"Respiratory hypoalgesia? Breath-holding, but not respiratory phase modulates nociceptive flexion reflex and pain intensity"

Jafari, Hassan ; Van de Broek, Karlien ; Plaghki, Léon ; Vlaeyen, Johan W.S. ; Van den Bergh, Omer ; Van Diest, Ilse

ABSTRACT

Several observations suggest that respiratory phase (inhalation vs. exhalation) and post-inspiratory breath-holds could modulate pain and the nociceptive reflex. This experiment aimed to investigate the role of both mechanisms. Thirty-two healthy participants received supra-threshold electrocutaneous stimulations to elicit both the Nociceptive Flexion Reflex (NFR) and pain, either during spontaneous inhalations or exhalations, or during three types of instructed breath-holds: following exhalation, at mid-inhalation and at full-capacity inhalation. Whether the electrocutaneous stimulus was applied during inhalation or exhalation did not affect the NFR or pain. Self-reported pain was reduced and the NFR was increased during breath-holding compared to spontaneous breathing. Whereas the type of breath-hold did not impact on self-reported pain, breath-holds at full-capacity inhalation and following exhalation were associated with a lower NFR amplitude compared to breath-holds at mid-inhalation. The present findings confirm that breath-holding can modulate pain (sensitivity) and suggest that both attentional distraction and changes in vagal activity may underlie the observed effects.

CITE THIS VERSION


Le dépôt institutionnel DIAL est destiné au dépôt et à la diffusion de documents scientifiques émanant des membres de l'UCLouvain. Toute utilisation de ce document à des fins lucratives ou commerciales est strictement interdite. L'utilisateur s'engage à respecter les droits d'auteur liés à ce document, principalement le droit à l'intégrité de l'œuvre et le droit à la paternité. La politique complète de copyright est disponible sur la page Copyright policy.

DIAL is an institutional repository for the deposit and dissemination of scientific documents from UCLouvain members. Usage of this document for profit or commercial purposes is strictly prohibited. User agrees to respect copyright about this document, mainly text integrity and source mention. Full content of copyright policy is available at Copyright policy.

Available at: http://hdl.handle.net/2078.1/182545
Respiratory hypoalgesia? Breath-holding, but not respiratory phase modulates nociceptive flexion reflex and pain intensity

Hassan Jafari a,⁎, Karlien Van de Broek a, Léon Plaghki b, Johan W.S. Vlaeyen a,c, Omer Van den Bergh a, Ilse Van Diest a,⁎⁎

a University of Leuven, Health Psychology, Leuven, Belgium
b Institute of Neuroscience (IoNS), Université catholique de Louvain, Brussels, Belgium
c Department of Clinical Psychological Science, Maastricht University, The Netherlands

A R T I C L E   I N F O

Article history:
Received 31 July 2015
Received in revised form 16 January 2016
Accepted 21 January 2016
Available online 22 January 2016

Keywords:
Pain
Nociceptive flexion reflex
Respiration
Breathing
Breath-hold
Hypoalgesia

A B S T R A C T

Several observations suggest that respiratory phase (inhalation vs. exhalation) and post-inspiratory breath-holds could modulate pain and the nociceptive reflex. This experiment aimed to investigate the role of both mechanisms. Thirty-two healthy participants received supra-threshold electrocutaneous stimulations to elicit both the Nociceptive Flexion Reflex (NFR) and pain, either during spontaneous inhalations or exhalations, or during three types of instructed breath-holds: following exhalation, at mid-inhalation and following exhalation. The present findings confirm that breath-holding can modulate pain (sensitivity) and suggest that both attentional distraction and changes in vagal activity may underlie the observed effects.

© 2016 Elsevier B.V. All rights reserved.

1. Introduction

Breathing techniques involving slow breathing are widely applied as a key element in many relaxation and meditation exercises, as well as in strategies to control pain (Bertisch et al., 2009; Brazier et al., 2006; Busch et al., 2012a; Grant and Rainville, 2009; Kitko, 2007; Mehling et al., 2005; Miller and Perry, 1990). Both clinical and experimental studies seem to confirm the potentially analgesic effects of instructed slow breathing, particularly, and various psychological (e.g., expectation, fear reduction, distraction from pain) and physiological (e.g., baroreceptor stimulation, vagal activation) factors may contribute to respiration-induced hypoalgesia.

