

Power of Words

Influence of Preexercise Information on Hypoalgesia after Exercise-Randomized Controlled Trial

Vaegter, Henrik Bjarke; Thinggaard, Peter; Madsen, Casper Høj; Hasenbring, Monika; Thorlund, Jonas Bloch

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1 **Power of words: influence of pre-exercise information on hypoalgesia after exercise – RCT**

2 Henrik Bjarke Vaegter^{1,2}, Peter Thinggaard³, Casper Høj Madsen³, Monika Hasenbring⁴, Jonas
3 Bloch Thorlund^{3,5}

4
5 *¹ Pain Research Group, Pain Center, Odense University Hospital, Odense, Denmark*

6 *² Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark*

7 *³ Research Unit for Musculoskeletal Function and Physiotherapy, Department of Sports Science and
8 Clinical Biomechanics, University of Southern Denmark, Odense, Denmark*

9 *⁴ Department of Medical Psychology and Medical Sociology, Faculty of Medicine, Ruhr University
10 Bochum, Bochum, Germany*

11 *⁵ Research Unit for General Practice, Department of Public Health, University of Southern
12 Denmark, Odense, Denmark*

13 **Original investigation for MSSE**

14 **Corresponding author:**

15 Henrik Bjarke Vaegter Ph.D.

16 Pain Research Group, Pain Center, University Hospital Odense

17 Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark

18 Heden 7-9, Indgang 200

19 DK – 5000 Odense C

20 Tel.: +45 65413869; fax: +45 65415064

21 E-mail address: henrik.bjarke.vaegter@rsyd.dk

22 ORCID ID: 0000-0002-7707-9947

23 **ABSTRACT**

24 **Purpose:** Exercise increases pressure pain thresholds (PPT) in pain-free individuals, known as
25 exercise-induced hypoalgesia (EIH). Positive pre-exercise information can elicit higher EIH
26 responses, but the effect of positive versus negative pre-exercise information on EIH is unknown.
27 The primary aim of this randomized controlled trial (RCT) was to compare EIH at the exercising
28 thigh muscle following an isometric squat exercise between individuals receiving positive versus
29 negative pre-exercise information about the effect of exercise on pain. Secondary aims were to
30 compare EIH at non-exercising muscles between groups, and to investigate the relationship between
31 participants' expectations and EIH.

32 **Methods:** Eighty-three participants were randomly assigned to brief positive (n=28), neutral (n=28)
33 or negative (n=27) verbal information. The neutral information group was included in the study as a
34 reference group. PPTs at the thigh and trapezius muscles were assessed before and after the
35 intervention (i.e. pre-exercise information+squat exercise). Expectations of pain relief were
36 assessed using a numerical rating scale (-10 (most negative) to 10 (most positive)).

37 **Results:** Change in quadriceps and trapezius PPTs after the squat exercise showed a large
38 difference between the positive and negative information groups (Quadriceps: 102 kPa 95% CI: 55
39 to 150; effect size: 1.2; Trapezius: 41 kPa 95 % CI: 16 to 65; effect size: 0.9). The positive
40 information group had a 22% increase in quadriceps PPT whereas the negative information group
41 had a 4% decrease. A positive correlation was found between expectations and increase in PPT.

42 **Conclusion:** Negative pre-exercise information caused hyperalgesia after the wall squat exercise
43 whereas positive or neutral pre-exercise information caused hypoalgesia. Positive pre-exercise
44 information did not change the magnitude of EIH compared to neutral information.

45
46 **Trial registration number:** NCT03678662

47 **Keywords:** exercise-induced hypoalgesia, expectations, pain threshold, pain tolerance, pain
48 sensitivity
49

50 INTRODUCTION

51 Exercise is guideline recommended treatment for a range of chronic pain conditions (1). Clinically
52 important improvements in pain are typically observed after 8 to 12 sessions of exercise therapy (2),
53 but as little as 1 session of exercise can influence the pain sensitivity. In pain-free individuals, a
54 single bout of aerobic or isometric exercise consistently results in higher pain thresholds and pain
55 tolerance (3-8). This phenomenon is known as exercise-induced hypoalgesia (EIH) (9-12). Several
56 mechanisms potentially responsible for hypoalgesia after exercise have been hypothesized and
57 investigated in humans including the release of endogenous opioids (13-15), and the ‘pain inhibits
58 pain’ or conditioned pain modulation (CPM) (16-18) phenomenon. In patients suffering from
59 chronic pain conditions, the EIH response has been reported to be lower or that exercise even elicits
60 a negative effect on pain thresholds or pain tolerance (i.e. hyperalgesia) (9, 19, 20).

