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1 **TITLE**

2 Regulation of primary afferent depolarization and homosynaptic post-activation depression during passive and
3 active lengthening, shortening and isometric conditions

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24 **ABSTRACT**

25 *Purpose* This study aimed to determine whether the modulation of primary afferent depolarization (PAD) and
26 homosynaptic post-activation depression (HPAD) are involved in the lower efficacy of Ia-afferent- α -motoneuron
27 transmission commonly observed during lengthening compared to isometric and shortening conditions.

28 *Methods* 15 healthy young individuals participated in two experimental sessions dedicated to measurement in
29 passive and active muscle states, respectively. In each session, PAD, HPAD and the efficacy of Ia-afferent- α -
30 motoneuron transmission were evaluated during lengthening, shortening and isometric conditions. PAD was
31 evaluated with D1 inhibition technique. Posterior tibial nerve stimulation was used to study HPAD and the
32 efficacy of the Ia-afferent- α -motoneuron transmission through the recording of the soleus Hoffmann reflex (H
33 reflex).

34 *Results* PAD was increased in lengthening than shortening (11.2%) and isometric (12.3%) conditions regardless
35 of muscle state ($P < 0.001$). HPAD was increased in lengthening than shortening (5.1%) and isometric (4.2%)

36 conditions in the passive muscle state ($P < 0.05$), while no difference was observed in the active muscle state. H
37 reflex was lower in lengthening than shortening (-8.2%) and isometric (-12.6%) actions regardless of muscle
38 lengths ($P < 0.001$).

39 *Conclusion* These results highlight the specific regulation of PAD and HPAD during lengthening conditions.
40 However, the differences observed during passive lengthening compared to shortening and isometric conditions
41 seem to result from an increase in Ia afferent discharge, while the variations highlighted during active
42 lengthening might come from polysynaptic descending pathways involving supraspinal centres that could
43 regulate PAD mechanism.

44
45 **KEYWORDS**

46 Muscle; H reflex; presynaptic inhibition; eccentric; concentric; electrical nerve stimulation; D1 inhibition.

47
48 **ABBREVIATIONS**

49

ANOVA	Analysis of variance
EMG	Electromyography
HPAD	Homosynaptic post-activation depression
H reflex	Hoffmann reflex
MVC	Maximal voluntary contraction
PSI	Presynaptic inhibition
PAD	Primary afferent depolarization
SOL	Soleus

50
51
52

53 INTRODUCTION

54
55 The eccentric modality is commonly used in sports and rehabilitation. Indeed, one of the advantages of
56 training based on eccentric contractions concerns the neuromuscular adaptations that it induces. These seems to
57 be greater than those observed following concentric and/or isometric training (Aagaard et al. 2000; Guilhem et
58 al. 2016). However, in human, it is now well established that neuromuscular output during lengthening is down-
59 regulated compared to shortening or isometric contractions. This has been evidenced by a reduction in voluntary
60 activation level (Doguet et al. 2017), electromyographic (EMG) activity (Westing et al. 1991; Komi et al. 2000;
61 Pasquet et al. 2000; Aagaard et al. 2000; Babault et al. 2003), and motor unit discharge rate (Linnao et al.
62 2003). Therefore, understanding the physiological mechanisms underlying the specific neural control of muscles
63 during lengthening contractions is of interest to optimize its practical use.

64
65 Corticospinal and spinal reflex pathways have been mostly investigated to determine the neurological
66 origin of such specific neural control during lengthening contractions (Duchateau and Enoka 2008).
67 Corticospinal excitability is reduced during lengthening compared with shortening and isometric contractions,
68 regardless of contraction intensity (Duclay et al. 2014). This reduction was not attributable to a greater cortical
69 inhibition, as demonstrated by a shorter duration of the cortical silent period following motor evoked potentials
70 during muscle lengthening (Duclay et al. 2011). It is now well established that modulation of corticospinal
71 excitability observed during muscle lengthening is mainly attributable to inhibition acting at the α -motoneuron
72 level (Duclay et al. 2014).

73
74 The efficacy of Ia-afferent- α -motoneuron transmission is also reduced by muscle lengthening whether
75 at rest (Pinniger et al. 2001; Duclay and Martin 2005) or during submaximal (Pinniger et al. 2001; Duclay and
76 Martin 2005) or maximal (Duclay and Martin 2005; Duclay et al. 2011) contractions. This reduction has been
77 associated with an increased recurrent inhibition (post-synaptic mechanism) (Barrué-Belou et al. 2018, 2019). It
78 has been hypothesized that this reduction could also be attributed, at least in part, to presynaptic inhibition (PSI)
79 mechanisms acting at the termination of the Ia afferent fibres (Romanò and Schieppati 1987; Abbruzzese et al.
80 1994; Pinniger et al. 2001; Nordlund et al. 2002; Duclay and Martin 2005; Duclay et al. 2011, 2014; Grosprêtre
81 et al. 2014).

82
83 PSI is produced by two mechanisms: i) PAD through inhibitory interneurons that mediate Ia PSI
84 (Rudomin and Schmidt 1999), and ii) HPAD due to an activity-dependent reduction in neurotransmitter release
85 at the Ia terminals (Hultborn et al. 1987). It is frequently assumed that PAD is controlled by supraspinal
86 command and modulated continuously during muscle activity through the discharge of the group Ia and II
87 afferents that originates from muscle spindles (Pierrot-Deseilligny and Burke 2005). Indeed this regulatory
88 mechanism would prevent α -motoneuron hyperactivity by increasing the activity of inhibitory interneurons,
89 reducing the efficiency of Ia- α -motoneurons transmission during muscle lengthening (Burke et al. 1978; Hulliger
90 et al. 1985; Pinniger et al. 2001; Nordlund et al. 2002; Duclay and Martin 2005; Duclay et al. 2011, 2014).
91 Experimental data are needed to provide evidence on the effect of lengthening contractions on PAD.

93 Because HPAD regulates the neurotransmitter release in the Ia- α -motoneuron synapse, it also has the
94 potential to be involved in the reduced efficacy of Ia- α -motoneuron transmission during muscle lengthening.
95 One study previously examined HPAD during passive and active lengthening and shortening conditions
96 (Nordlund et al. 2004). The authors found that HPAD reduces the efficacy of Ia- α -motoneuron transmission
97 during active shortening, active and passive lengthening, but not during passive shortening. However, they did
98 not directly compare the effect of muscle conditions (lengthening and shortening) in passive and active states.
99 Besides, the methodology used in the work of Nordlund et al. (2004) differed from that observed in previous
100 studies of the HPAD phenomenon, such as the choice of stimulation intensity, which did not allow optimal
101 observation of HPAD modulation. In view of the importance of such a mechanism in regulating efficacy of Ia-
102 afferent- α -motoneuron transmission, it seems necessary to combine the study of PAD with HPAD. This
103 association would provide a comprehensive view of PSI mechanisms during active and passive lengthening,
104 shortening and isometric conditions.

105

106 This study aimed to determine the modulation of PAD and HPAD during lengthening, shortening and
107 isometric conditions. We hypothesized that both PAD and HPAD are specifically modulated during passive and
108 active lengthening compared to shortening and isometric conditions.

109 **METHODS**

110 **Participants**

111 Fifteen adults (11 males and 4 females; age: 24 ± 4 years; height: 177 ± 8 cm; weight: 73 ± 12 kg)
112 without any history of neurological injuries or diseases gave written informed consent to participate in this study.
113 Approval for the project was obtained from the Ethics Committee on Non-interventional Research of the
114 University of Nantes (n°12102021). All procedures used in this study were conformed with the Declaration of
115 Helsinki (last modified in 2013). Moreover, all participants were asked to avoid any strenuous exercise for 48 h
116 before testing sessions.

117 **Study design**

118 All individuals participated in two experimental sessions, separated by at least ten days. During each
119 visit, muscles lengthening, shortening, and isometric were randomized among participants. The first session (≈ 2
120 h, passive session) was split into two parts. During the first part, H reflex (H_{50}) was evaluated at rest during
121 lengthening, shortening, and isometric conditions for soleus (SOL). In the second part PSI (PAD and HPAD)
122 was evaluated in passive state. In the second session (≈ 3 h, active session), the same variables (i.e., H_{50} , PAD
123 and HPAD) were evaluated in active state (**Fig.1**).

124

125 **Experimental set-up**

126 Mechanical data

127 Torque values for voluntary contractions were collected using an isokinetic dynamometer (Biodex,
128 Shirley, NY, USA). The output signal from the dynamometer was collected at 2,000 Hz using a commercial
129 acquisition system (CED power 1401-3A, Cambridge Electronic Design; Cambridge UK), displayed and stored
130 with the Signal 7 software (Cambridge Electronic Design; Cambridge UK).

131
132 Participants were tested in a seated position with the trunk inclined backward at 20° to the vertical, the
133 knee angle at 0° (complete extension) and ankle angle during isometric conditions at 0° (neutral ankle position).
134 The lateral malleolus was aligned with the axis of rotation of the dynamometer. The foot, trunk and thighs were
135 securely strapped to the footplate or the seat of the dynamometer. Participants were asked to cross their arms on
136 their chest during contractions. During the anisometric contractions, the range of motion for ankle joint was set
137 at 40°, from -20° (dorsiflexion) to +20° (plantar flexion), the pedal speed was set at 20°/s to perform the
138 movement and 40°/s to return to its initial position (**Fig.1**). For each session, the dynamometer movement cycles
139 lasted 3 s including 2 s to perform the movement (plantar flexion or dorsi flexion) and 1 s to return to its initial
140 position. Thus, for all our measurements the stimulations were delivered at 0° (middle of the range of motion).

