

1 Influence of experimental pain on the spatio-temporal activity of upper trapezius during  
2 dynamic lifting – an investigation using Bayesian spatio-temporal ANOVA

Bernard X.W. Liew<sup>1</sup>, Yu (Ryan) Yue<sup>2</sup>, Corrado Cescon<sup>3</sup>, Marco Barbero<sup>3</sup>, Deborah Falla<sup>1</sup>

**Affiliations:**

<sup>1</sup> Centre of Precision Rehabilitation for Spinal Pain (CPR Spine), School of Sport, Exercise and Rehabilitation Sciences, College of Life and Environmental Sciences, University of Birmingham, Birmingham, United Kingdom

<sup>2</sup> Paul H. Chook Department of Information Systems and Statistics, Zicklin School of Business, Baruch College, The City University of New York, United States

<sup>3</sup> Rehabilitation Research Laboratory 2rLab, Department of Business Economics, Health and Social Care, University of Applied Sciences and Arts of Southern Switzerland, Manno

3 **Address for reprint requests and other correspondence:** Bernard Liew, School of  
4 Sport, Exercise and Rehabilitation Sciences, Centre of Precision Rehabilitation for Spinal  
5 Pain (CPR Spine), College of Life and Environmental Sciences, University of  
6 Birmingham, Birmingham, United Kingdom; E-mail: [LiewB@adf.bham.ac.uk](mailto:LiewB@adf.bham.ac.uk);  
7 [liew\\_xwb@hotmail.com](mailto:liew_xwb@hotmail.com). Tel: +44 121 415 8526

8

9     **Abstract**

10     High-density surface electromyography (HDsEMG) provides a detailed analysis of a  
11     muscle's spatial distribution of activity. We applied a Bayesian spatio-temporal statistical  
12     method to quantify how acute nociception and task repetition alters the upper trapezius  
13     instantaneous spatial distribution of activity during dynamic muscular contractions. Ten  
14     male adults performed repeated lifting of a 1 kg box between shelves positioned at hip and  
15     shoulder heights with a cycle time of 3 s for 50 cycles under four conditions: baseline,  
16     isotonic and hypertonic saline injections (nociception) to the right upper trapezius, and 15  
17     minutes post injection. Activity of the right upper trapezius was measured using a 64-  
18     channel surface electrode grid. Statistical inference was performed using Integrated Nested  
19     Laplace Approximations (INLA), and significance was determined by a non-zero crossing  
20     of the Bayesian 95% credible intervals (CrI). The maximal decrease in activity after  
21     nociception was  $-38.1\mu\text{V}$  [95% CrI  $-40.9$  to  $-35.3$ ] at 30% of the lift cycle when compared  
22     to baseline. The maximal reduction in muscle activity between the early and later phases  
23     of lifting in the presence of nociception was by  $10.4\mu\text{V}$  [95% CrI  $8.2$  to  $12.6$ ]. A more  
24     holistic understanding of muscle behaviour is achieved using spatio-temporal inference  
25     than traditional reductionist methods.

26     **Keywords:** Pain, Electromyography, Motor control, Spatio-temporal, Bayesian

27

## 28 **1. Introduction**

29 High-density surface electromyography (HDsEMG) has been increasingly used to  
30 study how pain (Falla et al., 2017), fatigue (Abboud et al., 2016), and repetitive task  
31 execution (Samani et al., 2017) alter the spatial distribution of EMG amplitude. Changes in  
32 the spatial distribution of EMG amplitude reflect a variety of physiological (mal) adaptations.  
33 For example, the spatial distribution of intra-muscular activity may reflect the intrinsic  
34 variation of motor neuron activity for load distribution (Martinez Valdes et al., 2018); a non-  
35 uniform distribution of nociceptive input to motor neurons (Dideriksen et al., 2016); and a  
36 strategy to sustain consistent force outputs (Falla and Farina, 2008a). Intra-muscular  
37 coordination of the upper trapezius has been widely investigated, since this muscle is  
38 commonly implicated in the development of musculoskeletal pain and fatigue syndromes  
39 (Falla et al., 2017, Samani et al., 2017).

40 Excitation of nociceptors within the upper trapezius muscle via injection of  
41 hypertonic saline, has been shown to shift the barycentre of muscle activity caudally (Falla et  
42 al., 2009, Falla et al., 2017, Madeleine et al., 2006, Dideriksen et al., 2016). Whether motor  
43 adaptations to a noxious stimulus is specific to the site of nociception remains unclear (Falla  
44 et al., 2009, Gallina et al., 2018, Hug et al., 2013). For instance, a caudal shift in barycentre  
45 of upper trapezius activity occurred regardless of the site of nociception within the muscle  
46 (Falla et al., 2009, Dideriksen et al., 2016). At the vastus medialis, the region with the  
47 greatest reduction in EMG amplitude was at the site of nociception (Gallina et al., 2018);  
48 whereas Hug et al. (Hug et al., 2013) reported that the reduction in discharge rate of soleus  
49 motor units was greatest in the region of nociception, but this was not observed in all  
50 participants. It is evident from the topographical EMG amplitude maps of the two studies  
51 (Falla et al., 2009, Gallina et al., 2018), that different sites of nociception could change the  
52 spatial distribution of muscle activity differently. For example, a cranial injection to the upper

53 trapezius appear to reduce cranial muscle activity only, whilst a caudal injection to the same  
54 muscle appear to reduce muscle activity (albeit non-symmetrically) in both the cranial and  
55 caudal muscle regions (Falla et al., 2009).