61 It is well documented that specific pre-treatment information can modulate the
62 experience of pain (21-24) likely mediated by expectations of pain relief, and previous research has
63 reported that positive information about the effect of an acute bout of exercise on the pain
64 sensitivity elicits higher EIH responses (25). Currently, it is unknown how negative pre-exercise
65 information influences the EIH response. The lower EIH response from exercise observed in
66 patients with chronic pain (20) may be influenced by specific beliefs and negative expectations
67 build on inappropriate narratives, previous experiences with ineffective treatments, and episodic
68 hyperalgesia in response to exercise (26-28).

69 The primary aim of this randomized controlled trial (RCT) was to investigate if
70 individuals receiving positive pre-exercise information about the effect of an isometric squat
71 exercise on pain would experience a larger EIH response compared to individuals receiving
72 negative pre-exercise information. In addition, we aimed to investigate if the EIH response was
73 confined to the exercising muscle, if a graded relationship between groups (EIH in positive

74 information group > EIH in neutral information group > EIH in negative information group)
75 existed, and if the EIH response was associated with expectations of pain relief from the squat
76 exercise.

77

78 **MATERIALS AND METHODS**

79 The Consolidated Standards of Reporting Trials of Non-pharmacological Treatments (CONSORT
80 NPT) were used as guideline for reporting this trial (29). The trial was preregistered at
81 ClinicalTrials.gov (ID: NCT03678662), approved by the Danish Data Protection Agency
82 (18/49726) and the local ethics committee (S-20180019). All participants provided written informed
83 consent.

84

85 **Participants**

86 Pain-free individuals were recruited for this trial through advertisements on social media, posters on
87 billboards at the University of Southern Denmark and University College Lillebaelt, Odense,
88 Denmark. Individuals were eligible for participation if they met the following inclusion criteria:
89 between 18 and 50 years of age and adept in Danish language both verbally and written. Individuals
90 were excluded if any of the following criteria were present: pregnancy, former or present addictive
91 behavior, suffering from neurological or cardiovascular diseases, currently suffering from acute or
92 chronic pain, previous participation in pain and exercise studies. Eligible participants were
93 presented with written information about the study and procedures, but the true aim of the study
94 was not revealed to the participants.

95

96 **Randomization**

97 This RCT with a three-parallel group design and 1:1:1 group allocation was conducted in the
98 laboratory at the Pain Center at Odense University Hospital, Denmark from September 2018 to
99 November 2018.

100 The randomization sequence was computer generated in blocks of 6 and 9, prepared
101 by an independent study secretary who had no other involvement in the trial. The randomization
102 sequence was distributed and stored in sealed opaque envelopes handled only by experimenter 1
103 (CHM) who after group allocation delivered the pre-exercise specific group information.
104 Experimenter 1 was not involved in the recruiting or enrollment of the participants. All outcome
105 measurements (pain sensitivity and expectation ratings) were done by experimenter 2 (PT) who was
106 unaware of the participants` group allocation at all time. In addition, the researcher (JBT)
107 responsible for the statistical analyzes was blinded to group allocations.

108

109 **Interventions**

110 All participants participated in one session lasting approximately 30 min (Fig 1). At the beginning
111 of the session a thorough introduction to the procedures both verbally and via visual drawings and
112 demonstrations was given and all participants were familiarized with the definitions of pain
113 threshold and pain tolerance. Moreover, one pressure pain threshold assessment at the non-
114 dominant thigh which was not used for further assessment was performed. Participants were also
115 familiarized to the squat exercise through a picture, but did not perform the squat exercise during
116 the familiarization procedure.

117 Following the baseline pain sensitivity assessments participants were randomized into
118 one of three groups. The three groups received either (A) brief positive verbal suggestion on how
119 previous studies have shown that exercise can reduce the experience of pain (i.e. hypoalgesic
120 information), (B) neutral information elaborating on how to perform the exercise condition, or (C)

121 brief negative verbal suggestion on how previous studies have shown that exercise can induce pain
122 (i.e. hyperalgesic information) (See Table, Supplemental Digital Content 1, which describes the pre-
123 exercise information given to the 3 groups). The neutral information group was included as a
124 reference group which would help clarify whether a difference between the positive and negative
125 information groups was due to an increase or decrease in EIH. The information lasted 2-3 minutes
126 and was closely matched in duration for the positive, neutral and negative information groups.

127 Next, all participants performed a 3 minutes isometric wall squat exercise that has
128 previously demonstrated robust EIH responses in pain-free individuals (8, 30). Participants were
129 instructed to stand upright with their back against the wall, heels 45cm from the wall, feet parallel
130 and shoulder-width apart, and hands by their sides. A goniometer was aligned with the lateral
131 epicondyle of the right femur and participants were instructed to lower their back down the wall
132 until their hips were just above the knees and a knee joint angle of 100° flexion was reached. All
133 participants were asked to maintain this position for a maximum of 3 min or until fatigue. Just
134 before beginning the wall squat exercise participants were instructed to rate pain intensity in the
135 legs on a 0-10 numerical rating scale (NRS), with 0 defined as “no pain” and 10 “as worst
136 imaginable pain”. Pain intensity in the legs was assessed at 1, 2, and 3 min during the exercise.