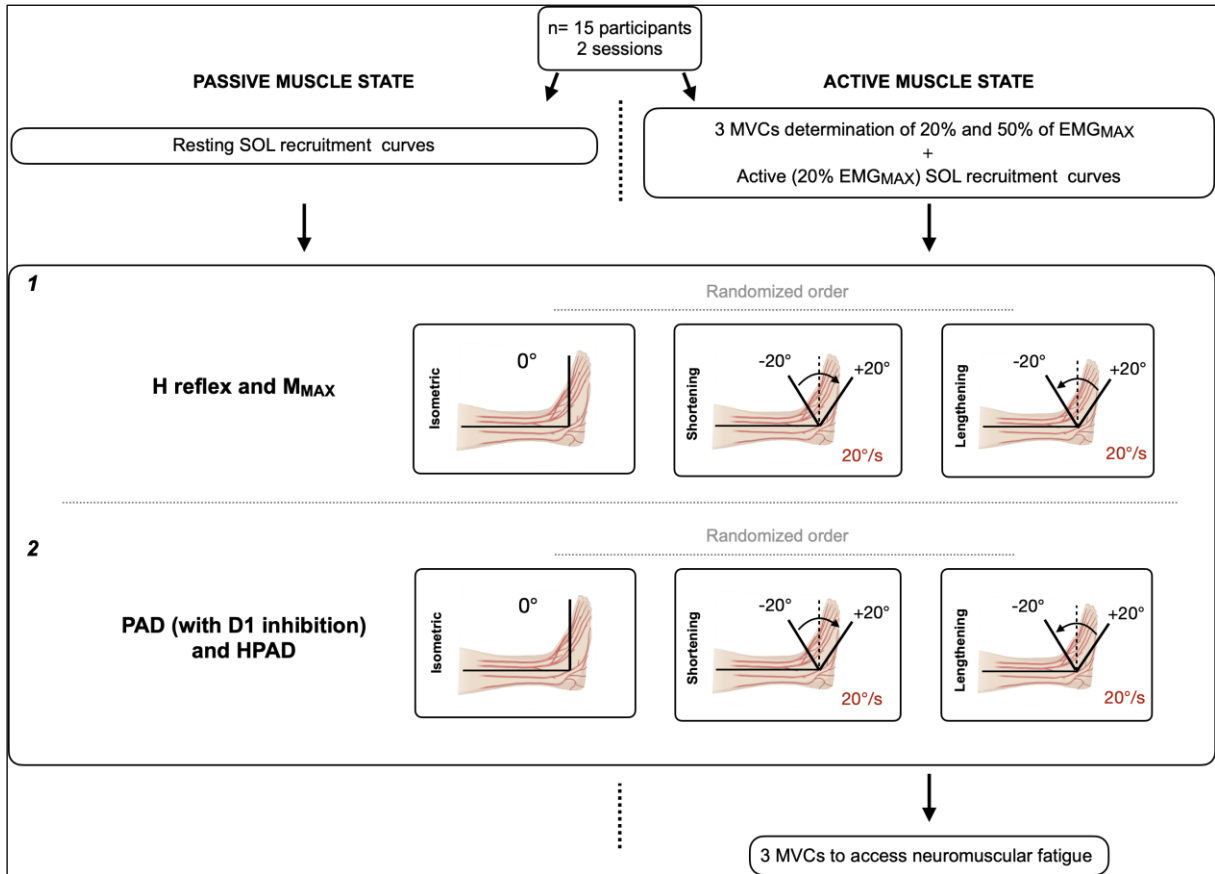
141 142 Electromyography

143 Electromyogram was recorded from SOL and tibialis anterior muscles with pairs of self-adhesive
144 surface electrodes (Meditrace 100; Covidien, Mansfield, MA, USA) in bipolar configuration with a 30 mm inter-
145 electrode distance. SOL electrodes were placed 2 cm below the muscle-tendon junction of the gastrocnemii.
146 Tibialis anterior electrodes were placed on the muscle belly parallel to the longitudinal axis of the muscle, one-
147 third of the distance between the head of the fibula and the tip of the medial malleolus. Low impedance (<5 kΩ)
148 between electrodes was obtained by shaving and gently abrading the skin and then cleaning it with alcohol.
149 Signals were amplified (1000x) with a bio-amplifier g. BSamp 0201a (Guger Technologies, Shieldberg,
150 Australia) bandpass filtered (5–500 Hz). The signals were acquired on a personal computer at a sampling rate of
151 1 kHz with a data-acquisition system (CED power 1401-3A, Cambridge Electronic Design; Cambridge UK) and
152 analyzed off-line by using Signal 7 analysis software (Cambridge Electronic Design; Cambridge UK).

153 154 Percutaneous electrical nerve stimulation

155 The electrophysiological responses (i.e., H reflex and M wave) of the SOL was evoked by percutaneous
156 stimulation of the posterior tibial nerve with a single rectangular pulse (1 ms) and high voltage (400 V),
157 delivered by a stimulator (Digitimer stimulator, model DS7, Hertfordshire, UK). Self-adhesive cathode (1 cm
158 diameter, Ag-AgCl) was placed in the popliteal fossa, and an anode (5 × 10 cm, Medicompex SA, Ecublens,
159 Switzerland) was placed on the anterior surface of the knee, over the patella. The stimulation site providing the
160 largest response amplitude was first located by a hand-held cathode ball electrode (0.5 cm diameter). Once the
161 position was determined, the cathode electrode was firmly fixed to this site with a strap and tape, as
162 recommended (Cattagni et al. 2018). Furthermore, the fibular nerve (D1 inhibition) was stimulated by placing
163 the cathode close to the head of the fibula and the anode near the medial part of the tibial head. The location of
164 the cathode was chosen to maximize and minimize the activation of the tibialis anterior and peroneal muscles,

165 respectively (Baudry and Duchateau 2012). The motor threshold for stimulation of the common peroneal nerve
 166 was determined as the lowest intensity that evoked at least three M waves out of five stimulations. Using the
 167 acquisition system CED, stimulations during isometric condition were delivered at 0°. Besides during
 168 lengthening and shortening conditions, stimulations were automatically delivered when the ankle angle passed 0°
 169 to avoid changes in H reflex size due to changes in muscle length (Budini and Tilp 2016).
 170



171
 172 **Figure 1. Diagram representing experimental design**

173 SOL: soleus; MVC: maximal voluntary contraction; H reflex: Hoffman reflex; PAD: primary afferent depolarization (with
 174 D1 methodology); HPAD: Homosynaptic post-activation depression; M_{MAX}: maximal M wave; 1: first part of session; 2:
 175 second part of session.
 176

177 **Experimental protocol**

178
 179 During the passive session, SOL H reflex passive isometric recruitment curve was first performed.
 180 Then, PAD and HPAD were randomly investigated with the use of submaximal conditioned and unconditioned
 181 posterior tibial nerve electrical stimulation during each conditions (lengthening, shortening, and isometric). The
 182 order of the conditions was randomized between participants. During all passive testings, participants were
 183 instructed to relax despite movements of the foot and electrical stimulations of the nerve.
 184

185 During the active session, recruitment curve of SOL was preceded by 3 maximal voluntary contractions
 186 (MVCs) to determine the maximal EMG activity of SOL. This maximum activity level was used to determine

187 the specific activation levels (20 and 50%) corresponding to the feedbacks provided to participants. Concerning
188 the EMG feedback method, participants were asked to maintain a level of EMG activity according to the visual
189 biofeedback displayed on a screen. For the EMG biofeedback, the root mean square (RMS) value of the EMG
190 signal was provided by a digital computing channel. This channel instantaneously computed the true RMS level
191 of the amplified EMG signal with an integration time of 500 ms. This method allowed to keep constant levels of
192 muscle activity during active lengthening, shortening and isometric conditions (Duclay et al. 2014). Then PAD
193 and HPAD were randomly investigated. At the end of active session, 3 additional MVCs were performed to
194 ensure that no neuromuscular fatigue was induced.

195

196 **Electrophysiological recordings**

197 H reflex and M wave recruitment curves

198 For both sessions (passive and active muscle states), H reflex and M wave recruitment curve from SOL
199 was obtained during isometric condition with the same methodology, the only difference was the presence of a
200 voluntary contraction at 20% of maximal EMG RMS level during the active state. The stimulation intensity was
201 gradually increased with a 0.5 mA increment from the H reflex threshold to the intensity at which the maximal H
202 reflex (H_{MAX}) was recorded for SOL. Then, the intensity was increased with a 1 mA increment until the intensity
203 for which no modification of the amplitude of M wave (i.e., plateau) was observed. Then, supramaximal
204 stimulations at 130% of this latter stimulation intensity were delivered to ensure the recording of a maximal M
205 wave (M_{MAX}) of SOL. Five stimulations were delivered at each stimulation intensity and an interstimulus
206 interval of 5 s was used. We used 5 H reflexes per increment since this number of evoked H reflex is sufficient to
207 obtain reliable data (Hopkins et al. 2000). From the recruitment curves, we determined the stimulation intensity
208 required to obtain a SOL H reflex with an amplitude of 25% (H_{TEST}) and 50% (H_{50}) of its maximum amplitude in
209 the ascending part of the recruitment. These stimulus intensities (H_{50} , H_{TEST} , M_{MAX}) were subsequently used to
210 evoke H reflex and M wave during passive lengthening, shortening, and isometric conditions. H_{50} stimulation
211 intensity was used to compare the efficacy Ia- α -motoneuron transmission between all modalities in both muscle
212 states (i.e. active and passive). H_{TEST} stimulation intensity was used to assess and compare the level of PAD and
213 HPAD between the different conditions in both muscle states. Submaximal H reflexes in the ascending portion
214 of the H reflex recruitment curve were used since they are more sensitive to change in inhibitory or facilitatory
215 inputs (Baudry et al. 2011). To study H reflex variation, 20 H_{50} , and 3 M_{MAX} were delivered for each condition
216 (lengthening, shortening and isometric) during passive and active states (**Fig.1**). Conditions were assessed in
217 randomized order and were each separated by a 5-min rest period.