56         Inconsistency in defining the nature of motor adaptations relative to the site of  
57 noxious stimulation could be due to a myriad number of plausible surface EMG spatial  
58 distribution patterns bringing about similar shifts in the barycentre. The sensitivity of  
59 inferring a complex spatial EMG distribution from its barycentre may also depend on the  
60 physical dimension and number of channels within the electrode grid. To understand the  
61 spatial distribution of EMG amplitude driving a change in the position of the barycentre,  
62 researchers have qualitatively drawn on observations from topographical EMG amplitude  
63 maps.

64         It is also unclear if the effect of nociception on the spatial distribution within the upper  
65 trapezius remains consistent during a repetitive dynamic task. Experimental pain induced a  
66 caudal shift in the barycentre of the upper trapezius during an isometric contraction, and this  
67 caudal shift persisted for the entire duration of the contraction (60 to 90s) (Falla et al., 2009,  
68 Madeleine et al., 2006). Although Falla et al. (Falla et al., 2017) collected EMG data over 50  
69 lifting repetitions, the authors did not investigate whether adaptations of the upper trapezius  
70 during nociceptor excitation changed across repetitions of this dynamic motor task. However,  
71 there is evidence from a pain-free cohort that repetitive dynamic movements resulted in a  
72 significant lateral shift of the upper trapezius's barycentre of activity (Samani et al., 2017).  
73 Knowing if motor adaptations to nociception is magnified or reduced by repeated  
74 performance is fundamental towards understanding the mechanisms related to the  
75 development of work-related neck-shoulder disorders.

76 HDsEMG data has a spatial component due to the two-dimensional coordinate system of  
77 the electrode grid. Since muscle activity is assessed across time, there is also a temporal  
78 component (Falla et al., 2017, Madeleine et al., 2006). Spatio-temporal HDsEMG has always  
79 been summarized into discrete metrics, such as the barycentre. In the present study, a discrete  
80 variable is one which has only magnitude and no space/time information. Although analysing  
81 spatio-temporal data in a discrete form does not provide a comprehensive understanding of  
82 physiological mechanisms, an advantage is that it allows for simpler statistical inference  
83 methods (e.g. Analysis of Variance [ANOVA]). However, performing statistical inference on  
84 discrete HDsEMG data is not without problems. As the number of repeated tests increases,  
85 either the inflation of the familywise Type I error rate gets severely inflated when no efforts  
86 are made to control the familywise error rate, or the statistical power diminishes when an  
87 attempt is made to control the familywise error rate.

88 In the present study, Bayesian spatio-temporal ANOVA (Wang et al., 2018, Yu et al.,  
89 2018) was used to perform a secondary analysis on previously published data investigating  
90 the influence of experimentally induced upper trapezius muscle pain on spatio-temporal  
91 activity of the upper trapezius during a repeated lifting task (Falla et al., 2017). The aim of  
92 the present study was to quantify the spatial distribution of upper trapezius activity that  
93 accounts for the reported shifts in its barycentre of activity under nociception (Falla et al.,  
94 2017). Three hypotheses are proposed: First, hypertonic saline injection to the cranial portion  
95 of the upper trapezius would only reduce muscle activity in the cranial region of the muscle  
96 (Falla et al., 2009). Second, the reduction in cranial muscle activity after hypertonic saline  
97 injection would be symmetrical in the medial-lateral direction (Falla et al., 2017). Third,  
98 hypertonic saline injection would reduce the activity of the lateral portion of the upper  
99 trapezius more during the early than later phase of lifting (Samani et al., 2017) - findings not  
100 observed in the original study (Falla et al., 2017).

## 101 **2. Methods**

### 102 2.1. Design, participants, task

103 This was a secondary analysis of a previously published study, where full details of the  
104 experimental procedures have been previously reported (Falla et al., 2017). The study was  
105 approved by the local Ethics Committee (#200538), conducted according to the Declaration  
106 of Helsinki and all participants provided written informed consent prior to their study  
107 inclusion. Ten healthy male volunteers with a mean (standard deviation [sd]) age, height and  
108 weight of 26.2 (3.1) years old, 1.78 (0.06) m, and 71.3 (9.2) kg, respectively, participated and  
109 all participants completed the study.

110 Participants attended a single laboratory session and were required to lift a 1 kg box  
111 between shelves positioned at hip and shoulder height, with a cycle time of 3 s for 50 cycles.  
112 An acoustic signal from a digital metronome was provided to the subjects during the task to  
113 standardize the duration of cycles. Subjects repeated the task four times: (1) baseline no  
114 injection, (2) isotonic saline (0.9%) injection to the cranial portion of right upper trapezius,  
115 (3) hypertonic saline (5.8%) injection to the same portion of the upper trapezius, and (4)  
116 recovery (15 mins post hypertonic injection). The order of conditions was not randomized.  
117 The rest interval between the repetitions was set to 15 minutes starting from the moment  
118 when the pain caused by the injections disappeared. Subjects practiced the movement  
119 sequence for ~1 min without the weight prior to data recording.

