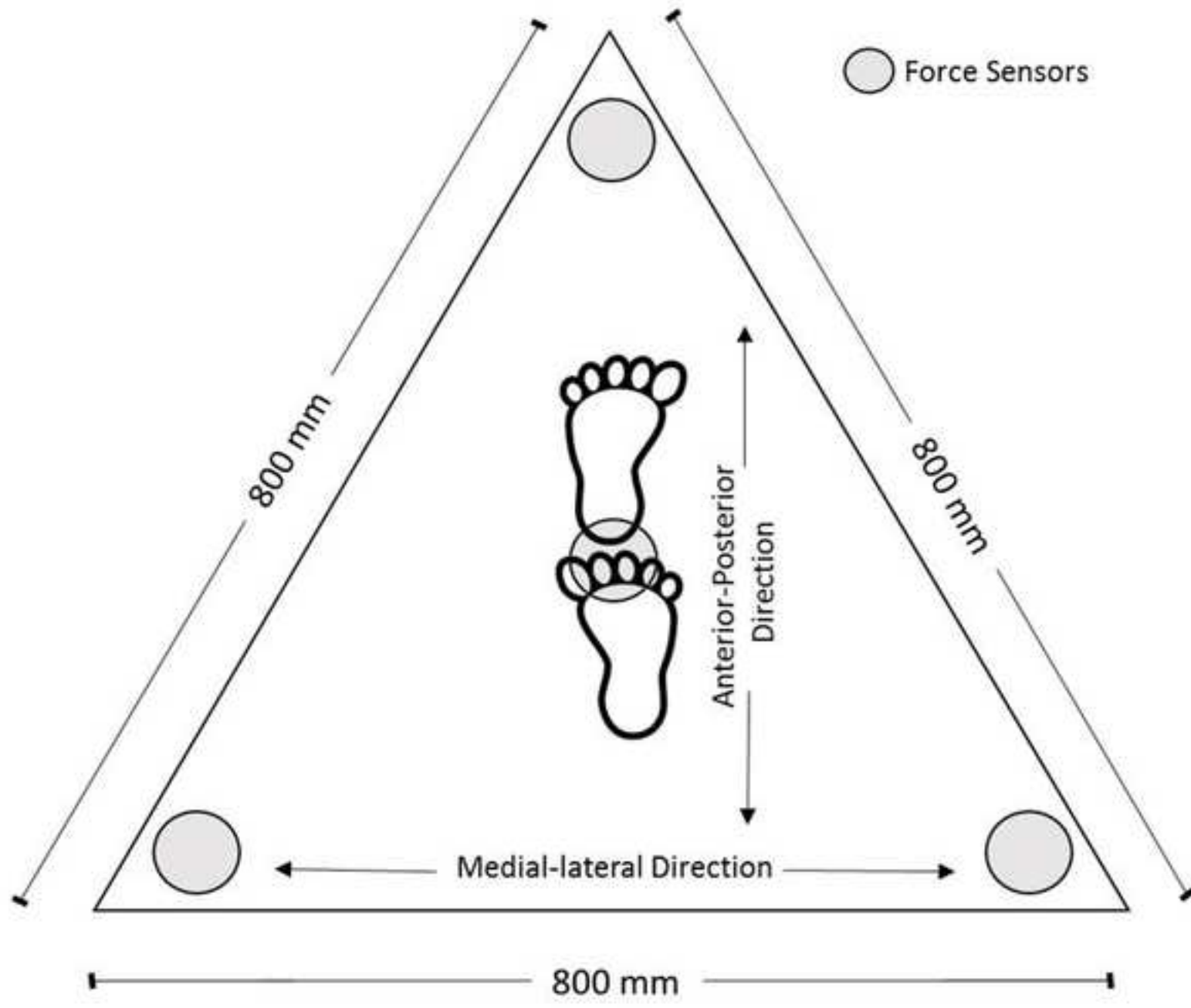
Fig 1 Schematic drawing representing the force platform size, sensor locations, and the tandem position of the subjects during the experiment