218

219 Assessment of primary afferent depolarization

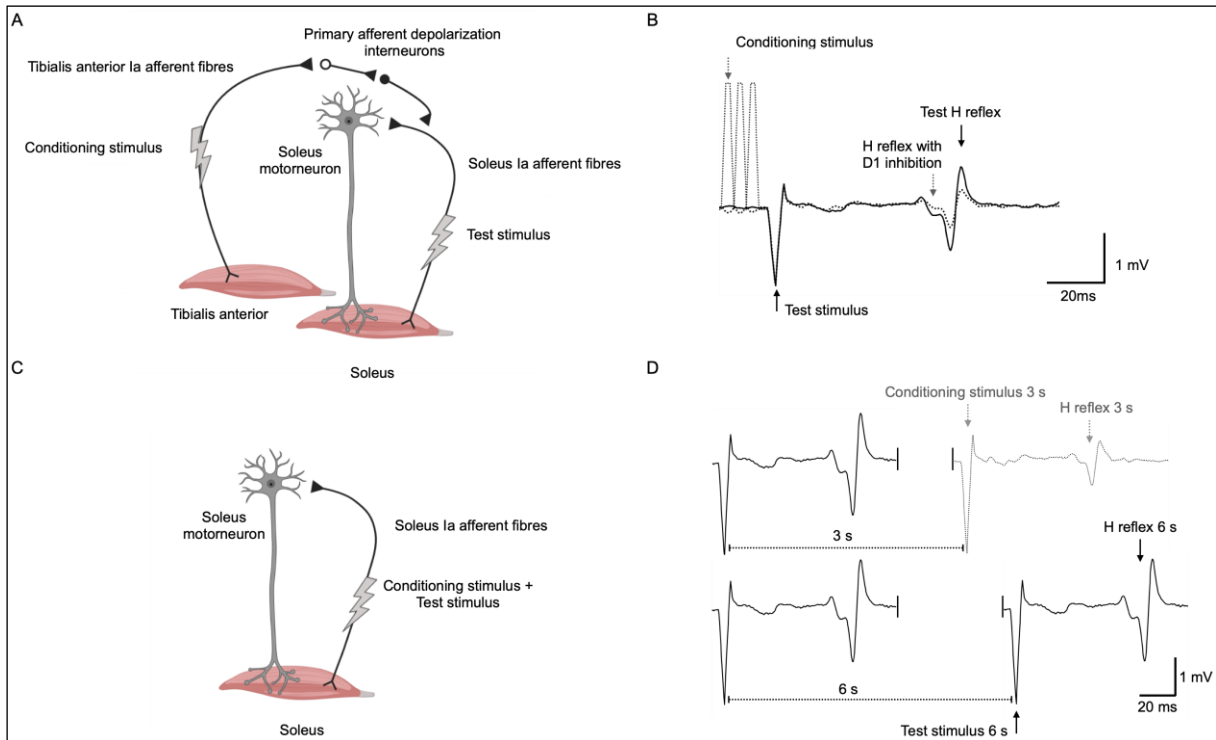
220 To study the mechanism of PAD, we used the D1 inhibition methodology (Mizuno et al. 1971). Indeed,
221 an activation of Ia terminals can also be evoked by an electrical volley on Ia afferent fibres in the nerve
222 supplying the antagonistic muscles α -motoneuron pool. This results in the so-called "D1" inhibition of the H
223 reflex (Mizuno et al. 1971)(**Fig.2A and B**). This depression depends on the excitability of PAD interneurons: the
224 larger the primary afferent depolarization excitability, the greater the presynaptic inhibition of the test afferent
225 volley and the greater the reflex depression (Achache et al. 2010). During passive and active lengthening
226 conditions, the reduction in H reflex could be more than 50 % between lengthening and shortening conditions

227 and therefore did not allow to reach an adequate H reflex of 50% in all conditions (Duclay et al. 2011). Thus, for
228 the study of D1 inhibition the intensity of stimulation for the test H reflex (H_{TEST}) was set at 25% of the H_{MAX}
229 amplitude recorded during the SOL H reflex recruitment curve. Before each condition the ratio H_{TEST}/M_{MAX} was
230 verified and adjusted to keep constant to ensure a similar sensitivity to excitatory and inhibitory inputs in the
231 different muscle states (Crone and Nielsen 1989; Baudry and Duchateau 2012). H_{TEST} was conditioned by a
232 stimulus applied to the fibular nerve to activate PAD interneurons responsible for presynaptic inhibition of the
233 Ia afferents from the SOL. Conditioned H reflex (H_{D1}) applied at the fibular nerve was a train of three 1 ms
234 stimulations at 300 Hz at an intensity of 1.2 x stimulation intensity of the tibialis anterior motor threshold. The
235 interval between the first shock of the train and the H_{TEST} was 21 ms (Aymard et al. 2000; Lamy et al. 2009;
236 Magalhães et al. 2015). A total of 20 H_{TEST} and 20 H_{D1} were randomly evoked during lengthening, shortening
237 and isometric conditions at rest (**Fig.3A**) and during active state (**Fig.3B**).

238

239 Assessment of homosynaptic post-activation depression

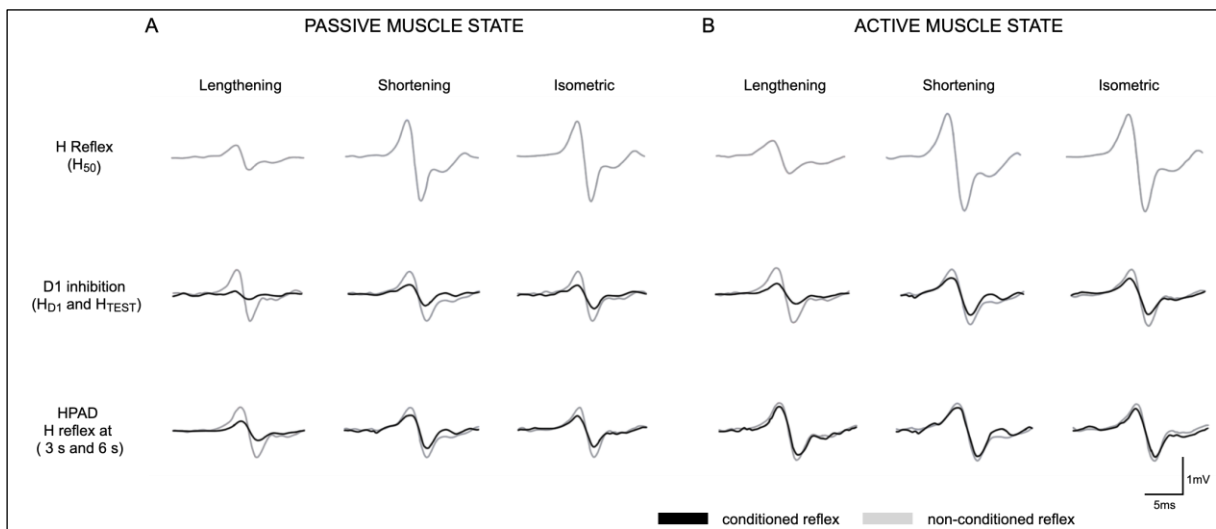
240 HPAD (**Fig.2C and D**) has been defined as an alteration in neurotransmitters release caused by repeated
241 contractions or stimulations (Crone and Nielsen 1989; Aymard et al. 2000; Lamy et al. 2009). Previous
242 activation of Ia fibres mediating the afferent volley of the H reflex produces a dramatic reflex depression at short
243 interval (1-2 s between two consecutive stimuli). In the present study, we used interstimuli interval of 3 s (0.33
244 Hz, each consecutive movement cycle) and 6 s (0.16 Hz, on every other cycle). It was verified that the amplitude
245 of the reflex evoked at 6 s (non-conditioned stimulus) remained constant throughout the experiment (**Fig.3**).
246 HPAD was investigated during passive (**Fig.3A**) and active states (**Fig.3B**) for each condition (lengthening,
247 shortening and isometric) with 20 stimuli at a 3 s interval (conditioned stimuli) and 20 stimuli at a 6 s interval
248 (non-conditioned stimuli) delivered in randomized order and separated by 5 min of rest.



249

250 **Figure 2. Schematic representation of the pathway involved in the recorded responses**

251 A) schematic representation of the pathways involved in D1 inhibition, open circle represents the excitatory interneuron and
 252 black circle the inhibitory interneuron, conditioning stimulus applied to the fibular nerve activates primary afferent
 253 depolarization interneurons acting on soleus Ia afferent fibres and reduces the amplitude of conditioned H reflex. B)
 254 representative traces showing the soleus H reflex evoked by posterior tibial nerve stimulation, the D1 inhibition evoked by
 255 fibular nerve stimulation preceding the posterior tibial nerve stimulation at a conditioning test interval of 21 ms. C)
 256 schematic representation of the pathway involved in homosynaptic post-activation depression, the repetitive activation of α -
 257 motoneuron pool reduces the amplitude of conditioned H reflex under the influence of neurotransmitter depletion. D)
 258 representative traces showing the soleus H reflex evoked by posterior tibial nerve stimulation at interval of 3s and interval of
 259 6s to investigate HPAD activity.



260

261 **Figure 3. Representative soleus electromyographic H reflex responses to different stimulation techniques during**
 262 **lengthening, shortening and isometric conditions**

263 H reflex: Hoffman reflex; D1 inhibition: primary afferent depolarization with D1 methodology; HPAD: homosynaptic post-
264 activation depression; H_{50} : submaximal H reflex; H_{D1} : conditioned H reflex; H_{TEST} : test H reflex; Typical recording of EMG
265 trace of submaximal H reflex, PAD and HPAD for one representative subjects. Trace corresponds to the recording obtained
266 at submaximal H reflex (H_{50}), conditioned and non-conditioned H reflex (H_{D1} and H_{TEST} , respectively) and H reflex with
267 different intervals (3 s and 6 s) during passive muscle state (panel A) and active muscle state (panel B).

268 **Data analysis**

269 Muscle torque

270 For MVCs, the torque produced by the plantar flexors during isometric contractions was recorded at 0°.
271 The MVC(s) torque was computed as the mean value recorded on the three tests before and after the test.

272

273 EMG activity

274 SOL EMG activity was quantified with a RMS over the 500 ms prior to stimulation and were
275 normalized to the corresponding amplitude of maximal RMS (RMS/RMS_{MAX}) and also to the corresponding
276 maximal M wave (RMS/M_{MAX}) for all three conditions. Tibialis anterior EMG RMS prior to the stimulation was
277 also analyzed during the same period of time.