120 The experimental muscle pain was induced by injection (27G cannula) of 0.4 ml sterile  
121 hypertonic saline (5.8%) into the upper division of the trapezius on the right side with the  
122 subject seated. Isotonic saline (0.4 ml, 0.9 %) was used as a control injection in a similar  
123 location. The location of the injection was defined as 15 mm cranial to the line between the  
124 acromion and the spinous process of the seventh cervical vertebra. The bolus was injected

125 over a 10-s period. The isotonic saline injection was given first however participants were  
126 blinded to each injection and were told that one or both might be painful.

## 127 2.2. HDsEMG

128 HDsEMG signals were recorded from the right upper trapezius using a 64-electrode  
129 adhesive electrode grid (ELSCH64NM3, OT Bioelettronica, Torino, Italy) (Figure 1). The 64  
130 electrodes were arranged in a 13 row by 5 column grid (1mm diameter, 8mm inter-electrode  
131 distance), with an absent electrode in the upper right corner. The electrode grid was placed  
132 with the fourth row along the line between the lateral edge of the acromion and C7, with the  
133 lateral column 10 mm distant from the innervation zone (Falla et al., 2017). The injections  
134 were performed lateral to the electrode grid (~ 10 mm) and corresponded to the 4th row of  
135 the grid.

136 EMG signals were amplified 2000 times and sampled at 2048 Hz (EMGUSB2, OT  
137 Bioelettronica, Torino, Italy). Four accelerometers were positioned on the box and the four  
138 signals were averaged to produce a single signal, which was subsequently rectified and  
139 filtered (low pass, 2<sup>nd</sup> order Butterworth at 10 Hz). A 50m/s<sup>2</sup> threshold on the filtered  
140 accelerometer signal was used to identify the contact instants of the box with each of the 2  
141 shelves, to obtain the beginning and end time points of a lifting repetition.

## 142 2.3. Signal processing

143 HDsEMG signals were filtered with a 2<sup>nd</sup> order Butterworth band-pass filter (10 – 400Hz).  
144 Each lift cycle was discretized into ten 10% time epochs. Single differential channels were  
145 extracted from each pair of electrodes in the horizontal direction, resulting in a 13 x 4 grid of  
146 51 bipolar channels, with one missing channel on the upper right corner. The single  
147 differential method was used to reduce the non-propagating components such as end of fibre  
148 effects, which is a common procedure in surface EMG processing. RMS values from each

149 differential channel were calculated for each 10% epoch. This produced a 10 x 51 (time by  
 150 channels) matrix of RMS values for each participant, condition, and each lifting repetition.  
 151 Twelve participant-condition combinations had less than 50 repetitions of HDsEMG data,  
 152 due to significant signal artefacts present within the accelerometer signals, precluding the  
 153 identification of a lifting repetition. The minimum number of lifting repetitions available was  
 154 39. Thirty-eight available repetitions were used from each participant and condition to allow  
 155 pairwise difference in EMG signals to be computed (see below). Lifting repetitions were  
 156 dichotomized into “early phase” (first 19 available repetitions) and “later phase” (second 19  
 157 available repetitions).

#### 158 2.4. Outcome variables

159 There were six outcome variables, with the first three being:

$$\Delta EMG_{i=1,2,3}^{early} = EMG_{hypertonic} - EMG_{baseline,isotonic,recovery} \quad (1)$$

160 where  $\Delta EMG_{i=1}^{early}$ ,  $\Delta EMG_{i=2}^{early}$ ,  $\Delta EMG_{i=3}^{early}$  represented the difference in the 10x51 matrix  
 161 values of EMG RMS ( $\mu V$ ) at each epoch between hypertonic saline injection vs baseline,  
 162 hypertonic vs isotonic injections, and hypertonic injection vs recovery during the early lift  
 163 phase, respectively. A negative  $\Delta EMG_{i=1,2,3}^{early}$  indicated a reduction in EMG amplitude with the  
 164 hypertonic saline injection, relative to its comparator. The other three outcomes were:

$$\Delta EMG_{phase}^{i=1,2,3} = \Delta EMG_{later}^{i=1,2,3} - \Delta EMG_{early}^{i=1,2,3} \quad (2)$$

165 where  $\Delta EMG_{phase}^{i=1,2,3}$  represented the difference in the 10x51 matrix values of EMG RMS  
 166 ( $\mu V$ ) at each epoch between the later and early phase of lifting. If  $\Delta EMG_{early}^{i=1,2,3}$  is negative,  
 167 than a positive  $\Delta EMG_{phase}^{i=1,2,3}$  indicates a greater reduction in EMG amplitude in the early than  
 168 later phase.