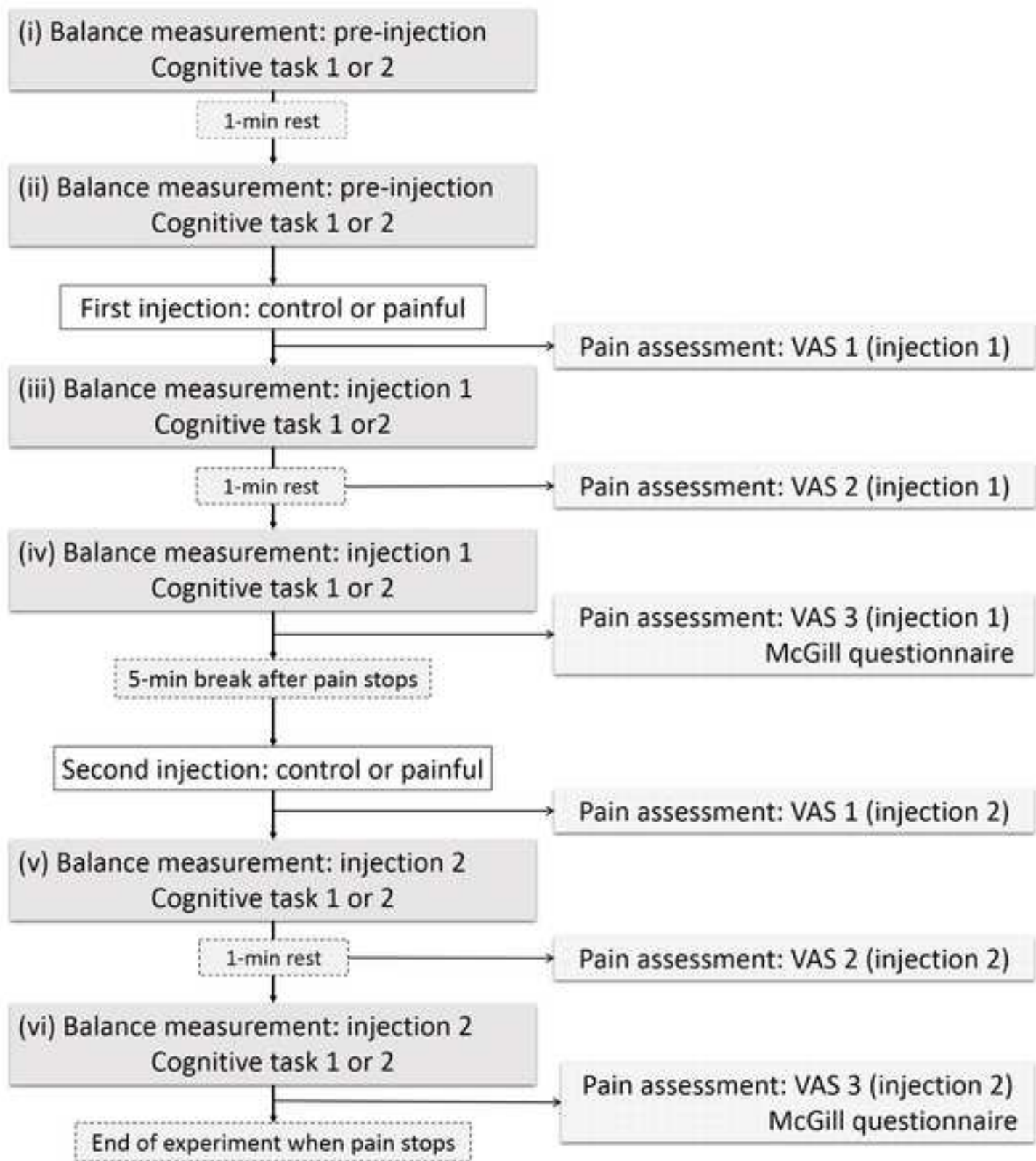
Fig 2 Study design overview: pain assessments were performed immediately after each injection and each balance measurement; the order of the saline injections was randomized in a balanced way