278

279 Evoked potentials

280 The average values from peak-to-peak amplitudes of H_{50} , M_{MAX} , H_{D1} , H_{TEST} , and H reflex evoked every
281 3 s and 6 s responses were calculated. For H reflex variation, the H_{50}/M_{MAX} ratio was computed. The M wave
282 elicited concomitantly with the H_{50} (M_{H50}), which represented a small fraction of the M_{MAX} (M_{H50}/M_{MAX}) was
283 measured to control the stability of the stimulus intensity (Schieppati 1987). Concerning D1 inhibition, we
284 expressed the H_{D1} value as a percentage of the H_{TEST} value (H_{D1}/H_{TEST} ratio) and we calculated the H_{TEST}/M_{MAX} .
285 For homosynaptic post-activation depression we expressed the average value of the H reflex amplitude evoked
286 every 3 s as a percentage to the H reflex amplitude evoked every 6 s (3 s/6 s ratio). All ratios were calculated for
287 lengthening, shortening and isometric conditions for both states.

288

289 **Statistical analysis**

290 All descriptive statistics presented in the text, tables and figures are mean values \pm standard deviation.
291 The significance level for all analyses was set at $P < 0.05$. Data normality was verified using the Shapiro–Wilk
292 normality test and sphericity was assumed. In addition, Student's paired t tests were used to compare MVC
293 before the test and MVC after the test during active session. Separate one-way repeated measures ANOVAs
294 were used to test differences between conditions (lengthening, shortening and isometric) for RMS/RMS_{MAX} ratio,
295 RMS/M_{MAX} ratio and tibialis anterior EMG RMS. Two-factors [condition (lengthening, shortening and
296 isometric) \times muscle state (Passive muscle state vs. Active muscle state)] ANOVAs with repeated measures on
297 condition and muscle state were used to compare maximal M_{MAX} amplitude, M_{H50}/M_{MAX} , H_{50}/M_{MAX} ,
298 H_{TEST}/M_{MAX} , H_{D1}/H_{TEST} and 3 s/6 s ratio for SOL. When a main effect or an interaction was found, a post-hoc
299 analysis was made using the Tukey test. ANOVAs and post-hoc tests were performed using GraphPad Prism
300 software (version 8.0; GraphPad Software Inc., San Diego, CA, USA).

301 **RESULTS**

302 **MVC Torque and EMG activity**

303 In the active session, we assessed plantar flexor MVC torque before and after the experimental protocol
 304 to determine if the experimental session induced neuromuscular fatigue. We did not observe a significant
 305 difference in plantar flexor MVC torque ($t_{(14)} = 1.407$, $P = 0.181$, $d = 0.363$) between pre-testing (163.3 ± 46.9
 306 N.m) and post-testing (161.7 ± 47.6 N.m). We also compared SOL RMS/RMS_{MAX}, RMSM/M_{MAX} and tibialis
 307 anterior EMG RMS between lengthening, shortening and isometric conditions to confirm that participants
 308 performed similar level of agonist and antagonist muscle activity. The statistical analysis did not reveal a
 309 significant condition effect on SOL RMS/RMS_{MAX} ($F_{(1,4,19,9)} = 3.177$; $P = 0.177$; $\eta_p^2 = 0.185$), RMS/M_{MAX} ($F_{(1,3,18,9)} = 1.612$;
 310 $P = 0.225$; $\eta_p^2 = 0.103$) and tibialis anterior EMG RMS ($F_{(2,28)} = 2.149$; $P = 0.135$; $\eta_p^2 = 0.133$)
 311 (Table 1).

312
 313
 314
 315
 316
 317
 318

	Lengthening	Shortening	Isometric
Passive muscle state			
M _{MAX} (mV)	9.9 ± 1.62	9.8 ± 1.41	9.7 ± 1.32
M _{H50} / M _{MAX} (%)	2.2 ± 0.40	3.4 ± 0.43	3.2 ± 0.34
H _{TEST} / M _{MAX} (%)	9.3 ± 0.51	10.9 ± 0.65	10.1 ± 0.52
Active muscle state			
M _{MAX} (mV)	13.1 ± 0.42	12.9 ± 0.61	12.8 ± 0.66
M _{H50} / M _{MAX} (%)	6.0 ± 0.54	5.9 ± 0.56	6.2 ± 0.39
H _{TEST} / M _{MAX}	10.1 ± 0.66	10.3 ± 0.49	10.4 ± 0.33
SOL RMS / M _{MAX} (%)	3.3 ± 0.27	3.4 ± 0.29	3.2 ± 0.31
SOL RMS / RMS _{MAX} (%)	51.22 ± 0.23	52.17 ± 0.29	50.88 ± 0.22
Tibialis anterior RMS (mV)	0.23 ± 0.04	0.25 ± 0.04	0.24 ± 0.03

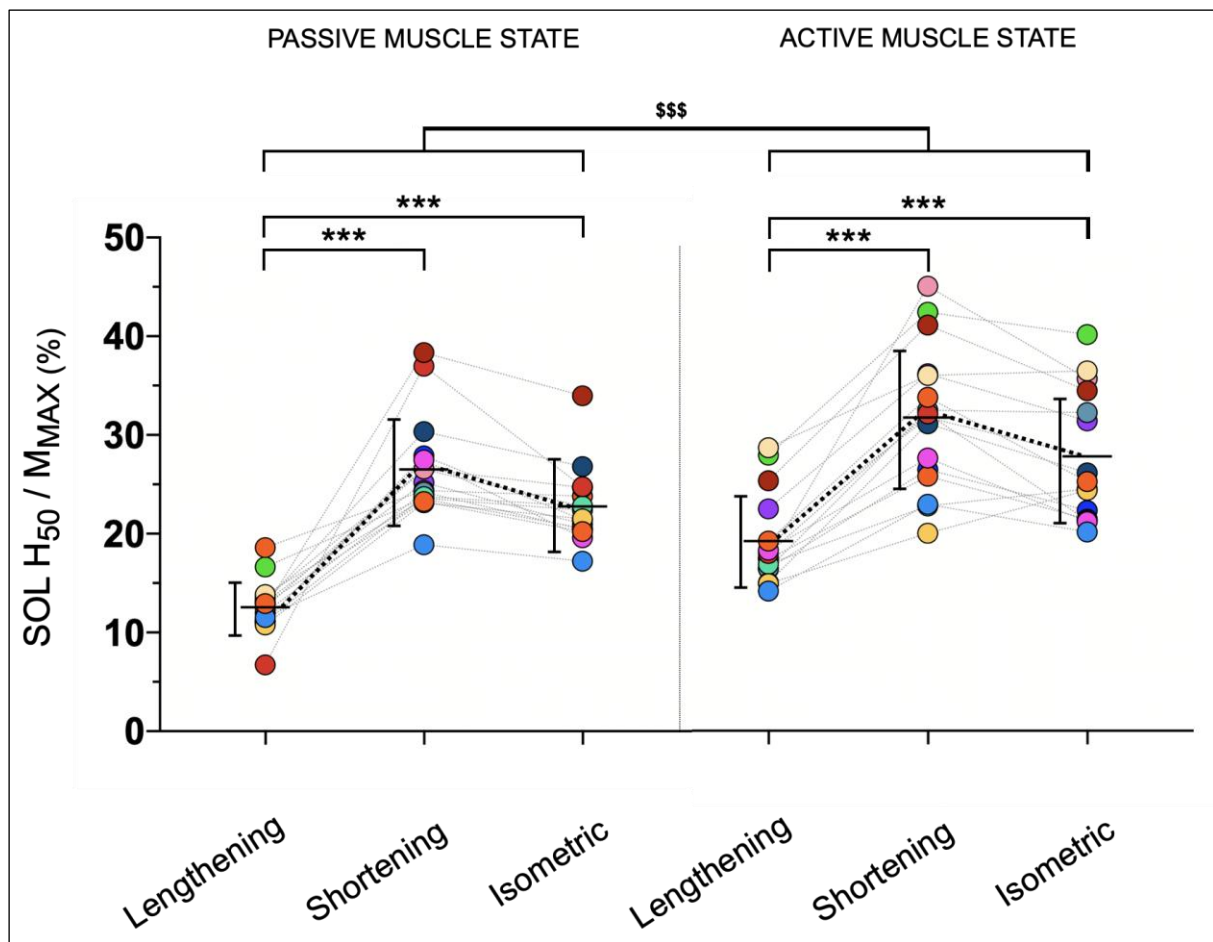
319
 320 **Table 1: Effect of conditions and muscle states on amplitudes of soleus evoked potentials and soleus and tibialis**
 321 **anterior electromyographic activity.**

322 Absolute and individual data (n=15) are expressed as mean ± standard deviation. SOL: soleus; TA: tibialis anterior; M_{MAX}:
 323 maximal M wave; M_{H50}: M wave corresponding to H reflex at 50% of its maximal value; H₅₀: Submaximal H reflex at 50%

324 of its maximal value; H_{TEST} : H reflex corresponding to its test value; RMS: root mean square; RMS_{MAX} : maximal root mean
325 square value. *Significant difference at $P < 0.001$: Lengthening vs Shortening and isometric conditions.
326