137

138 **Outcomes**

139 The primary outcome in this trial was pressure pain threshold (PPT) at the dominant quadriceps
140 muscle and secondary outcomes were PPT at the non-dominant trapezius muscle, cuff pressure pain
141 tolerance (cPTT) at the right lower leg, and ratings of expectations about EIH. Order of the
142 assessments was as presented above. Leg dominance was assessed by asking the participant what
143 leg they would use to kick a ball.

144 Seated with arms resting in the lap and without footrest, PPTs were assessed with
145 handheld pressure algometer (Somedic Sales AB, Sweden). Two assessment sites were located and
146 marked. Site one was located in the middle of the dominant quadriceps muscle, fifteen cm proximal
147 to the base of patella. Site two was located in the non-dominant upper trapezius muscle, ten cm
148 from the acromion in direct line with the 7th cervical vertebra. The stimulation area was 1 cm² and
149 the rate of pressure increase was 30 kPa/s. The first time the pressure was perceived as minimal
150 pain, the participant pressed a button and the pressure intensity defined the PPT. Two PPT
151 assessments were completed for each site and the average was used for statistical analysis.

152 Computer-controlled cuff algometry (CPAR, Nocitech, Denmark) was used to assess
153 cuff pressure pain tolerance (cPTT). Due to positioning of the plinth and the cuff algometer cPTT
154 was always performed on the right leg. A 10 cm blood pressure cuff (VBM, Sulz, Germany)
155 connected to an air tank was placed 8 cm distally from the base of the patella around the right calf
156 muscle. The pressure increased with a rate of 1 kPa/s and the maximal limit of pressure was 100
157 kPa; participants were unaware of this limit. Participants quantified the pain intensity induced by
158 the pressure using an electronic 0-10 cm visual analogue scale (VAS) with 0 indicating “no pain”
159 and 10 “maximal pain”. When the pain intensity reached the extreme of 10 cm on the VAS, the
160 pressure was terminated, and the pressure value was defined as the cPTT.

161 To assess the effect of the intervention on expectations of EIH, a manipulation check
162 was performed immediately after the post intervention pain assessment. Participants were asked to
163 retrospectively rate how they had expected the wall-squat exercise to affect PPTs at the quadriceps
164 and trapezius muscles and cPTT at the lower leg. The questions for pain threshold and pain
165 tolerance were asked as “*If you think back to the time just before you did the squat exercise. What*
166 *impact did you expect that the squat exercise would have on how much pressure would be needed*
167 *before you experienced the first sensation of pain?”* and “*If you think back to the time just before*

168 *you did the squat exercise. What impact did you expect that the squat exercise would have on how*
169 *much pressure would be needed before you could not tolerate more pressure?"* Each question was
170 scored from -10 to +10 where -10 indicated the expectation of a lot less pressure needed to reach
171 PPT or cPTT (hyperalgesia) and +10 indicated the expectation of a lot more pressure needed to
172 reach PPT or cPTT (hypoalgesia). Zero indicated no change in pressure needed to reach PPT or
173 cPTT.

174

175 **Statistical analysis**

176 The study was powered to detect a large difference in EIH response (i.e. effect size of 0.80)
177 between the group exposed to positive verbal information and the group exposed to negative verbal
178 information. Using G*power (version 3.1.9.2., Dusseldorf, Germany) we estimated that 26
179 participants were required in each group to be able to detect such a difference with a power of 80%
180 and a two-sided significance level of 0.05. In addition, a similar number of individuals were
181 recruited for a reference group receiving neutral information. To account for a ceiling effect in the
182 assessment of pain tolerance in approximately 8% of participants (6) we planned to include a total
183 of 84 participants (i.e. 28 participants per group).

184 *Main analysis on the primary outcome:* To investigate the effect of the intervention on the primary
185 outcome, the absolute change (before vs after the squat exercise) in PPT at the quadriceps muscle
186 was compared between the two positive and negative information groups using student's unpaired *t*-
187 test as change score in quadriceps PPT was normally distributed (Shapiro-Wilk test: $P > 0.05$).

188 *Exploratory analyses on the primary outcome:* To explore the hypothesis of a graded quadriceps
189 EIH response between all three groups (EIH in positive information group $>$ EIH in neutral
190 information group $>$ EIH in negative information group) a linear test for trend (linear regression)
191 was performed. In addition, to explore whether a difference in the primary outcome was due to an

192 increase or decrease in EIH after positive or negative information, the absolute change in PPT was
193 also compared between the neutral information group and the positive information group, and
194 between the neutral information group and the negative information group, respectively using
195 student's unpaired *t*-test.