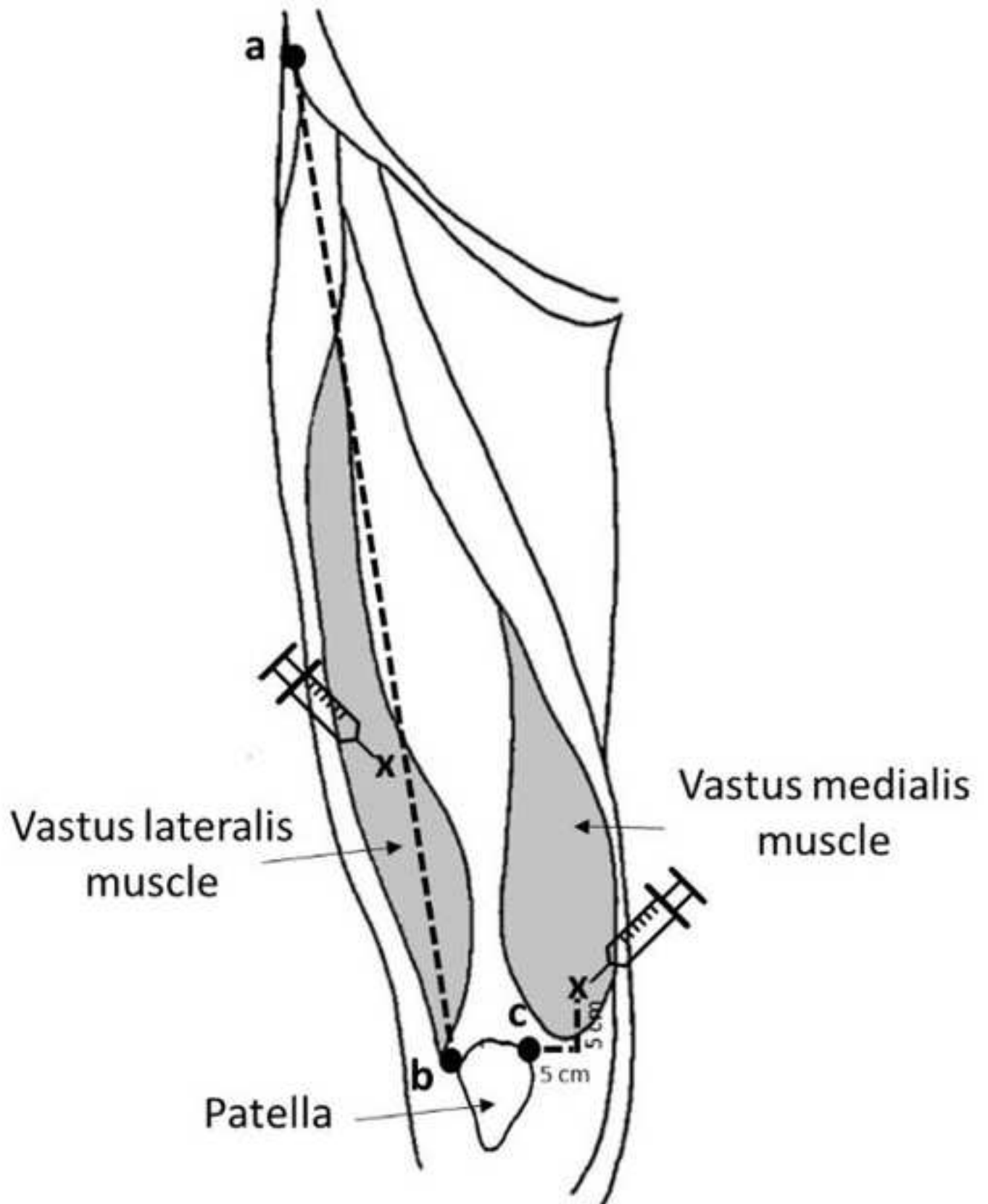
Fig 3 Injections sites for vastus lateralis muscle, performed at two thirds of the distance from the anterior spina iliaca (a) to the lateral side of the patella (b); and for the vastus medialis muscle, performed 5 cm proximal and 5 cm medial to the medial corner of the patella (c),