327 **Evoked potentials: H reflex and M wave**

328 For H_{50}/M_{MAX} ratio, we observed significant condition effect ($F_{(2,28)} = 93.412$; $P < 0.001$; $\eta_p^2 = 0.870$),
329 and muscle state ($F_{(1,14)} = 16.588$; $P = 0.001$; $\eta_p^2 = 0.542$), but no significant condition x muscle state interaction
330 was found ($F_{(2,28)} = 0.667$; $P = 0.521$; $\eta_p^2 = 0.045$). H_{50}/M_{MAX} ratio during lengthening was significantly ($P <$
331 0.001) reduced by 13.2% and 9.4% compared with shortening and isometric conditions, respectively. H_{50}/M_{MAX}
332 was greater in active compared with passive muscle state by 5.5% regardless of condition (**Fig 4**). Regarding
333 M_{MAX} , we did not observe significant condition effect ($F_{(2,28)} = 0.422$; $P = 0.660$; $\eta_p^2 = 0.029$), in contrast we
334 observed a significant muscle state effect ($F_{(1,14)} = 43.293$; $P < 0.001$; $\eta_p^2 = 0.479$) but no significant interaction
335 was found ($F_{(2,28)} = 1.416$; $P = 0.260$; $\eta_p^2 = 0.092$). M_{MAX} amplitude was greater in active compared with passive
336 muscle state by 4.1% regardless of condition. For M_{H50}/M_{MAX} , ANOVAs did not show a statistically significant
337 condition effect ($F_{(2,28)} = 2.522$; $P = 0.098$; $\eta_p^2 = 0.153$) in contrast we observed a statistically significant muscle
338 state effect ($F_{(1,14)} = 42,526$; $P < 0.001$; $\eta_p^2 = 0.567$) but no significant interaction was found ($F_{(2,28)} = 2.135$; $P =$
339 0.137 ; $\eta_p^2 = 0.132$). In fact, M_{H50}/M_{MAX} ratio was greater in active compared with passive muscle state by 2.9%
340 regardless of condition. Concerning H_{TEST}/M_{MAX} ratio we did not observe significant condition effect ($F_{(2,28)} =$
341 3.020 ; $P = 0.051$; $\eta_p^2 = 0.192$), muscle state ($F_{(1,14)} = 2.514$; $P = 0.135$; $\eta_p^2 = 0.152$) or condition x muscle state
342 interaction ($F_{(2,28)} = 0.325$; $P = 0.632$; $\eta_p^2 = 0.023$) (**Table 1**).
343



344

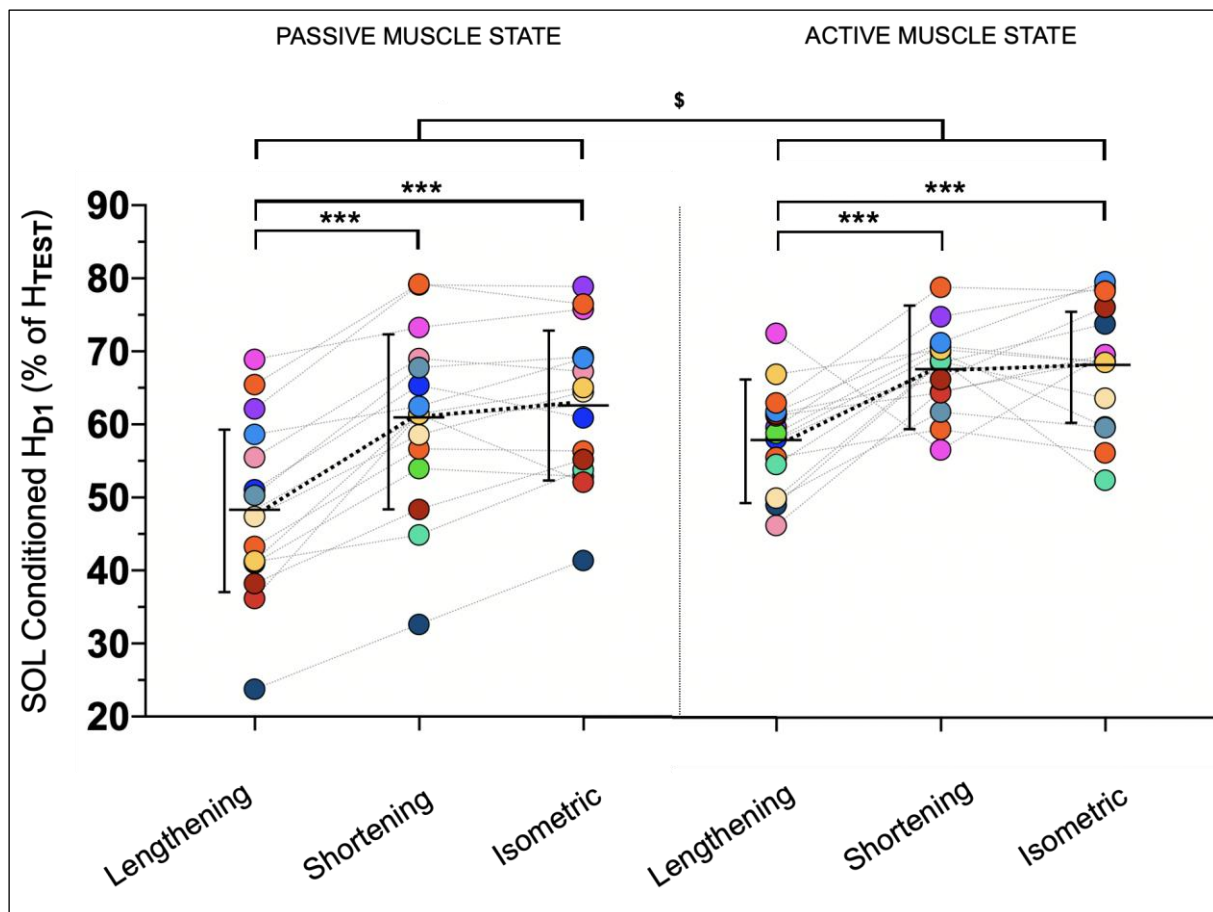
345 **Figure 4. Changes in H reflex during lengthening, shortening and isometric conditions in resting and active states**

346 Absolute and individual data (n=15) are expressed as mean \pm standard deviation. Changes in H reflex corresponding to 50%
 347 of maximal SOL H reflex normalized to the corresponding maximal M wave during lengthening, shortening and isometric
 348 conditions. Modulations of these ratios was investigated during resting (panel A) and active (Panel B) states. ***Significant
 349 difference at $P < 0.001$ for condition effect. \$\$\$ Significant difference at $P < 0.001$ for muscle state effect.

350 **D1 inhibition**

351 The two factors repeated measures ANOVAs revealed significant condition effect ($F_{(2,28)} = 51.065$; $P <$
 352 0.001 ; $\eta_p^2 = 0.785$) and muscle state ($F_{(1,14)} = 6.994$; $P = 0.019$; $\eta_p^2 = 0.333$) for H_{D1}/H_{TEST} ratio (**Fig.5**). No
 353 condition x muscle state interaction was found ($F_{(2,28)} = 1.374$; $P = 0.270$; $\eta_p^2 = 0.089$). H_{D1}/H_{TEST} ratio during
 354 lengthening was significantly ($P < 0.001$) decreased by 11.2% and 12.3% compared to shortening and isometric
 355 conditions, respectively. Furthermore, H_{D1}/H_{TEST} ratio was greater in active compared with passive muscle state
 356 by 7.3% regardless of condition.

357



358

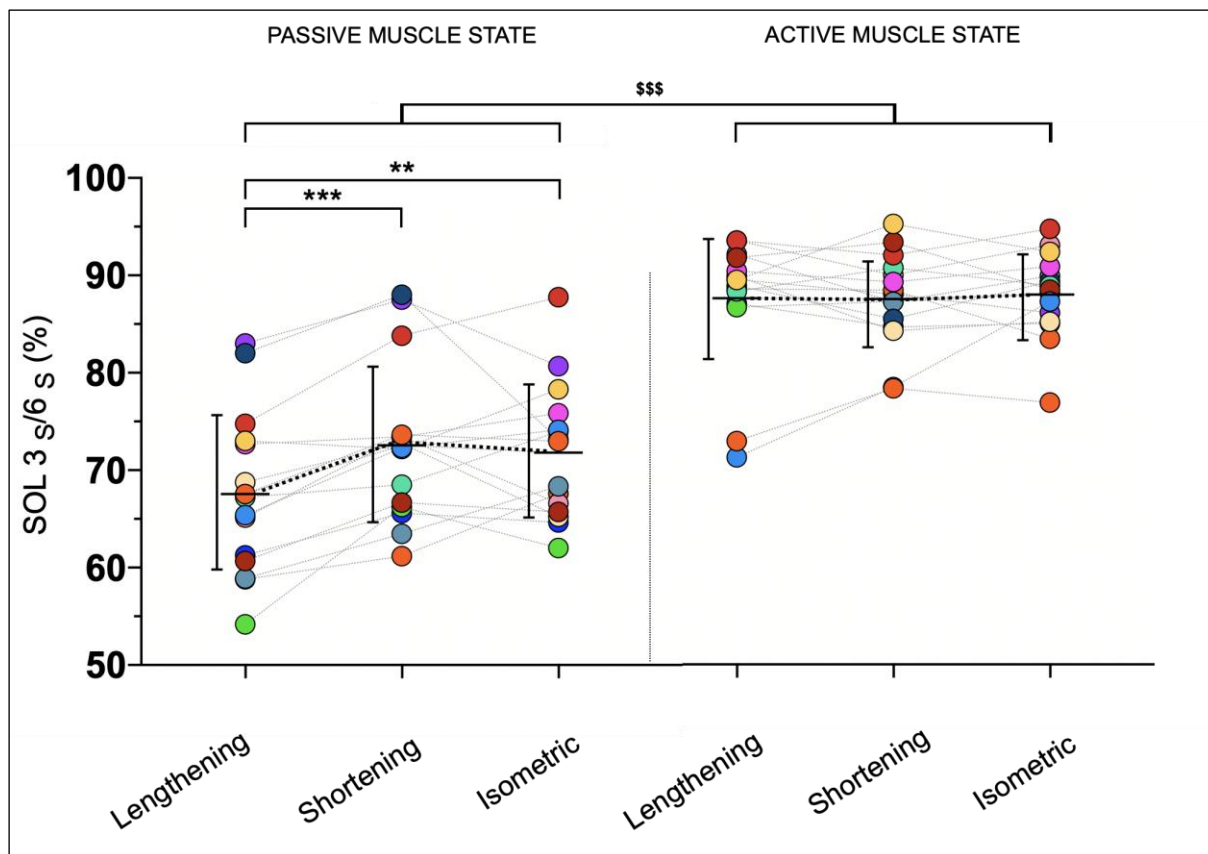
359 **Figure 5. Changes in primary afferent depolarization during lengthening, shortening and isometric conditions in**
 360 **resting and active states**

361 Absolute and individual data ($n=15$) are expressed as mean \pm standard deviation. Conditioned SOL H reflex (H_{D1}),
 362 (conditioned by stimulation of fibular nerve) are expressed in percentage of his non conditioned H reflex (H_{TEST}) in resting
 363 state (panel A) and active state (panel B) during lengthening, shortening and isometric actions. The electrical intensity to
 364 evoke H_{TEST} were normalized in each condition (lengthening, shortening and isometric). ***Significant difference at $P <$
 365 0.001 for condition effect. \$ Significant difference at $P < 0.05$ for muscle state effect.