196 *Exploratory analyses on secondary outcomes:* For exploration of secondary outcomes, the absolute
197 change (before vs after the squat exercise) in PPT at the trapezius muscle and cPTT at the lower leg
198 were compared between the two positive and negative information groups using student's unpaired
199 *t*-tests as change scores in trapezius PPT and cPTT were normally distributed (Shapiro-Wilk test: P
200 > 0.05). As for the primary outcome, the absolute changes in trapezius PPT and cPTT were also
201 explored between the neutral information group and the positive information group, and between
202 the neutral information group and the negative information group, respectively using student's
203 unpaired *t*-test. As we did not hypothesize a graded EIH response on the secondary outcomes tests
204 for trend were not performed.

205 For primary and secondary outcomes, Cohen's *d* effect sizes (ES) were calculated and
206 categorized as large ($ES \geq 0.80$), moderate ($ES=0.5$) and small ($ES=0.2$) using Cohen's criteria
207 (31). To explore differences between all 3 groups in ratings of expectations and pain intensity
208 experienced during the wall squat exercise separate one-way analysis of variances (ANOVA) were
209 used. In case of significant ANOVAs, Bonferroni corrected *t*-tests were used for between group
210 comparisons. Pearson's correlation coefficients were used to investigate correlations between the
211 expectation ratings and the EIH responses after the wall squat exercise. Effect sizes for Pearson
212 product-moment correlations coefficients were categorized large ($ES \geq 0.50$), moderate ($ES=0.3$)
213 and small ($ES=0.1$) using Cohen's criteria (31). All statistical analyses were performed using Stata
214 15.1 (StataCorp, College Station, TX, USA) and *P* values of 0.05 or less were considered
215 significant unless otherwise specified.

216

217 **RESULTS**

218 Eighty-four individuals were assessed for eligibility, but one was excluded due to pregnancy. A
219 total of 83 participants underwent randomization into one of the three information groups (Table 1).
220 All participants completed the pain sensitivity assessments and the full 3 min wall-squat exercise
221 and no adverse events were reported. The 3 min wall squat exercise was rated as moderately painful
222 (Table 1) with no significant differences between groups at any time during the squat exercise (one-
223 way ANOVAs: $F(2,82) < 1.11$, $P > 0.33$).

224

225 *Primary outcome*

226 A large difference in change in PPT (ES: 1.2) at the quadriceps muscle was observed between the
227 positive and negative information groups (102 kPa 95 % CI: 55 to 150, $P < 0.001$). The positive
228 information group experienced a 22 % increase in thigh PPT (85 kPa 95% CI: 46 to 125), whereas
229 the negative information group experienced a 4 % decrease in thigh PPT (-16 kPa 95% CI: -43 to
230 11). A graded response between groups were observed in thigh PPT (positive information > neutral
231 information > negative information) (test for trend, $P < 0.001$) (Figure 2 and Table 2). Compared to
232 the neutral information group, the negative information group had a significantly smaller EIH
233 response at the exercising quadriceps muscle (-75 kPa 95% CI: -122 to -28, $P = 0.002$) whereas
234 there was no significant difference between the positive information group and the neutral
235 information group (26 kPa 95% CI: -28 to 81, $P = 0.33$).

236

237 *Secondary outcomes*

238 Change in the non-exercising trapezius PPT showed a large difference (ES: 0.9) between the
239 positive and negative information groups (41 kPa 95 % CI: 16 to 65, $P = 0.002$). The positive

240 information group had a 10 % increase in trapezius PPT whereas the negative information group
241 had a 7 % decrease in PPT (Figure 3 and Table 2). Compared to the neutral information group, the
242 negative information group had a significantly smaller EIH response at the non-exercising trapezius
243 muscle (-41 kPa 95% CI: -67 to -158, $P = 0.002$) whereas there was no significant difference
244 between the positive information group and the neutral information group (0 kPa 95% CI: -27 to 27,
245 $P = 0.98$).

246 Seventeen participants (21%), 6 in the positive information group, 6 in the neutral
247 information group and 5 in the negative information group reached the maximum capacity of the
248 computer-controlled cuff algometry (100kPa) at baseline and were therefore not included in the
249 pain tolerance analysis. Change in cPTT at the lower leg showed a moderate difference (ES: 0.6)
250 between positive and negative information groups (6.3 kPa 95 % CI: -0.1 to 12.6, $P = 0.054$). The
251 positive information group had a 13 % increase in lower leg cPTT whereas the negative information
252 group had a 2 % increase in cPTT (Table 2). Compared to the neutral information group, the
253 negative information group had a smaller change in pain tolerance after exercise (-7.0 kPa 95% CI:
254 -13.9 to -0.01, $P = 0.050$) whereas there was no significant difference between the positive
255 information group and the neutral information group (-0.7 kPa 95% CI: -5.7 to 4.37, $P = 0.78$).