A series of positive findings stem from clinical studies (Friesner et al., 2006; Mehling et al., 2005; Park et al., 2013; Yildirim and Sahin, 2004; but see Downey and Zun, 2009). However, those studies do not allow for strong conclusions as they often lack necessary control conditions and do not implement respiratory measures. Recently, experimental studies have started to investigate the effect of instructed slow breathing on laboratory-induced pain (Arsenault et al., 2013; Busch et al., 2012a, 2012b; Martin et al., 2012; Zautra et al., 2010; Zunhammer et al., 2013). For example, one study found that slow deep breathing increased both thermal pain threshold and tolerance (Chalaye et al., 2009), suggesting that an increased vagal activity resulting from slow deep breathing could mediate the analgesic effect. Also, another study (Zautra et al., 2010) reported on a reduction in self-reported thermal pain by slow breathing. In a recent study, slow deep breathing was found to prevent the development of oesophageal pain hypersensitivity. Vagal blockade with atropine abolished this effect, pointing to a critical role of the vagus (Botha et al., 2014). In yet another study, slow breathing did not change the Nociceptive Flexion Reflex (NFR), but did reduce self-reported pain, decreased heart rate, and increased heart rate variability (HRV) (Martin et al., 2012). Interestingly, changes in HRV in the latter study were not correlated with changes in any of the pain outcomes, which made the authors conclude that efferent cardiac vagal outflow could not explain the pain-reducing effect of slow deep breathing. Thus, also experimental studies have documented an effect of slow deep breathing on pain, but it is still unclear which mechanisms critically contribute to such effect.

A few experimental studies have also investigated whether the NFR or pain ratings differ according to whether the painful stimulus was presented during the inspiratory or expiratory phase of the respiratory cycle. As vagal outflow to the heart is thought to be higher during expiration compared to inspiration (Appelhans and Lueckern, 2006; Eckberg, 2003), potentially anti-nociceptive effects of vagal efferent outflow could produce a reduced pain (sensitivity) during the expiratory
and conducted according to the guidelines laid down in the Declaration of Helsinki. Of the 50 participants, five were excluded because they met at least one exclusion criterion. Among the people that were invited, six did not show up without providing any specific reason. From the remaining 39 healthy people, seven were excluded because no proper NFR could be obtained with stimulus intensities remaining below the participant’s pain tolerance threshold. Thirty-two participants (22 females, 10 males), aged between 18 and 30 (M = 20.7, SD = 2.5), completed the experiment.

2.2. Instruments and measurements

The experiment was programmed using Affect 4.0 software (Spruyt et al., 2010), including psychophysiological recordings (respiration and EMG), pain ratings and stimuli presentations (breath holding task, electrocutaneous stimulation).

2.2.1. Respiratory recording and breathing–holding task

A pneumograph chest belt (respiratory belt Philips and Bird Company, USA) was used to record respiratory activity. This device is sensitive to air pressure changes inside a tube caused by breathing-related expansions of the chest. Because our main interest was to investigate changes in respiration with respect to a within-subject manipulation, no calibration procedure to transform the recorded signal into absolute volumes was performed. The belt was fixed around the subjects’ upper abdomen adjacent to the lower thoracic rib region, and DC-coupled to a differential aneroid pressure transducer (Coulbourn V72-25B, Coulbourn Instruments, Allentown, Pennsylvania). The signal was sampled and stored at 1000 Hz.

The breath-holding task comprised three types of instructed breath-holds, corresponding to voluntary breath-holds of 4 s at three different levels of Maximum Inspiratory Thoracic Expansion (MITE): at 50% of MITE (mid-inhalation breath-hold), at 80% of MITE (full-capacity inhalation breath-hold) and post-expiration (exhalation breath-hold). Participants’ MITE was assessed prior to the experimental procedure. To this end, participants performed three maximal inhalations. The peak value of the inhalation with the greatest amplitude served as an approximation of the participant’s maximal inspiratory capacity. The amplitudes representing 50% and 80% of the participant’s MITE were calculated accordingly. During the instructed breath-holding task, the amplitudes representing exhalation, 50% and 80% of MITE were displayed with horizontal lines on a monitor in front of the participant. Also, the respiratory signal (pneumographic chest belt) was displayed on the monitor, providing the participant with continuous feedback of his or her ongoing respiratory activity. Participants were instructed to keep the respiratory signal by means of a breath-hold at a specific horizontal target line for 4 s whenever such instruction appeared on the monitor. The task comprised 10 mid-inhalation, 10 full-inhalation and 10 exhalation breath-holds instructed in a random order with 15 to 25 millisecond time interval.