366 Homosynaptic post-activation depression

367 For 3 s/6 s ratio (**Fig. 6**), we observed significant effects of condition ($F_{(2,28)} = 4.982$; $P = 0.014$; $\eta_p^2 =$
 368 0.262), muscle state ($F_{(1,14)} = 65.740$; $P < 0.001$; $\eta_p^2 = 0.824$) and condition x muscle state interaction ($F_{(2,28)} =$
 369 4.739; $P = 0.017$; $\eta_p^2 = 0.253$). In the passive muscle state, 3 s/6 s ratio during lengthening was significantly ($P <$
 370 0.001 and $P = 0.011$) reduced by 5.1% and 4.2% compared with shortening and isometric conditions,
 371 respectively. In the active muscle state, there was no significant effect of condition on the 3 s/6 s ratio ($P =$
 372 1.000). In each condition, the 3 s/6 s ratio was significantly greater ($P < 0.001$) in the active state than in the
 373 passive state.

374



375
 376 **Figure 6. Changes in homosynaptic post-activation depression during lengthening, shortening and isometric**
 377 **conditions in resting and active states**
 378 Absolute and individual data (n=15) are expressed as mean \pm standard deviation. SOL H reflex amplitude at a 3 s interval
 379 expressed in percentage of its value at a 6 s interval, in resting (panel A) and active (panel B) during lengthening, shortening
 380 and isometric conditions. The electrical intensity to evoke H reflex were normalized in each condition. ***Significant
 381 difference at $P < 0.001$; **Significant difference at $P > 0.01$ for condition effect. \$\$\$ Significant difference at $P < 0.001$ for
 382 muscle state effect.

383 DISCUSSION

384 To provide new insights on the regulation of PSI according to condition, estimations of PAD with the
 385 H_{D1}/H_{TEST} ratio and HPAD with 3 s/6 s ratio were investigated during muscle lengthening, shortening and
 386 isometric conditions in both passive and active states. We found a lower H_{D1}/H_{TEST} ratio during lengthening
 387 compared with shortening and isometric conditions, regardless of muscle state (passive or active). We also found
 388 a lower 3 s/6 s ratio during lengthening condition compared with the other, but only in the passive state. In
 389 addition, we reported a lower H_{50}/M_{MAX} during the lengthening compared with the shortening and isometric
 390 conditions for both states. Taken together, these results suggest that i) PAD and HPAD increase during
 391 lengthening condition at rest, and ii) only PAD increase during active lengthening compared to shortening and
 392 isometric conditions.

393 **Primary afferent depolarization**

394 It has been previously demonstrated that certain methodological requirements must be respected to
395 ensure accurate analysis of the H reflex in different experimental conditions because it may be altered by
396 recording and analysis conditions. Because of the foot movement, the efficacy of tibial nerve stimulation at a
397 given intensity may change between experimental conditions, especially during limb movement (Pierrot-
398 Deseilligny and Mazevet 2000). The study of PAD was only carried out with the D1 inhibition technique.
399 Previous experiments on the cortical control of primary afferent depolarization have confirmed the reliability of
400 the D1 inhibition method in estimating of the activity of primary afferent depolarization interneurons (Meunier
401 and Pierrot-Deseilligny 1998). The D1 inhibition method provides similar results than other experimental
402 methods estimating PAD such as the study of heteronomous monosynaptic Ia facilitation (Hultborn et al. 1987)
403 or monosynaptic Ia excitation peak in post-stimulus time histograms (Katz et al. 1988). To avoid changes in the
404 efficacy of tibial nerve stimulation at a given intensity between experimental conditions, we systematically
405 checked the H_{TEST} amplitude during experiments so that the same H_{TEST} amplitude was evoked between
406 experimental conditions. Moreover, regarding the H_{TEST} values normalized to the maximal M wave (H_{TEST}/M_{MAX}
407 ratio) we showed no difference between the different conditions. Thus, only modulations of inhibitory and
408 excitatory inputs regulated the conditioned H reflex amplitude (Baudry and Duchateau 2012).

409
410 Besides, it is essential to mention the thixotropic effect of the neuromuscular spindle (post excitatory
411 facilitation phenomenon), which is able to modify the H reflex amplitude (Pinniger et al. 2001). The thixotropic
412 properties of intrafusal muscle can distort neuromuscular spindle discharge and must be considered when
413 interpreting unexpected changes in spindle discharge, reflex behaviour or perception, especially when they occur
414 after a muscle contraction. In our study and during each movement cycle, the dynamic contractions were
415 followed by a stretch (return to the initial position at -20° of plantar flexion (for lengthening) and $+20^\circ$ of plantar
416 flexion (for shortening) to remove any thixotropic effects (Proske et al. 1993).

417
418 Therefore, this current study provided experimental evidence that presynaptic mechanisms, especially
419 PAD, is involved in the specific neural control of lengthening. In fact, we found that lengthening induced a
420 reduction of H_{D1}/H_{TEST} ratio of 11.5% and 14.6% compared to shortening and isometric conditions respectively.
421 These results therefore suggest that the amount of PAD interneurons activity increases during lengthening
422 compared to shortening and isometric conditions. This result agrees with the increased PAD during passive
423 lengthening and is consistent with previous investigations on the effects of local muscle-tendon vibration on
424 PAD (Desmedt and Godaux 1978). Since vibration also activates Ia afferents originating from muscle spindles
425 (Burke 1980), it induces an increase in PAD activity (Nielsen and Petersen 1994; Souron et al. 2019). However,
426 this argument does not fully explain the differences observed during active state, because the firing pattern of
427 single motor units by the stimulation of Ia afferents was not affected differently according to shortening and
428 lengthening conditions (Petersen et al. 2007). In fact primary and secondary endings, behave in a qualitatively
429 similar manner in the different contractions tested: shortening and lengthening contractions, with or without
430 additional load (Burke et al. 1978). Although other receptors such as golgi tendon organ or cutaneous receptors
431 can participate in regulation of PAD interneurons activity, the most accurate hypothesis actually suggested is the

432 modulations by polysynaptic descending pathways involving a subcortical mechanism that can regulate PAD
433 interneurons activity (Grosprêtre et al. 2014).

434

435 Although these results experimentally confirm the importance of PAD activity during active
436 lengthening, it is not the only mechanism that can modify the efficacy of Ia-afferent- α -motoneuron transmission.
437 Indeed, it has recently been shown that recurrent inhibition can also reduce the excitability of motoneurons pool
438 via Renshaw cells, which are regulated by descending neural drive and/or peripheral neural mechanisms (Barrué-
439 Belou et al. 2018, 2019). This demonstrates that both presynaptic and recurrent inhibition are involved in the
440 decline of the efficacy of Ia-afferent- α -motoneuron transmission observed during lengthening contractions.
441 Modulation of these two inhibitor mechanisms may coexist but there is no evidence that one of these
442 mechanisms influences each other.

443

444 Reciprocal inhibition is another source of H reflex modulation (Pierrot-Deseilligny and Burke 2005;
445 Achache et al. 2010; Duclay et al. 2011, 2014). The strength of reciprocal inhibition is related to the intensity of
446 antagonist muscle activity (Nielsen and Pierrot-Deseilligny 1996). To ensure that our experimental conditions
447 did not induce a different level of reciprocal inhibition, we compared tibialis anterior activity during the different
448 conditions. We found no difference in tibialis anterior activity between all conditions, as previously observed
449 (Amiridis et al. 1996; Duclay et al. 2011). Although we do not exclude a role of reciprocal inhibition on efficacy
450 of Ia-afferent- α -motoneuron transmission during lengthening condition, our results suggest that the possible
451 involvement of this mechanism did not alter the relevance of our findings. However, as shown in the literature,
452 the effect of condition is not the only one that can modify the efficacy of Ia-afferent- α -motoneuron transmission.

453

454 As previously observed (Fumoto et al. 2002; Tucker et al. 2005), our study confirmed an increased
455 efficacy of Ia-afferent- α -motoneuron transmission from passive to active muscle states since the SOL H_{50}/M_{MAX}
456 was 5.5% greater in the active muscle state than in the passive one, regardless of conditions. It is well established
457 that during a voluntary contraction, the supraspinal command reaching the α -motoneuron pool via the
458 descending neural pathways increases the sensitivity of the α -motoneurons to Ia afferent feedback, increasing the
459 efficacy of spinal transmission (Tucker et al. 2005). However, this does not always translate into an increase in
460 the H/M ratio as the M wave can also be increased by voluntary control. In our case it increased by 4.1%. We
461 showed that H_{DI}/H_{TEST} ratio increased by 7.1% from passive to active muscle states, indicating a decreased PAD
462 activity with muscle contraction, regardless of condition. These results agree with previous reports investigating
463 the effect of muscle state on the modulation of PAD during isometric contractions (Hultborn et al. 1987; Chen
464 and Perez 2022). It was assumed that the reduction of PAD interneuron activity on α -motoneurons during muscle
465 contraction would be driven by the supraspinal command to facilitate the excitation of voluntary activated α -
466 motoneurons by the Ia-afferent- α -motoneuron pathway (Hultborn et al. 1987; Rudomin and Schmidt 1999).

467

468 Interestingly, the regulation of PAD between passive and active muscle state is not influenced by
469 conditions. Indeed, the quantity of PAD remains higher during lengthening compared to the other muscle
470 conditions. It can be hypothesized that during a voluntary movement the supraspinal control increases the

471 excitability threshold of the PAD interneurons to facilitate the efficiency of the Ia-afferent- α -motoneuron
472 transmission.