256 Participants receiving positive information or neutral information had higher
257 expectations to the effect of the squat exercise on pain sensitivity compared with the negative
258 information group. The difference in expectations between participants receiving positive
259 information or neutral information was not significant (Table 3; one-way ANOVAs: $F(2,82) > 7.80$,
260 $P \leq 0.001$).

261 A positive correlation of moderate size was observed between expectation ratings and
262 change in quadriceps PPT ($r=0.35$, $P=0.002$) and a positive correlation of small-moderate size was
263 observed between expectation ratings and change in cPTT ($r=0.26$, $P=0.03$) after the wall squat

264 exercise. No correlation between ratings of expectations and change in trapezius PPT ($r=-0.02$,
265 $P=0.84$) was observed.

266

267 **DISCUSSION**

268 The main finding of the present study was that participants receiving negative pre-exercise
269 information experienced hyperalgesia (i.e. a decrease in PPT) after the wall squat exercise
270 compared with individuals receiving positive or neutral pre-exercise information. Importantly,
271 positive information did not change the magnitude of EIH compared to neutral information.
272 Exercise expectations matched the EIH response on a group level supporting that expectations are
273 likely a large contributor to the observed EIH response. The absence of EIH after negative
274 information was observed in the exercising body part as well as in a remote non-exercising body
275 part indicating that negative expectations influence pain-inhibitory mechanisms on a more systemic
276 level. This is the first study investigating the effect of negative pre-exercise information on the pain
277 response of exercise and the complete blockage of EIH after negative information is similar to what
278 has been demonstrated for CPM (32).

279 The observed changes in the neutral information group in PPT and pain tolerance at
280 the exercising and non-exercising muscles after the 3 min wall squat exercise are in line with the
281 magnitude of hypoalgesia previously observed after isometric exercises (4, 8, 16, 33). Previous
282 research exploring the effect of verbal suggestions and manipulation of expectations has reported
283 that verbal suggestion can induce positive expectations of hypoalgesia with small to large treatment
284 effects (34). Our results are comparable to a previous study observing enhanced hypoalgesia after
285 positive pre-exercise EIH education (25); however, although we observed a graded response in EIH
286 at the quadriceps the between group difference (i.e. positive vs negative information) was primarily
287 caused by the hyperalgesic response following negative information rather than an increase in EIH

288 following positive information. The modest effect of the positive information in this study could be
289 due to the relative short information intervention (i.e. 2-3 min) compared to previous studies using a
290 positive EIH education lasting for 15 minutes (25), suggesting a larger effect after an intervention
291 with longer duration, however the influence of duration is currently unknown. However, the
292 expectation ratings corresponded well to the group allocation with a clear polarization between the
293 positive and negative information groups validating the brief verbal information intervention used
294 in our study. Of note, although clear group differences in EIH were observed the correlations
295 between expectations and EIH were less clear with a moderate correlation between expectation
296 ratings and change in quadriceps PPT and no correlation between expectation ratings and trapezius
297 PPT. This may be explained by the fact the exercise intervention was focused on the quadriceps
298 muscle and that participants for that reason had less clear expectations about the effect on the non-
299 exercising trapezius muscle.

300 Pre-treatment information is a well-recognized factor known to modulate treatment
301 outcome (22, 35-37), which the results of the present study support. Former experiences and
302 treatment history may shape individual expectations and these seem to persist over time and transfer
303 to other therapeutic approaches (38). Some individuals with chronic pain may have expectations
304 shaped by previous unhelpful information or narratives from healthcare professionals, non-evidence
305 based web sources or negative treatment experiences which may explain why the EIH response is
306 less consistent in individuals with chronic pain (9, 26).

307

308 **Clinical implications**

309 The findings of this study have important clinical implications. The participants in the neutral
310 information group reported positive expectations of the effect of exercise suggesting that the
311 general impression is that exercise is beneficial for pain. However, this impression or expectation

312 may easily be changed. The participants receiving negative information had no expectations of a
313 hypoalgesic response to exercise, consistent with the observed hyperalgesic response. The results
314 suggest that expectations were greatly affected by the information given to the participants and play
315 an important role in the pain response to an acute exercise bout.

316 To our knowledge, this is the first study investigating the effect of negative pre-
317 exercise information on the pain response of exercise and reporting a complete absence of EIH after
318 negative information. This could be related to the psychological phenomenon of “bad is stronger
319 than good” previously proposed by Baumeister and co-workers (39). Clinicians should therefore be
320 careful how they frame information about exercise and pain to avoid negative narratives, but also be
321 aware that positive information did not change the magnitude of EIH compared to neutral
322 information. Likely this also applies to information in relation to delivery of other types of
323 treatment interventions. The results high-light, that clinicians should thoroughly and systematically
324 assess expectations, knowledge, previous experiences and exercise preferences prior to any exercise
325 prescription in order to optimize the outcome.