169 2.5. Statistical inference

170 A two-way mixed-effects spatio-temporal ANOVA model with a random subject-intercept  
171 of the form was fitted,

$$y_i = \eta(x_i) + b_{g_i} + e_i \text{ for } i = 1, \dots, n \quad (3)$$

172 where  $n$  is the total number of data points for all participant-condition combinations after  
173 converting the data into a column vector,  $y_i$  is the  $\Delta EMG$  in equations (1) and (2),  $x_i =$   
174  $(t_i, s_i)$  is the fixed effect of lifting cycle ( $t_i$ ) and spatial location of the electrode grid ( $s_i$ ),  $g_i$   
175 is the subject indicator,  $b_{g_i}$  is the random effect such that  $b_{g_i} \sim^{iid} N(0, \delta)$  with  $\delta > 0$ , and  
176  $e_i \sim^{iid} N(0, \sigma^2)$  is the random error.  $t_i$  represents the 10 epochs of the lifting cycle, whilst  $s_i$   
177 represents the 51 bipolar channels. The predictor  $\eta$  can be further decomposed into main and  
178 interaction effects as follows:

$$\eta(x_i) = \eta_1(t_i) + \eta_2(s_i) + \eta_{12}(t_i, s_i) \quad (4)$$

179 where  $\eta_1$  is the main temporal effect of lifting cycle,  $\eta_2$  is the main spatial effect of  
180 electrode grid location, and  $\eta_{12}$  is the spatio-temporal interaction effect. We fitted model (3)  
181 under a fully Bayesian framework. For the  $\eta_1$  main temporal effect, a first order  
182 autoregressive (AR1) prior was used (Wang et al., 2018). For the spatial effect  $\eta_2$ , a  
183 stochastic partial differential equation (SPDE) spatial prior was used. For the interaction  
184 effect  $\eta_{12}$ , a separable spatio-temporal prior was used (Cameletti et al., 2013).

185 The resulting Bayesian mixed model can be efficiently estimated using integrated nested  
186 Laplace approximations (INLA) (Wang et al., 2018). INLA provides accurate approximated  
187 posterior distributions of all parameters (e.g.  $\beta$  coefficients) given the data, needed to make  
188 fully Bayesian inference (i.e. posterior mean with credible intervals [CrI]). The technical  
189 details of INLA can be found in the supplementary material. For the main and interaction

190 effects, we calculated the posterior joint probabilities for a change in any EMG channel  
191 across the electrode grid to produce a topographical map of probabilities (Bolin and  
192 Lindgren, 2015). The probability map provides useful visualization of the certainty of where  
193 and when any EMG amplitude changes occur. To quantify the magnitude of EMG changes  
194 on all spatial locations and across the lifting cycles, and to determine if these changes were  
195 significant, the mean and 95% CrI was calculated. Significant changes were defined within a  
196 Bayesian framework, by a non-zero crossing of the 95% CrI. We provide the data, code, and  
197 results in a public repository (Liew et al., 2018).

### 198 **3. Results**

#### 199 3.1. Comparing pairwise injection conditions during early lift phase

##### 200 3.1.1. Main and interaction effects

201 There were significant spatial main and spatial-temporal interaction effects in EMG  
202 changes. To clarify, a spatial main effect is the influence of different EMG channel locations  
203 on EMG values (independent of lifting cycle); temporal main effect is the influence of  
204 different lifting cycles on EMG values (independent of channel location); and spatio-  
205 temporal interaction is the influence of different EMG channel locations at each lifting cycle  
206 on the EMG values. At the spatial main effect level, there was a  $> 0.95$  probability that EMG  
207 changes were present between hypertonic saline injection and isotonic saline injection, and  
208 recovery conditions largely in the cranial half of the electrode grid (Fig. 2). At the interaction  
209 level, the period with the greatest number of spatial locations with  $> 0.95$  probability of EMG  
210 changes was at 30% lift cycle between hypertonic injection-baseline conditions, 30% lift  
211 cycle between hypertonic-isotonic saline injections, and 30% between hypertonic injection-  
212 recovery conditions (Fig. 3).

##### 213 3.1.2. *Effect size of EMG RMS change ( $\mu V$ )*

214 The maximal decrease in EMG RMS within the electrode grid after hypertonic saline  
215 injection was  $-38.1\mu\text{V}$  [95% CrI  $-40.9$  to  $-35.3$ ] at 30% lift cycle when compared to baseline  
216 (Fig. 4). The maximal decrease in EMG RMS within the electrode grid after hypertonic saline  
217 injection was  $-28.8\mu\text{V}$  [95% CrI  $-31.4$  to  $-26.2$ ] at 30% lift cycle when compared to recovery  
218 (Fig. 4). The maximal increase in EMG RMS within the electrode grid after hypertonic saline  
219 injection was  $6.7\mu\text{V}$  [95% CrI  $4.1$  to  $-9.3$ ] at 80% of the lift cycle and this was compared to  
220 the recovery condition (Fig. 4).