473 **Homosynaptic post activation depression**

474 Previous studies generally analysed HPAD by calculating a percentage between H reflexes triggered at
475 a high stimulation rate and H reflexes at a low stimulation rate, such as 2s/8s (Aymard et al. 2000; Lamy et al.
476 2009), 1 s/6 s (Achache et al. 2010) or 1 s/5 s (Nordlund et al. 2004). In the current study we chose intervals of 3
477 s and 6 s corresponding to the experimental movement cycles. Indeed, the dynamometer movement cycles were
478 of 3 s duration, comprising 2 s for performing the movement (plantar flexion or dorsi flexion) and 1 s for the
479 return of the pedal to its initial position. Thus, for all our HPAD measurements, either the stimulation was
480 delivered during one movement cycle (3 s) or every other cycle (6 s). In the present study, HPAD with the 3 s/6 s
481 ratio in the passive isometric state was about 71%. Although this indicated that we induced less inhibition than
482 previous reports, this also showed that our methodology was appropriate to induce HPAD.

483

484 The 7.1% and 5.9% lower 3 s/6 s ratio observed in the passive lengthening compared to the passive
485 shortening and isometric conditions, respectively, demonstrated a specific HPAD increase during passive muscle
486 lengthening. These results agree with previous findings on local vibration applied to the homonymous tendon
487 (Pierrot-Deseilligny and Burke 2005). In fact, conditioning vibration applied to the homonymous tendon
488 activates homonymous post-activation depression, due to repetitive activation of the Ia- motoneurone synapse,
489 and this also contributes to the vibratory-induced depression of the reflex (Hultborn et al. 1996). During
490 lengthening, mechanical stress is greater than during shortening or isometric conditions and leads to a higher
491 discharge frequency of the muscle spindles (Matthews 2011). This higher discharge frequency could potentially
492 induce earlier depletion of neurotransmitters (GABA) and thus increase HPAD during lengthening. Our results
493 concerning a strong involvement of HPAD during passive muscle lengthening are confirmed by those of
494 Nordlund et al. (2004) who found that HPAD activity could reduce the efficacy of Ia-afferent- α -motoneuron
495 transmission. However, our current findings showing an effect of HPAD activity during passive shortening differ
496 from Nordlund's conclusion reported that HPAD could not reduce efficacy of Ia-afferent- α -motoneuron
497 transmission. These latter results need to be taken with caution since the methodology used by the authors to
498 study HPAD was not in agreement with previous researches (Crone and Nielsen 1989; Aymard et al. 2000;
499 Lamy et al. 2009; Achache et al. 2010; Racinais and Cresswell 2013; Souron et al. 2019). For example,
500 Nordlund et al. (2004) set a stimulation intensity evoking H_{MAX} to assess HPAD. This implies that the H reflex
501 evoked with low frequency would have been different between muscle conditions while in our study the low-
502 frequency H reflex was kept constant between the different conditions, in agreement with the methodology
503 commonly used (Crone and Nielsen 1989; Aymard et al. 2000; Lamy et al. 2009; Achache et al. 2010; Racinais
504 and Cresswell 2013; Souron et al. 2019). Furthermore, H_{MAX} is less sensitive to modulation than a submaximal H
505 reflex in the ascending part of its recruitment curve (Pierrot-Deseilligny and Mazevet 2000). The possibility to
506 observe a HPAD modulation therefore is broadly lower at H_{MAX} than at H_{50} .

508 In contrast to the passive muscle state, no significant differences were found between the conditions in
509 the active muscle state, suggesting that condition has no effect on HPAD during voluntary muscle contraction.
510 These results are consistent with the hypothesis that the group Ia afferents discharge from neuromuscular
511 spindles conditioned by gamma drive activity is identical during lengthening and shortening conditions in active
512 muscle state (Burke et al. 1978). We reported that the 3 s/6 s ratio was about 17% greater in the active state than
513 the passive muscle state. This result confirmed a HPAD reduction due to muscle activation, as previously
514 observed with different methodologies during isometric (Burke 1980; Crone and Nielsen 1989) and dynamic
515 conditions (Nordlund et al. 2004). It has been proposed that the enhanced Ia firing during voluntary contraction
516 causes a background level of post-activation depression, and this can only be enhanced slightly by the additional
517 depression caused by a preceding H reflex. This interpretation is supported by the difference between the amount
518 of HPAD observed at rest and during contraction, which disappears when the activity of Ia afferents is blocked
519 by ischaemia (Hultborn et al. 1996; Pierrot-Deseilligny and Burke 2005). It has been also proposed that a
520 possible modulation of neuromuscular spindle activity due to muscle stiffness or an alteration in the sensitivity
521 of static and dynamic receptors regulated by gamma drive would explain the reduction of HPAD during muscle
522 contraction (Pinniger et al. 2001).

523

524 To conclude, this study provides the evidence that PAD and HPAD have a specific behaviour during
525 lengthening at rest and during active state. During passive lengthening, the higher level of Ia afferents discharge
526 seems to explain the greater activity of these two inhibitory mechanisms. However, during active lengthening,
527 neural activity reading appear to be more complex, involving descending polysynaptic pathways with different
528 functions in regulating the activity of peripheral mechanisms such as PAD interneurons or neuromuscular
529 spindle sensibility. Previous work has shown the importance of muscle length (degree of lengthening) on the
530 efficacy of Ia-afferent- α -motoneuron transmission. Further work should determine whether PAD and HPAD are
531 involved during lengthening at different muscle lengths and in particular at long muscle length inducing strong
532 inhibition.

533 **COMPETING INTERESTS**

534 The authors have no relevant financial or non-financial interests to disclose.

535 **REFERENCES**

- 536 Aagaard P, Simonsen EB, Andersen JL, et al (2000) Neural inhibition during maximal eccentric and concentric
537 quadriceps contraction: effects of resistance training. *J Appl Physiol* (1985) 89:2249–2257.
538 <https://doi.org/10.1152/jappl.2000.89.6.2249>
539 Abbruzzese G, Morena M, Spadavecchia L, Schieppati M (1994) Response of arm flexor muscles to magnetic
540 and electrical brain stimulation during shortening and lengthening tasks in man. *J Physiol* 481 (Pt 2):499–507.
541 <https://doi.org/10.1113/jphysiol.1994.sp020458>
542 Achache V, Roche N, Lamy J-C, et al (2010) Transmission within several spinal pathways in adults with
543 cerebral palsy. *Brain* 133:1470–1483. <https://doi.org/10.1093/brain/awq053>
544 Amiridis IG, Martin A, Morlon B, et al (1996) Co-activation and tension-regulating phenomena during

545 isokinetic knee extension in sedentary and highly skilled humans. *Eur J Appl Physiol Occup Physiol* 73:149–
546 156. <https://doi.org/10.1007/BF00262824>

547 Aymard C, Katz R, Lafitte C, et al (2000) Presynaptic inhibition and homosynaptic depression: a comparison
548 between lower and upper limbs in normal human subjects and patients with hemiplegia. *Brain* 123 (Pt 8):1688–
549 1702. <https://doi.org/10.1093/brain/123.8.1688>

550 Babault N, Pousson M, Michaut A, Van Hoecke J (2003) Effect of quadriceps femoris muscle length on neural
551 activation during isometric and concentric contractions. *Journal of Applied Physiology* 94:983–990.
552 <https://doi.org/10.1152/jappphysiol.00717.2002>

553 Barrué-Belou S, Marque P, Duclay J (2018) Recurrent inhibition is higher in eccentric compared to isometric
554 and concentric maximal voluntary contractions. *Acta Physiol (Oxf)* 223:e13064.
555 <https://doi.org/10.1111/apha.13064>

556 Barrué-Belou S, Marque P, Duclay J (2019) Supraspinal Control of Recurrent Inhibition during Anisometric
557 Contractions. *Med Sci Sports Exerc* 51:2357–2365. <https://doi.org/10.1249/MSS.0000000000002042>

558 Baudry S, Duchateau J (2012) Age-related influence of vision and proprioception on Ia presynaptic inhibition in
559 soleus muscle during upright stance. *J Physiol* 590:5541–5554. <https://doi.org/10.1113/jphysiol.2012.228932>

560 Baudry S, Maerz AH, Gould JR, Enoka RM (2011) Task- and time-dependent modulation of Ia presynaptic
561 inhibition during fatiguing contractions performed by humans. *J Neurophysiol* 106:265–273.
562 <https://doi.org/10.1152/jn.00954.2010>

563 Budini F, Tilp M (2016) Changes in H-reflex amplitude to muscle stretch and lengthening in humans. *Rev*
564 *Neurosci* 27:511–522. <https://doi.org/10.1515/revneuro-2016-0001>

565 Burke D (1980) Muscle spindle function during movement. *Trends in Neurosciences* 3:251–253.
566 [https://doi.org/10.1016/0166-2236\(80\)90093-4](https://doi.org/10.1016/0166-2236(80)90093-4)

567 Burke D, Hagbarth KE, Löfstedt L (1978) Muscle spindle activity in man during shortening and lengthening
568 contractions. *J Physiol* 277:131–142. <https://doi.org/10.1113/jphysiol.1978.sp012265>

569 Cattagni T, Merlet AN, Cornu C, Jubeau M (2018) H-reflex and M-wave recordings: effect of pressure
570 application to the stimulation electrode on the assessment of evoked potentials and subject's discomfort. *Clin*
571 *Physiol Funct Imaging* 38:416–424. <https://doi.org/10.1111/cpf.12431>

572 Chen B, Perez MA (2022) Altered regulation of Ia afferent input during voluntary contraction in humans with
573 spinal cord injury. *Elife* 11:e80089. <https://doi.org/10.7554/eLife.80089>

574 Crone C, Nielsen J (1989) Methodological implications of the post activation depression of the soleus H-reflex
575 in man. *Exp Brain Res* 78:28–32. <https://doi.org/10.1007/BF00230683>

576 Desmedt JE, Godaux E (1978) Mechanism of the vibration paradox: excitatory and inhibitory effects of tendon
577 vibration on single soleus muscle motor units in man. *J Physiol* 285:197–207.
578 <https://doi.org/10.1113/jphysiol.1978.sp012567>

579 Doguet V, Nosaka K, Guével A, et al (2017) Muscle length effect on corticospinal excitability during maximal
580 concentric, isometric and eccentric contractions of the knee extensors. *Exp Physiol* 102:1513–1523.
581 <https://doi.org/10.1113/EP086480>