326

327 **Limitations**

328 This study has limitations. First, the ratings of EIH expectations were completed at the end of the
329 experimental session as a manipulation check and it may therefore not reflect the true pre-exercise
330 expectations, potentially enhancing the relationship between expectations and EIH. However, had
331 expectations been assessed before the exercise it could have revealed the hypothesis of the trial to
332 the participants. Second, an unexpected high number of participants reached the cuff-algometry’s
333 maximum capacity at baseline resulting in a smaller sample for the analysis of pain tolerance.
334 Third, participants were pain-free young adults; therefore results cannot be directly transferred to a
335 clinical population.

336

337 **Conclusion**

338 Participants receiving negative pre-exercise information experienced hyperalgesia after the wall
339 squat exercise compared with individuals receiving positive or neutral pre-exercise information.
340 The difference between groups in exercise response was primarily driven by the absence of an EIH
341 response in those receiving negative information as positive information did not change the
342 magnitude of EIH compared to neutral information. The findings have clinical implications as
343 clinicians should consider how they frame information about exercise and pain to avoid negative
344 outcomes. Future studies should investigate interactions between information, expectations and
345 exercise-induced hypoalgesia in individuals with chronic pain.

346

347 **Acknowledgement**

348 We declare that the results of this study are presented clearly, honestly, and without fabrication,
349 falsification, or inappropriate data manipulation. The results of the present study do not constitute
350 endorsement by ACSM.

351

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354

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454 **Figure captions:**

455 **Figure 1:** Illustration of the experimental procedure. Pressure pain thresholds (PPTs) were assessed
456 at the thigh and shoulder with handheld algometry, and pressure pain tolerance (cPTT) were
457 assessed at the lower leg with computer-controlled cuff algometry. PPTs and cPTT were assessed
458 before randomization and after the information interventions.

459

460 **Figure 2:** Absolute mean change (95% CI) in pressure pain threshold (PPT) at the exercising
461 quadriceps muscle for the positive information group (n=28), the neutral information group (n=28),
462 and the negative information group (n=27) assessed with handheld algometry after a 3 min
463 isometric wall squat exercise. *, significantly different compared with other groups.