### 221 3.2. *Influence of lift phase on the effects of hypertonic injection*

#### 222 3.2.1. *Main and interaction effects*

223 There were significant spatial main and spatial-temporal interaction effects in EMG  
224 changes between lifting phases. At the spatial main effect level, there was a  $> 0.95$   
225 probability that the effects of hypertonic saline injection changed between the early and later  
226 lifting phases, independent of lifting cycle (Fig. 5). At the interaction level, the period with  
227 the greatest number of spatial locations with  $> 0.95$  probability of EMG changes happening  
228 between lifting phases was at 80% lift cycle between hypertonic injection-baseline  
229 conditions, 80% lift cycle between hypertonic-isotonic saline injections, and 40% lift cycle  
230 between hypertonic injection-recovery conditions (Fig. 6).

#### 231 3.2.2. *Effect size of EMG RMS change ( $\mu\text{V}$ )*

232 The reduction in EMG activity with hypertonic saline injection was predominantly greater  
233 during the early than in the later lifting phase, although there were some spatial locations  
234 where the reduction was less in the early than later lifting phase (Fig. 7). The maximal  
235 difference in EMG RMS reduction within the electrode grid during the early phase after  
236 hypertonic saline injection was  $10.4\mu\text{V}$  [95% CrI  $8.2$  to  $12.6$ ] more than the later phase at

237 80% lift cycle when compared to baseline; and by  $5.8\mu\text{V}$  [95% CrI 3.6 to 8.0] more than the  
238 later phase at 20% lift cycle when compared to recovery (Fig. 7).

#### 239 **4. Discussion**

240 The main aim of the present study was to quantify the spatial distribution of upper  
241 trapezius activity under nociception that accounts for the reported shifts in its barycentre of  
242 activity. The Bayesian spatio-temporal ANOVA method used presently revealed three new  
243 findings which partially supported our hypotheses. First, an acute noxious stimulus to the  
244 cranial upper trapezius reduced muscle activity within the same muscle region, and slightly  
245 increased activity in the caudal-most portion of the muscle. Second, there was a greater  
246 reduction of muscle activity detected on the medial compared to the lateral part of the  
247 recording surface during acute nociception. Third, differences in the effects of acute  
248 nociception between lifting phases predominantly lay in the cranial-caudal axis, rather than in  
249 the medial-lateral axis.

250 The present study provides evidence that the intra-muscular adaptation to acute  
251 nociception may be specific to the site of nociceptive stimulus (Gallina et al., 2018). Such an  
252 adaptation may be aimed at mechanically unloading the painful muscle region (Gallina et al.,  
253 2018). Location specific responses to acute nociception was observed in a previous study  
254 (Gallina et al., 2018), but not others (Dideriksen et al., 2016, Falla et al., 2009). Dideriksen et  
255 al. (Dideriksen et al., 2016) reported that the regional discharge rate of motor units of the  
256 upper trapezius was similar regardless of nociception site. Dideriksen et al. (Dideriksen et al.,  
257 2016) identified cranial motor units from the cranial six rows of the electrode grid, whilst  
258 caudal motor units were identified from the caudal six rows. The smaller the spatial  
259 separation of the motor units' sources, the more homogeneous will be their behaviour (Falla  
260 et al., 2017). However, the spatial correlation between extracted motor units were not

261 considered during statistical inference, which may negatively influence the statistical model's  
262 validity (Dideriksen et al., 2016).

263 This is the first study to quantify the influence of acute nociception on the instantaneous  
264 spatial activity change of the upper trapezius. The periods of greatest reduction in amplitude  
265 of the cranial region of the upper trapezius during acute nociception lay within periods when  
266 the cranial region was most active (20% to 70% of lifting cycle). This may be an optimal  
267 motor strategy to unload painful tissues as this represents a phase within the lifting cycle  
268 when mechanical load on the muscle would be greatest. The influence of acute nociception  
269 on a muscle's spatial distribution of activity appears to differ between dynamic and isometric  
270 contractions. Sustained isometric contraction results in greater activity within the cranial  
271 region of the upper trapezius (Madeleine et al., 2006, Falla et al., 2008). This increase in  
272 muscle activity may augment tissue loading to the cranial region of the muscle. To reduce  
273 pain associated with hypertonic saline injection, more activity should be reduced in the  
274 cranial region of the upper trapezius as the contraction duration increases to mechanically  
275 unload this region. This would mean observing a greater caudal shift in the upper trapezius  
276 barycentre as isometric contraction duration increases in the presence of nociception. Instead,  
277 previous studies observe that that caudal shift in the upper trapezius's barycentre remains  
278 constant regardless of isometric contraction duration (Madeleine et al., 2006, Falla et al.,  
279 2008).

280 The mechanisms explaining why nociception reduced muscle activity more when there  
281 was higher versus lower baseline amplitude is unclear. It may be that pain intensity was  
282 greatest between 20% to 70% of the lifting cycle, resulting in greater inhibition on the  
283 motoneuron pool (Farina et al., 2004). However, subjective pain recordings within a  
284 movement cycle in a repetitive dynamic task are difficult to collect. Alternatively, the  
285 inhibition to the recruited motoneurons of the upper trapezius may remain invariant, but the

286 central excitability to the motorneurons may depend on the shoulder elevation angle. The  
287 relationship between central excitability of a muscle and shoulder elevation angles, has been  
288 shown for the infraspinatus (Lin et al., 2015), but not for the upper trapezius.