Fig 4 Representation of the experimental pain distribution reported areas after isotonic (top, blue in the online version) and hypertonic (bottom, red in the online version saline injections (A); the individual distributions are superimposed in the anatomical drawings

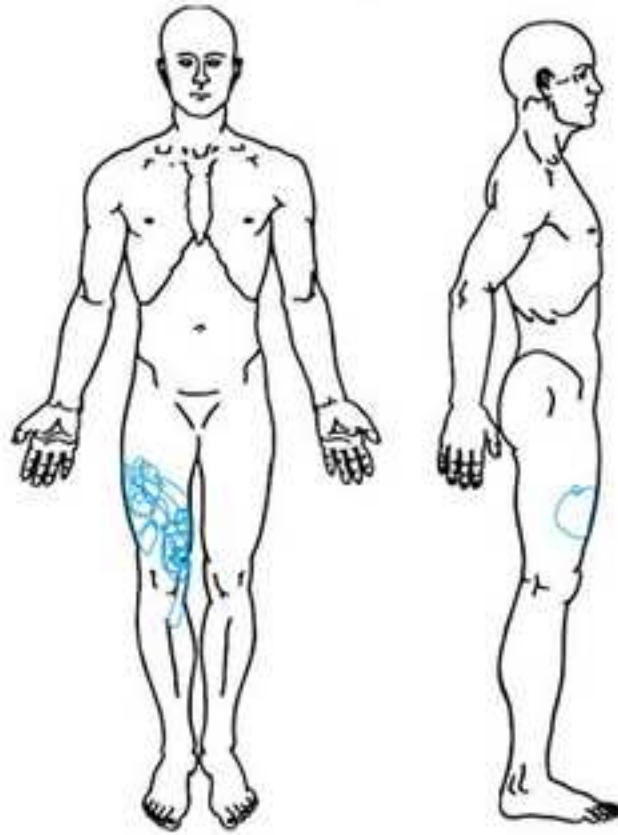
Figure 1







Isotonic injection



Hypertonic injection

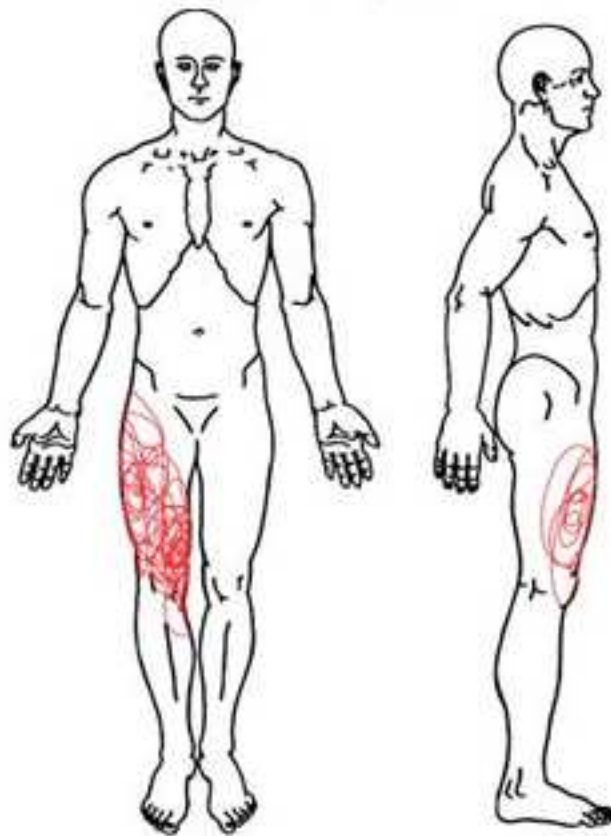


Table 1 – McGill Pain Questionnaire scores (median [Range]) for each category and total pain rating index for the pain experienced after isotonic and hypertonic injections.