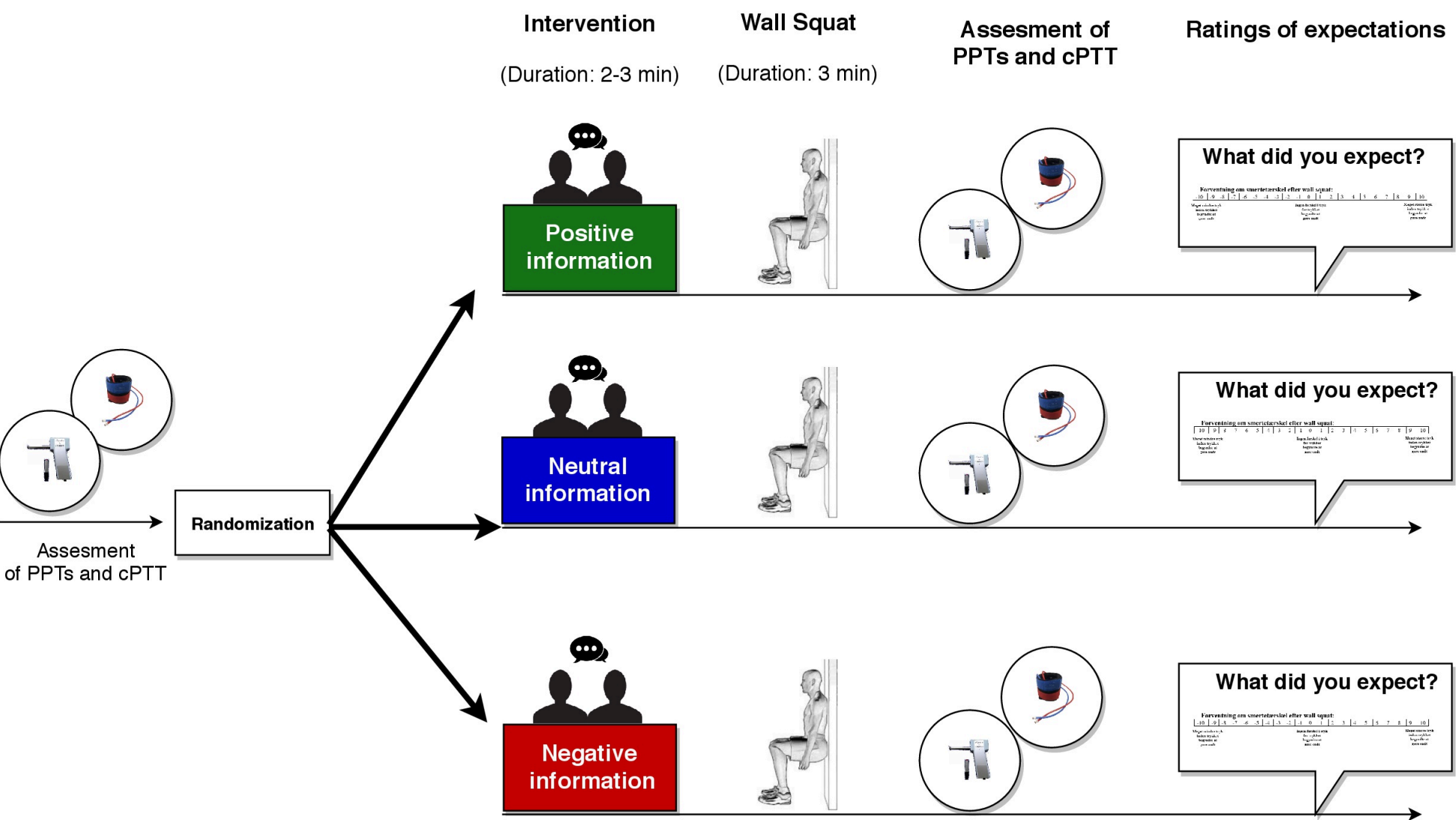
464

465 **Figure 3:** Absolute mean change (95% CI) in pressure pain threshold (PPT) at the non-exercising
466 trapezius muscle for the positive information group (n=28), the neutral information group (n=28),
467 and the negative information group (n=27) assessed with handheld algometry after a 3 min
468 isometric wall squat exercise. *, significantly different compared with other groups.

469

470 **Supplemental Digital Content 1:** Table that describes the pre-exercise information given to the 3
471 groups. (Docs)

472



Intervention
(Duration: 2-3 min)

Wall Squat
(Duration: 3 min)

Assesment of PPTs and cPTT

Ratings of expectations

Positive information

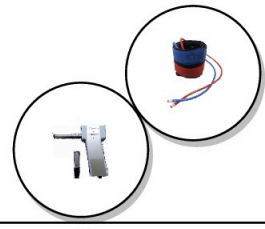


What did you expect?

Forventning om smertestærkel efter wall squat:

0	1	2	3	4	5	6	7	8	9	10
Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag
Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag

Neutral information

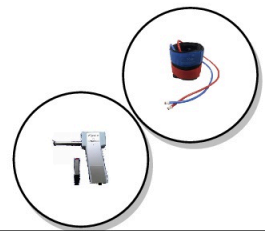


What did you expect?

Forventning om smertestærkel efter wall squat:

0	1	2	3	4	5	6	7	8	9	10
Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag
Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag

Negative information



What did you expect?

Forventning om smertestærkel efter wall squat:

0	1	2	3	4	5	6	7	8	9	10
Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag
Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag	Meget ubehag

Assesment of PPTs and cPTT

Randomization

Table 1: Baseline characteristics and pain intensity during wall squat for the 3 groups.

	Positive information group (n = 28)	Neutral information group (n = 28)	Negative information group (n = 27)
Female, n (%)	17 (60.7)	13 (46.4)	15 (55.6)
Age (years)	27.9 ± 5.0	28.0 ± 6.0	26.0 ± 4.7
BMI (kg/m ²)	25.2 ± 3.5	24.4 ± 3.1	24.5 ± 2.9
Pain intensity during wall squat exercise:			
1 min (NRS: 0-10)	3.3 ± 1.4	2.9 ± 1.1	3.2 ± 1.4
2 min (NRS: 0-10)	6.1 ± 1.8	5.6 ± 1.6	6.0 ± 1.8
3 min (NRS: 0-10)	7.9 ± 1.7	7.3 ± 1.7	7.7 ± 1.5

BMI=Body mass index;

NRS=Numeric Rating Scale

Table 2: Handheld pressure pain thresholds (PPTs) at the exercising quadriceps muscle and the non-exercising trapezius muscle as well as change in computer-controlled cuff pressure pain tolerance (cPTT) at the right lower leg after 3 min of isometric wall squat exercise in participants receiving different pre-exercise information. Data are reported as raw values at baseline (i.e. before randomization, information and exercise), after exercise and absolute change scores from baseline. *, significantly different compared with other groups.