289 The medial-lateral coordinate of the upper trapezius's barycentre was reported to remain  
290 invariant with acute nociception (Falla et al., 2017, Madeleine et al., 2006, Dideriksen et al.,  
291 2016). The barycentre approach decomposes the shift in the centroid of muscle activity along  
292 two Cardinal axes within the plane of the electrode grid. The present study observed greater  
293 medial than lateral reductions of the EMG amplitude in the cranial two thirds of the upper  
294 trapezius with acute nociception. This means that the shift in the centroid of muscle activity  
295 under nociception would be caudal-laterally rather than purely within the longitudinal axis of  
296 the grid.

297 The reductive effect of acute nociception on muscle activity was greater in the early, than  
298 later lifting phases, which was most apparent in the cranial upper trapezius. Based on the  
299 mechanical unloading hypothesis (Gallina et al., 2018), additional muscle activity to sustain  
300 lifting ought to be recruited from the caudal upper trapezius, which has no noxious stimulus  
301 induced. It appears that compensatory motor adaptations associated with repetitive task  
302 performance and pain are competing in dynamic motor tasks. Speculatively, the caudal upper  
303 trapezius may receive more inhibitory afferent input, due to the accumulation of local  
304 extracellular potassium ions associated with prolonged contractions (Falla and Farina,  
305 2008b). In addition, pain was decreasing from its maximum intensity in the later lifting phase  
306 (Falla et al., 2017). Given the greater nociceptive afferent distribution to the cranial than  
307 caudal region (Dideriksen et al., 2016), the reduction in pain intensity may preferentially  
308 reduce the inhibitory afferent input to the former compared to the latter region of the upper  
309 trapezius. It is unknown if compensatory neuromuscular adaptations associated with

310 repetitive task performance (including fatigue) and pain are competing in dynamic motor  
311 tasks in clinical pain conditions.

312 This current work has several limitations. First, it was previously reported that acute  
313 nociception resulted in a similar caudal shift of the barycentre of upper trapezius activity  
314 between genders (Falla et al., 2008). Instead, the difference between genders lie in the  
315 interaction between nociceptive stimulation and fatigue, on the neuromuscular adaption of the  
316 upper trapezius (Falla et al., 2008). Given that only male participants were presently  
317 investigated, the influence of task repetition on the intramuscular adaptations observed with  
318 acute nociception should be generalized to female participants with caution.

319 Second, an injection was performed at a single location only in the present study. This  
320 limits the ability to conclude if intramuscular adaptations to nociception are dependent on the  
321 site of noxious stimulation within the upper trapezius. Nevertheless, the present study  
322 provides a specific intramuscular “signature” of how the upper trapezius activity shifts  
323 caudally relative to a specific site of nociception. Such knowledge, and indeed the proposed  
324 statistical method, is essential for future study designs where multiple sites of injection are  
325 used to investigate a muscle’s response to the site of nociceptive activity.

326 Third, changes in EMG amplitudes during dynamic contractions could be attributed to  
327 alterations in muscle geometry (Farina et al., 2001). The influence of altered muscle  
328 geometry on EMG activation cannot be eliminated but may be mitigated by averaging the  
329 EMG signals across lifting cycles (Farina et al., 2001). By including subject-level random  
330 effects into our statistical models, we simultaneously performed two procedures: (1)  
331 estimating a weighted average effect of acute nociception on EMG alterations per participant,  
332 and (2) using each participant’s weighted average effect to estimate the overall group-level  
333 effect of acute nociception on the muscle’s activity.

334 5. Conclusions

335 Motor adaptations to acute nociception appears to be region-specific in the upper  
336 trapezius, with a greater medial than lateral reduction in muscle activity. There also appears  
337 to be competing motor adaptations induced by nociception and repetitive task performance.  
338 Hence, mechanical unloading of painful tissues does not solely drive the motor adaptations  
339 observed with acute nociception during low-load lifting. The methods used in the present  
340 study provides a robust statistical inference method for spatio-temporal data, allowing a  
341 richer mechanistic insight into the motor adaptations that occur in response to pain

342 **Acknowledgements**

343 None

344

345



346

## Appendix

### 347 **Integrated nested Laplace approximation (INLA) method**

348 Rue et al. (Rue et al., 2009) developed INLA for approximate Bayesian inference as an  
 349 alternative to traditional Markov chain Monte Carlo methods. The INLA framework can  
 350 be briefly described as follows. First of all,  $\mathbf{y} = (y_1, \dots, y_n)$  is a vector of observed  
 351 variables and the mean  $\mu_i$  (for observation  $y_i$ ) is linked to the linear predictor  $\eta_i$ . The  
 352 linear predictor can include terms such as fixed effect covariates and different types of  
 353 random effects (e.g. spatial or temporal correlated effects, random intercepts, smoothing  
 354 splines etc.). The vector of all latent effects will be denoted by  $\mathbf{x}$ , and it includes the linear  
 355 predictor and the various random effects previously mentioned. In addition, the  
 356 distribution of  $\mathbf{y}$  will depend on some vector of hyperparameters  $\theta_1$ .