582 Duchateau J, Enoka RM (2008) Neural control of shortening and lengthening contractions: influence of task
583 constraints. *J Physiol* 586:5853–5864. <https://doi.org/10.1113/jphysiol.2008.160747>

584 Duclay J, Martin A (2005) Evoked H-reflex and V-wave responses during maximal isometric, concentric, and
585 eccentric muscle contraction. *J Neurophysiol* 94:3555–3562. <https://doi.org/10.1152/jn.00348.2005>

586 Duclay J, Pasquet B, Martin A, Duchateau J (2014) Specific modulation of spinal and cortical excitabilities
587 during lengthening and shortening submaximal and maximal contractions in plantar flexor muscles. *J Appl*
588 *Physiol* (1985) 117:1440–1450. <https://doi.org/10.1152/jappphysiol.00489.2014>

589 Duclay J, Pasquet B, Martin A, Duchateau J (2011) Specific modulation of corticospinal and spinal excitabilities
590 during maximal voluntary isometric, shortening and lengthening contractions in synergist muscles. *J Physiol*
591 589:2901–2916. <https://doi.org/10.1113/jphysiol.2011.207472>

592 Fumoto M, Komiyama T, Nishihira Y (2002) Soleus H-reflex dynamics during fast plantarflexion in humans. *J*
593 *Electromyogr Kinesiol* 12:367–374. [https://doi.org/10.1016/s1050-6411\(02\)00030-5](https://doi.org/10.1016/s1050-6411(02)00030-5)

594 Grosprêtre S, Papaxanthis C, Martin A (2014) Modulation of spinal excitability by a sub-threshold stimulation of
595 M1 area during muscle lengthening. *Neuroscience* 263:60–71.
596 <https://doi.org/10.1016/j.neuroscience.2014.01.013>

597 Guilhem G, Doguet V, Hauraix H, et al (2016) Muscle force loss and soreness subsequent to maximal eccentric
598 contractions depend on the amount of fascicle strain in vivo. *Acta Physiol (Oxf)* 217:152–163.
599 <https://doi.org/10.1111/apha.12654>

600 Hopkins JT, Ingersoll CD, Cordova ML, Edwards JE (2000) Intrasession and intersession reliability of the soleus
601 H-reflex in supine and standing positions. *Electromyogr Clin Neurophysiol* 40:89–94

602 Hulliger M, Nordh E, Vallbo AB (1985) Discharge in muscle spindle afferents related to direction of slow
603 precision movements in man. *J Physiol* 362:437–453. <https://doi.org/10.1113/jphysiol.1985.sp015687>

604 Hultborn H, Illert M, Nielsen J, et al (1996) On the mechanism of the post-activation depression of the H-reflex

605 in human subjects. *Exp Brain Res* 108:450–462. <https://doi.org/10.1007/BF00227268>

606 Hultborn H, Meunier S, Pierrot-Deseilligny E, Shindo M (1987) Changes in presynaptic inhibition of Ia fibres at
607 the onset of voluntary contraction in man. *J Physiol* 389:757–772.
608 <https://doi.org/10.1113/jphysiol.1987.sp016681>

609 Katz R, Meunier S, Pierrot-Deseilligny E (1988) Changes in presynaptic inhibition of Ia fibres in man while
610 standing. *Brain* 111 (Pt 2):417–437. <https://doi.org/10.1093/brain/111.2.417>

611 Komi PV, Linnamo V, Silventoinen P, Sillanpää M (2000) Force and EMG power spectrum during eccentric and
612 concentric actions. *Med Sci Sports Exerc* 32:1757–1762. <https://doi.org/10.1097/00005768-200010000-00015>

613 Lamy J-C, Wargon I, Mazevet D, et al (2009) Impaired efficacy of spinal presynaptic mechanisms in spastic
614 stroke patients. *Brain* 132:734–748. <https://doi.org/10.1093/brain/awn310>

615 Linnamo V, Moritani T, Nicol C, Komi PV (2003) Motor unit activation patterns during isometric, concentric
616 and eccentric actions at different force levels. *J Electromyogr Kinesiol* 13:93–101.
617 [https://doi.org/10.1016/s1050-6411\(02\)00063-9](https://doi.org/10.1016/s1050-6411(02)00063-9)

618 Magalhães FH, Elias LA, da Silva CR, et al (2015) D1 and D2 Inhibitions of the Soleus H-Reflex Are
619 Differentially Modulated during Plantarflexion Force and Position Tasks. *PLoS One* 10:e0143862.
620 <https://doi.org/10.1371/journal.pone.0143862>

621 Matthews PBC (2011) Muscle Spindles: Their Messages and Their Fusimotor Supply. In: *Comprehensive*
622 *Physiology*. John Wiley & Sons, Ltd, pp 189–228

623 Meunier S, Pierrot-Deseilligny E (1998) Cortical control of presynaptic inhibition of Ia afferents in humans. *Exp*
624 *Brain Res* 119:415–426. <https://doi.org/10.1007/s002210050357>

625 Mizuno Y, Tanaka R, Yanagisawa N (1971) Reciprocal group I inhibition on triceps surae motoneurons in man.
626 *J Neurophysiol* 34:1010–1017. <https://doi.org/10.1152/jn.1971.34.6.1010>

627 Nielsen J, Petersen N (1994) Is presynaptic inhibition distributed to corticospinal fibres in man? *J Physiol*
628 477:47–58. <https://doi.org/10.1113/jphysiol.1994.sp020170>

629 Nielsen J, Pierrot-Deseilligny E (1996) Evidence of facilitation of soleus-coupled Renshaw cells during
630 voluntary co-contraction of antagonistic ankle muscles in man. *J Physiol* 493 (Pt 2):603–611.
631 <https://doi.org/10.1113/jphysiol.1996.sp021407>

632 Nordlund MM, Thorstensson A, Cresswell AG (2004) Conditioning Ia-afferent stimulation reduces the soleus
633 Hoffman reflex in humans when muscle spindles are assumed to be inactive. *Neurosci Lett* 366:250–253.
634 <https://doi.org/10.1016/j.neulet.2004.05.044>

635 Nordlund MM, Thorstensson A, Cresswell AG (2002) Variations in the soleus H-reflex as a function of
636 activation during controlled lengthening and shortening actions. *Brain Res* 952:301–307.
637 [https://doi.org/10.1016/s0006-8993\(02\)03259-6](https://doi.org/10.1016/s0006-8993(02)03259-6)

638 Pasquet B, Carpentier A, Duchateau J, Hainaut K (2000) Muscle fatigue during concentric and eccentric
639 contractions. *Muscle Nerve* 23:1727–1735. [https://doi.org/10.1002/1097-4598\(200011\)23:11<1727::aid-](https://doi.org/10.1002/1097-4598(200011)23:11<1727::aid-mus9>3.0.co;2-y)
640 [mus9>3.0.co;2-y](https://doi.org/10.1002/1097-4598(200011)23:11<1727::aid-mus9>3.0.co;2-y)

641 Petersen NT, Butler JE, Carpenter MG, Cresswell AG (2007) Ia-afferent input to motoneurons during shortening
642 and lengthening muscle contractions in humans. *Journal of Applied Physiology* 102:144–148.
643 <https://doi.org/10.1152/jappphysiol.00362.2006>

644 Pierrot-Deseilligny E, Burke D (2005) *The Circuitry of the Human Spinal Cord: Its Role in Motor Control and*
645 *Movement Disorders*. Cambridge University Press

646 Pierrot-Deseilligny E, Mazevet D (2000) The monosynaptic reflex: a tool to investigate motor control in
647 humans. Interest and limits. *Neurophysiol Clin* 30:67–80. [https://doi.org/10.1016/s0987-7053\(00\)00062-9](https://doi.org/10.1016/s0987-7053(00)00062-9)

648 Pinniger GJ, Nordlund M, Steele JR, Cresswell AG (2001) H-reflex modulation during passive lengthening and
649 shortening of the human triceps surae. *J Physiol* 534:913–923. <https://doi.org/10.1111/j.1469-7793.2001.00913.x>

650 Proske U, Morgan DL, Gregory JE (1993) Thixotropy in skeletal muscle and in muscle spindles: a review. *Prog*
651 *Neurobiol* 41:705–721. [https://doi.org/10.1016/0301-0082\(93\)90032-n](https://doi.org/10.1016/0301-0082(93)90032-n)

652 Racinais S, Cresswell AG (2013) Temperature affects maximum H-reflex amplitude but not homosynaptic
653 postactivation depression. *Physiological Reports* 1:. <https://doi.org/10.1002/phy2.19>

654 Romanò C, Schieppati M (1987) Reflex excitability of human soleus motoneurons during voluntary shortening
655 or lengthening contractions. *J Physiol* 390:271–284. <https://doi.org/10.1113/jphysiol.1987.sp016699>

656 Rudomin P, Schmidt RF (1999) Presynaptic inhibition in the vertebrate spinal cord revisited. *Exp Brain Res*
657 129:1–37. <https://doi.org/10.1007/s002210050933>

658 Schieppati M (1987) The Hoffmann reflex: a means of assessing spinal reflex excitability and its descending
659 control in man. *Prog Neurobiol* 28:345–376. [https://doi.org/10.1016/0301-0082\(87\)90007-4](https://doi.org/10.1016/0301-0082(87)90007-4)

660 Souron R, Baudry S, Millet GY, Lapole T (2019) Vibration-induced depression in spinal loop excitability
661 revisited. *J Physiol* 597:5179–5193. <https://doi.org/10.1113/JP278469>

662 Tucker KJ, Tuncer M, Türker KS (2005) A review of the H-reflex and M-wave in the human triceps surae. *Hum*
663 *Mov Sci* 24:667–688. <https://doi.org/10.1016/j.humov.2005.09.010>

664 Westing SH, Cresswell AG, Thorstensson A (1991) Muscle activation during maximal voluntary eccentric and

665 concentric knee extension. *Eur J Appl Physiol Occup Physiol* 62:104–108. <https://doi.org/10.1007/BF00626764>
666