	Positive information group (n = 28)			Neutral information group (n = 28)			Negative information group (n = 27)		
	Baseline Mean ± SD	After wall squat Mean ± SD	Absolute change from baseline Mean (95%CI)	Baseline Mean ± SD	After wall squat Mean ± SD	Absolute change from baseline Mean (95%CI)	Baseline Mean ± SD	After wall squat Mean ± SD	Absolute change from baseline Mean (95%CI)
Quadriceps PPT (kPa)	394 ± 154	479 ± 195	85 (46 – 125)	426 ± 201	484 ± 212	59 (22 – 65)	419 ± 229	403 ± 246	-16 (-43 – 11)*
Trapezius PPT (kPa)	252 ± 95	277 ± 121	25 (6 – 44)	257 ± 83	283 ± 97	25 (5 – 46)	245 ± 101	229 ± 113	-16 (-32 – 1)*
Lower leg cPTT (kPa) (n = 66)	59.0 ± 20.4	66.5 ± 19.7	7.5 (4.5 – 10.4)	66.2 ± 15.2	74.3 ± 19.4	8.2 (3.9 – 12.4)	61.3 ± 14.1	62.6 ± 18.6	1.2 (-4.6 – 7.1)*

kPa=Kilopascal

Table 3: Participant-rated expectations about change in pressure pain thresholds (PPTs) at the exercising quadriceps muscle and the non-exercising trapezius muscle as well as in pressure pain tolerance (cPTT) at the right lower leg after 3 min of isometric wall squat exercise. The questions for pain threshold and pain tolerance were asked as “*If you think back to the time just before you did the squat exercise. What impact did you expect that the squat exercise would have on how much pressure would be needed before you experienced the first sensation of pain?*” and “*If you think back to the time just before you did the squat exercise. What impact did you expect that the squat exercise would have on how much pressure would be needed before you could not tolerate more pressure?*” Each question was scored from -10 to +10 where -10 indicated the expectation of a lot less pressure needed to reach PPT or cPTT (hyperalgesia) and +10 indicated the expectation of a lot more pressure needed to reach PPT or cPTT (hypoalgesia). Zero indicated no change in pressure needed to reach PPT or cPTT. *, significantly different compared with other groups.

	Positive information group (n = 28) Mean ± SD (95%CI)	Neutral information group (n = 28) Mean ± SD (95%CI)	Negative information group (n = 27) Mean ± SD (95%CI)
Exp Δ Quadriceps PPT (NRS: -10 – 10)	4.6 ± 4.1 (3.0 – 6.2)	3.1 ± 4.4 (1.4 – 4.9)	-0.6 ± 4.4 (-2.3 – 1.2)*
Exp Δ Trapezius PPT (NRS: -10 – 10)	2.4 ± 3.7 (0.9 – 3.8)	2.0 ± 2.9 (0.8 – 3.1)	-0.7 ± 2.7 (-1.8 – 0.34)*
Exp Δ Lower leg cPTT (NRS: -10 – 10)	4.8 ± 4.2 (3.1 – 6.4)	3.0 ± 4.2 (1.3 – 4.6)	-0.4 ± 4.6 (-2.2 – 1.4)*

‘Exp’: Expectations. ‘PPT’: Pressure pain threshold. cPTT=Cuff pressure pain tolerance. NRS=Numeric Rating Scale

Supplementary Table 1: Pre-exercise information given to the 3 groups.

	Positive information group	Neutral information group	Negative information group
<p>The information given to each of the three groups</p>	<p>In a few minutes, you will do a wall squat exercise lasting 3 minutes in which you will be in a squat position against the wall for 3 minutes. After the wall squat exercise, the assessment of how you experience pressure pain that was just done will be assessed again. While doing the wall squat exercise, you will be asked to indicate whether the exercise causes any pain in the thigh muscles while standing in the squat position.</p> <p>What we know from previous studies about the effect of exercise e.g. cycling or walking on the experience of pressure pain is that a stronger pressure is needed before people experience that the pressure starts to hurt and also that a stronger pressure is needed before people cannot endure more pressure after exercise than before exercise. You may have heard that exercise can provide pain relief.</p> <p>Whether this is also the case after a squat exercise, such as the one you will be doing in a little while, has not yet been investigated, but we expect this to be the case, so that a stronger pressure is needed before you feel that the pressure begin to hurt and that you can endure a greater pressure than before.</p>	<p>In a few minutes, you will do a wall squat exercise lasting 3 minutes in which you will be in a squat position against the wall for 3 minutes. After the wall squat exercise, the assessment of how you experience pressure pain that was just done will be assessed again. While doing the wall squat exercise, you will be asked to indicate whether the exercise causes any pain in the thigh muscles while standing in the squat position.</p>	<p>In a few minutes, you will do a wall squat exercise lasting 3 minutes in which you will be in a squat position against the wall for 3 minutes. After the wall squat exercise, the assessment of how you experience pressure pain that was just done will be assessed again. While doing the wall squat exercise, you will be asked to indicate whether the exercise causes any pain in the thigh muscles while standing in the squat position.</p> <p>What we know from previous studies is that exercise e.g. cycling can induce muscle pain during exercise but also after exercise. You may be familiar with the experience of pain or soreness in your muscles after exercise.</p> <p>Whether this is also the case after a squat exercise, such as the one you will be doing in a little while, has not yet been investigated, but we expect this to be the case, so that less pressure is needed before you feel that the pressure begin to hurt and that you can endure less pressure than before.</p>