357 The distribution of the vector of latent effects  $\mathbf{x}$  is assumed to be Gaussian Markov random  
 358 field (GMRF). This GMRF will have a zero mean and precision matrix  $\mathbf{Q}(\theta_2)$  (inverse of  
 359 covariance matrix), with  $\theta_2$  a vector of hyperparameters. The vector of all hyperparameters  
 360 in the model will be denoted by  $\theta = (\theta_1, \theta_2)$ .

361

362 The aim of the INLA methodology is to approximate the posterior marginals of the model  
 363 effects ( $\mathbf{x}$ ) and hyperparameters ( $\theta$ ). This is achieved by exploiting the computational  
 364 properties of GMRF and the Laplace approximation for multidimensional integration.

365

366 The joint posterior distribution of the effects and hyperparameters can be expressed as:

$$\begin{aligned} \pi(\mathbf{x}, \theta | \mathbf{y}) &\propto \pi(\theta) \pi(\mathbf{x} | \theta) \prod_{i \in I} \pi(y_i | x_i, \theta) \\ &\propto \pi(\theta) |\mathbf{Q}(\theta)|^{\frac{1}{2}} \exp \left\{ -\frac{1}{2} \mathbf{x}^T \mathbf{Q}(\theta) \mathbf{x} + \sum_{i=1}^{n_y} \log(\pi(y_i | x_i, \theta)) \right\} \end{aligned}$$

367

368 Notation has been simplified by using  $\mathbf{Q}(\theta)$  to represent the precision matrix of the latent  
 369 effects. Also,  $|\mathbf{Q}(\theta)|$  denotes the determinant of that precision matrix.  $n_y$  denotes the vector  
 370 of values of the response variable.

371

372 The computation of the marginal distributions for the latent effects and hyperparameters  
 373 can be done considering that

$$\pi(x_i | \mathbf{y}) = \int \pi(x_i | \theta, \mathbf{y}) \pi(\theta | \mathbf{y}) d\theta$$

374 and

$$\pi(\theta_j | \mathbf{y}) = \int \pi(\theta | \mathbf{y}) d\theta_{-j}$$

375 Note how in both expressions integration is done over the space of the hyperparameters  
 376 and that a good approximation to the joint posterior distribution of the hyperparameters is  
 377 required.

378 To approximate  $\pi(\theta | \mathbf{y})$ , we use the Laplace approximation:

$$\tilde{\pi}(\theta|\mathbf{y}) \propto \frac{\pi(\mathbf{x}, \theta | \mathbf{y})}{\tilde{\pi}_G(\mathbf{x}|\theta, \mathbf{y})} \Big|_{x=x^*(\theta)}$$

379 Where  $\tilde{\pi}_G(\theta|\mathbf{y})$  is the Gaussian approximation to  $\pi(\theta|\mathbf{y})$ , and  $x^*(\theta)$  is the mode of  $\mathbf{x}$  for  
 380 a given configuration of  $\theta$ .

381 Rue et al. (Rue et al., 2009) approximate  $\pi(\mathbf{x}|\mathbf{y})$  using:

$$\tilde{\pi}(x_i|\mathbf{y}) = \sum_k \tilde{\pi}(x_i|\theta_k, \mathbf{y}) \times \tilde{\pi}(\theta_k|\mathbf{y}) \times \Delta_k$$

382 Here,  $\Delta_k$  are the weights associated with a vector of values  $\theta_k$  of the hyperparameters in a  
 383 grid.

384 The approximation  $\tilde{\pi}(\theta_k|\mathbf{y})$  can take different forms and be computed in different  
 385 ways. Rue et al. (Rue et al., 2009) discuss how this approximation should be in order to  
 386 reduce the numerical error.