McGill scores	Injection		P-value
	Isotonic	Hypertonic	
Sensory	1 [0-18]	8.5 [2-23]*	0.023
Affective	0 [0-7]	0 [0-4]	0.174
Evaluative	0 [0-1]	1.5 [0-4]*	0.001
Miscellaneous	0 [0-7]	2.5 [0-10]*	0.004
Total pain rating index	2.5 [0-33]	16 [5-30]*	0.001

*Statistically significant ($P < 0.05$) higher than isotonic condition (Wilcoxon Signed Rank Test with Bonferroni correction).

Table 2 – Mean (\pm SD) of the cognitive tasks performances before and during both injections type (hypertonic and isotonic) and three-way repeated measures ANOVA results (F; P).

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Task performance	Condition	Cognitive task		ANOVA (F; P value)			
		Counting forward	Counting backward	Time	Injection	Task	Time x Injection x Task
Total answers	Before control injection	63.3 \pm 7.5	31.3 \pm 13.5				
	After control injection	63.5 \pm 8.1	30.4 \pm 15.0	0.05; 0.833	0.22; 0.644	68.0; <0.001*	0.28; 0.608
	Before painful injection	63.3 \pm 10.4	32.1 \pm 12.7				
	After painful injection	63.3 \pm 9.1	32.3 \pm 12.7				
Total correct answers	Before control injection	63.3 \pm 7.5	30.9 \pm 13.9				
	After control injection	63.5 \pm 8.1	29.8 \pm 8.1	0.05; 0.819	0.06; 0.815	64.8; <0.001*	0.39; 0.540
	Before painful injection	63.3 \pm 10.4	30.9 \pm 14.2				
	After painful injection	63.3 \pm 9.0	31.3 \pm 13.5				

* Statistically significant ($P < 0.05$).

Table 3 – Mean (\pm SD) of center of pressure (CoP) variables represented as the difference between the measures after and before each injection (isotonic injection considered as control, hypertonic injection considered as painful) and two-way repeated measures ANOVA results (F; *P*).

CoP Variable	Control injection		Painful injection		ANOVA (F; <i>P</i> value)		
	Counting forward	Counting backward	Counting forward	Counting backward	Injection	Task	Injection x task
Total area (cm ²)	28.9\pm78.5^a	-25.1 \pm 138.7	84.5\pm145.5^{a,b}	12.8\pm53.9^b	1.84; 0.196	0.75; 0.400	7.78; 0.049*
AP Velocity (cm/s)	-0.36 \pm 2.24	-0.07 \pm 1.66	-0.39 \pm 1.82	1.07 \pm 2.35	0.61; 0.446	5.92; 0.028*	1.168; 0.614
ML Velocity (cm/s)	0.98\pm1.93^{c,d}	-0.73\pm2.23^d	-1.71\pm2.61^{c,e}	-0.34\pm1.92^e	3.90; 0.067	6.68; 0.697	4.69; 0.021*
AP SaEn (a. u.)	0.007 \pm 0.067	0.003 \pm 0.089	0.041 \pm 0.081	0.001 \pm 0.048	0.73; 0.406	1.51; 0.238	1.01; 0.331
ML SaEn (a. u.)	0.019 \pm 0.050	0.003 \pm 0.038	0.004 \pm 0.045	0.104 \pm 0.052	0.12; 0.116	0.12; 0.738	0.10; 0.755

* Statistically significant ($P < 0.05$). ^{a, b, c, d, e} Statistically significant difference between conditions detected in post-hoc tests ($P < 0.05$).

Author Contribution Statement

RPH, TP, NV and TGN conceived and designed research. EYS and TP conducted experiments. EYS and RPH analyzed data. EYS, RPH, ICNS, TP, NV and TGN wrote the manuscript. All authors read and approved the manuscript.