Power of Words

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

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

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ABSTRACT

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

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

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

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

Trial registration number: NCT03678662

Keywords: exercise-induced hypoalgesia, expectations, pain threshold, pain tolerance, pain sensitivity

INTRODUCTION

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

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

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

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

MATERIALS AND METHODS

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

Participants

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

Randomization

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

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

Interventions

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

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

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

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

Outcomes

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

Seated with arms resting in the lap and without footrest, PPTs were assessed with handheld pressure algometer (Somedic Sales AB, Sweden). Two assessment sites were located and marked. Site one was located in the middle of the dominant quadriceps muscle, fifteen cm proximal to the base of patella. Site two was located in the non-dominant upper trapezius muscle, ten cm from the acromion in direct line with the 7^{th} cervical vertebra. The stimulation area was 1 cm^2 and the rate of pressure increase was 30 kPa/s. The first time the pressure was perceived as minimal pain, the participant pressed a button and the pressure intensity defined the PPT. Two PPT assessments were completed for each site and the average was used for statistical analysis.

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

To assess the effect of the intervention on expectations of EIH, a manipulation check was performed immediately after the post intervention pain assessment. Participants were asked to retrospectively rate how they had expected the wall-squat exercise to affect PPTs at the quadriceps and trapezius muscles and cPTT at the lower leg. 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.

Statistical analysis

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

Main analysis on the primary outcome: To investigate the effect of the intervention on the primary outcome, the absolute change (before vs after the squat exercise) in PPT at the quadriceps muscle was compared between the two positive and negative information groups using student´s unpaired *t*-test as change score in quadriceps PPT was normally distributed (Shapiro-Wilk test: $P > 0.05$).

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

increase or decrease in EIH after positive or negative information, the absolute change in PPT was also compared between the neutral information group and the positive information group, and between the neutral information group and the negative information group, respectively using student´s unpaired *t*-test.

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

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

RESULTS

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

Primary outcome

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

Secondary outcomes

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

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

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

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

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

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

DISCUSSION

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

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

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

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

Clinical implications

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

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

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

Limitations

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

Conclusion

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

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

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Figure captions:

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

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

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

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

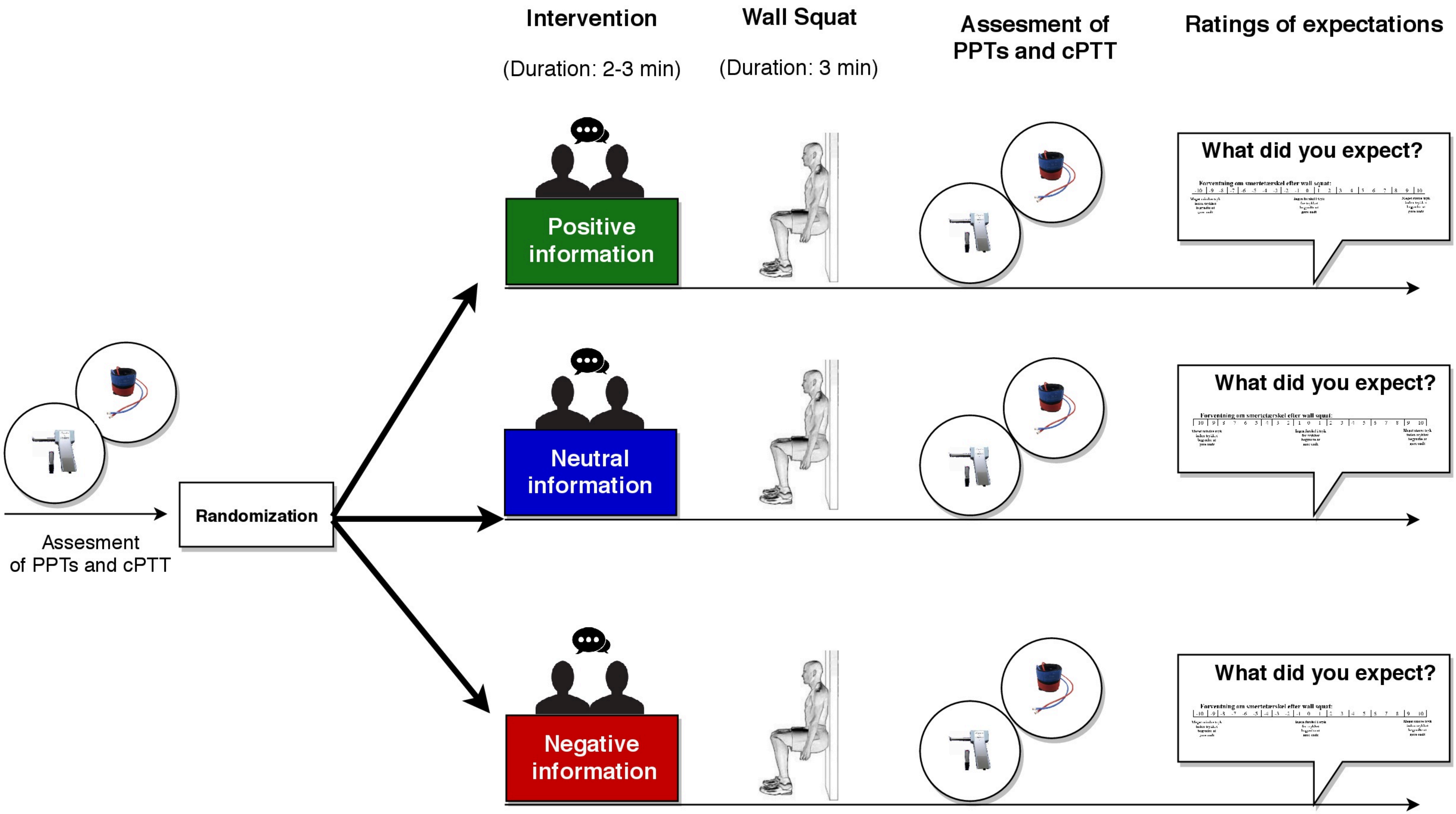
Intervention
(Duration: 2-3 min)
Wall Squat
(Duration: 3 min)
Assesment of PPTs and cPTT
Ratings of expectations
Positive information
Neutral information
Negative information
What did you expect?
What did you expect?
What did you expect?
Randomization
Assesment of PPTs and cPTT

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
The information given to each of the three groups	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. 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. 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.	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.	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. 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. 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.