387

388

389

391 **References**

- 392 Abboud, J., Nougrou, F., Lardon, A., Dugas, C. & Descarreaux, M. 2016. Influence of  
 393 Lumbar Muscle Fatigue on Trunk Adaptations during Sudden External Perturbations.  
 394 *Front Hum Neurosci*, 10, 576, doi: 10.3389/fnhum.2016.00576.
- 395 Bolin, D. & Lindgren, F. 2015. Excursion and contour uncertainty regions for latent Gaussian  
 396 models. *J R Stat Soc Series B Stat Methodol*, 77, 85-106, doi: doi:10.1111/rssb.12055.
- 397 Cameletti, M., Lindgren, F., Simpson, D. & Rue, H. 2013. Spatio-temporal modeling of  
 398 particulate matter concentration through the SPDE approach. *Adv Stat Anal*, 97, 109-  
 399 131, doi: 10.1007/s10182-012-0196-3.
- 400 Dideriksen, J. L., Holobar, A. & Falla, D. 2016. Preferential distribution of nociceptive input  
 401 to motoneurons with muscle units in the cranial portion of the upper trapezius muscle.  
 402 *J Neurophysiol*, 116, 611-8, doi: 10.1152/jn.01117.2015.
- 403 Falla, D., Arendt-Nielsen, L. & Farina, D. 2008. Gender-specific adaptations of upper  
 404 trapezius muscle activity to acute nociceptive stimulation. *Pain*, 138, 217-25, doi:  
 405 10.1016/j.pain.2008.04.004.
- 406 Falla, D., Arendt-Nielsen, L. & Farina, D. 2009. The pain-induced change in relative  
 407 activation of upper trapezius muscle regions is independent of the site of noxious  
 408 stimulation. *Clin Neurophysiol*, 120, 150-7, doi: 10.1016/j.clinph.2008.10.148.
- 409 Falla, D., Cescon, C., Lindstroem, R. & Barbero, M. 2017. Muscle Pain Induces a Shift of the  
 410 Spatial Distribution of Upper Trapezius Muscle Activity During a Repetitive Task: A  
 411 Mechanism for Perpetuation of Pain With Repetitive Activity? *Clin J Pain*, 33, 1006-  
 412 1013, doi: 10.1097/ajp.0000000000000513.
- 413 Falla, D. & Farina, D. 2008a. Motor units in cranial and caudal regions of the upper trapezius  
 414 muscle have different discharge rates during brief static contractions. *Acta Physiol*  
 415 (*Oxf*), 192, 551-8, doi: 10.1111/j.1748-1716.2007.01776.x.
- 416 Falla, D. & Farina, D. 2008b. Non-uniform adaptation of motor unit discharge rates during  
 417 sustained static contraction of the upper trapezius muscle. *Exp Brain Res*, 191, 363-  
 418 70, doi: 10.1007/s00221-008-1530-6.
- 419 Farina, D., Arendt-Nielsen, L., Merletti, R. & Graven-Nielsen, T. 2004. Effect of  
 420 experimental muscle pain on motor unit firing rate and conduction velocity. *J*  
 421 *Neurophysiol*, 91, 1250-9, doi: 10.1152/jn.00620.2003.
- 422 Farina, D., Merletti, R., Nazzaro, M. & Caruso, I. 2001. Effect of joint angle on EMG  
 423 variables in leg and thigh muscles. *IEEE Eng Med Biol Mag*, 20, 62-71,
- 424 Gallina, A., Salomoni, S. E., Hall, L. M., Tucker, K., Garland, S. J. & Hodges, P. W. 2018.  
 425 Location-specific responses to nociceptive input support the purposeful nature of  
 426 motor adaptation to pain. *Pain*, 159, 2192-2200, doi:  
 427 10.1097/j.pain.0000000000001317.
- 428 Hug, F., Hodges, P. W. & Tucker, K. J. 2013. Effect of pain location on spatial reorganisation  
 429 of muscle activity. *J Electromyogr Kinesiol*, 23, 1413-20, doi:  
 430 10.1016/j.jelekin.2013.08.014.
- 431 Liew, B., Yu, Y., Cescon, C., Barbero, M. & Falla, D. 2018. HDsEMG data analysis using R-  
 432 INLA. *Mendeley Data*, v1, DOI <http://dx.doi.org/10.17632/8hdb83vdt.1>, doi:  
 433 <http://dx.doi.org/10.17632/8hdb83vdt.1>.
- 434 Lin, Y. L., Christie, A. & Karduna, A. 2015. Excitability of the infraspinatus, but not the  
 435 middle deltoid, is affected by shoulder elevation angle. *Exp Brain Res*, 233, 1837-43,  
 436 doi: 10.1007/s00221-015-4255-3.

- 437 Madeleine, P., Leclerc, F., Arendt-Nielsen, L., Ravier, P. & Farina, D. 2006. Experimental  
438 muscle pain changes the spatial distribution of upper trapezius muscle activity during  
439 sustained contraction. *Clin Neurophysiol*, 117, 2436-45, doi:  
440 10.1016/j.clinph.2006.06.753.
- 441 Martinez Valdes, E., Negro, F., Falla, D., De Nunzio, A. M. & Farina, D. 2018. Surface EMG  
442 amplitude does not identify differences in neural drive to synergistic muscles. *J Appl*  
443 *Physiol* (1985), doi: 10.1152/jappphysiol.01115.2017.
- 444 Rue, H., Martino, S. & Chopin, N. 2009. Approximate Bayesian inference for latent Gaussian  
445 models by using integrated nested Laplace approximations. *J R Stat Soc Series B Stat*  
446 *Methodol*, 71, 319-392, doi: doi:10.1111/j.1467-9868.2008.00700.x.
- 447 Samani, A., Srinivasan, D., Mathiassen, S. E. & Madeleine, P. 2017. Variability in spatio-  
448 temporal pattern of trapezius activity and coordination of hand-arm muscles during a  
449 sustained repetitive dynamic task. *Exp Brain Res*, 235, 389-400, doi: 10.1007/s00221-  
450 016-4798-y.
- 451 Wang, X., Yu, Y. & Faraway, J. 2018. *Bayesian Regression Modeling with INLA*, Boca  
452 Raton, FL, Chapman and Hall/CRC.
- 453 Yu, Y., Bolin, D., Rue, H. & Wang, X. 2018. Bayesian Generalized Two-way ANOVA  
454 Modeling for Functional Data Using INLA. *Statistica Sinica*, doi:  
455 10.5705/ss.202016.0055.
- 456