2.2.2. Electrocutaneous stimulation and pain rating

To elicit pain and the NFR, a constant current stimulator (Digitimer DS5, U.K.) generated electrocutaneous stimuli. Each stimulation consisted of a volley of ten 1 ms rectangular pulses with 1 ms interpulse interval (total duration = 20 ms). A bar shaped bipolar stimulating electrode with two round electrodes (8 mm diameter, 30 mm inter-electrode distance) was fixed well with a Velcro strap over the retromalleolar pathway of the sural nerve of the left leg. Electrocutaneous stimuli were triggered manually by the experimenter.

A computerized online Numerical Rating Scale (NRS) (McMahon et al., 2013) was used for the pain ratings, which ranged from 0 (no pain) to 100 (worst possible pain). Pain tolerance was defined as a rating of 90 on this NRS, and was determined for each participant by administering stimuli with incremental steps of 2 mA up until a rating of 90 on the NRS was reached.
2.2.3. Nociceptive flexion reflex

The NFR is a polysynaptic spinal withdrawal reflex that is elicited following the activation of nociceptive A-delta afferent. It is considered a measure of sensitivity to pain at the spinal level that can be modulated by higher brain structures (Miller et al., 1979; Rhudy et al., 2005). Based on the observed EMG response, the intensity of stimulation required to elicit the NFR is used as an objective index of nociceptive threshold, and the electromyography response amplitude measures the NFR (Rhudy and France, 2007; Sandrini et al., 2005; Skljarevski and Ramadan, 2002). For the NFR recording, two 8 mm Ag/AgCl electrodes (2 cm center to center distance) were placed over the left biceps femoris muscle, 10 cm above the popliteal fossa, with a reference electrode attached over the antero-lateral aspect of the tibial bone plateau (see Fig. 1). To avoid recording of motion artefact and noise, the disposable recording electrodes were integrated in an adhesive cloth that stuck firmly to the skin, preventing their displacement. To elicit the NFR, electrocutaneous stimulation was applied over the sural nerve at the back of the lateral malleolus of the same side leg. NFR was defined as biceps femoris electromyographic (EMG) activity in the 85–180 millisecond period after stimulus.

The NFR threshold (NFRT) was conceptualized as the stimulation required to elicit a stable series of responses. The NFRT was determined for each participant using an up–down staircase method (4–2–1–0.5 mA staircase procedure). The stimulation level was increased with 4 mA once the NFR could be observed. Then, the stimulus intensity was decreased in steps of 2 mA until the NFR was no longer detected, and increased and decreased again for two more times with steps of 1 mA and 0.5 mA, respectively. The average of the two last ascending stimulations capable of eliciting the NFR was taken as NFRT. Participants rated the pain generated by each stimulus in this procedure using the digital NRS. For safety purposes, when no NFR could be observed with intensities that were rated lower than 90 on the NRS and/or lower than 35 mA, the experiment was discontinued. The intensity of the electrocutaneous stimulation delivered for the remainder of the study for eliciting the NFR was set to 120% of each participant’s NFRT. This procedure of NFR measurement and testing is frequently used in recent studies and the standards are well established (Rhudy et al., 2005; Rhudy and France, 2007; Sandrini et al., 2005; Sarton et al., 1997; Skljarevski and Ramadan, 2002).

The EMG signal was recorded at 1000 Hz, using an Isolated Bioamplifier Model V75-04 (Coulbourn Instruments, Allentown, Pennsylvania) with a band pass filter of 8–1000 Hz. EMG recordings started 200 ms (baseline) prior until 800 ms following the electrical stimulus.

2.3. Experimental design and procedure

The experiment took place at the Health Psychology Psychophysiology Laboratories of the University of Leuven. Participants were seated in an adjustable dentist’s chair in a semi-reclined position with a knee flexion of approximately 140 degrees and a neutral position of the ankle. The participants read and signed the informed consent form. Following this, participants were fitted with the electrodes and the electrodes’ wires were taped to the skin. Participants were asked to lay relaxed and to avoid any unnecessary voluntary movement or contraction of the muscles. Next, the participant’s pain tolerance and NFR threshold were determined (see Sections 2.2.2 and 2.2.3). Following this, participants were instructed how to perform the breath-holding task and practiced it for 2 min.

The actual experiment consisted of a spontaneous breathing and a breath-holding block for each participant (see Fig. 2). Participants were counterbalanced across the two possible order sequences. Participants rated their pain level on the NRS scale that appeared on the monitor following each pain stimulus. The NFRT and pain ratings were recorded with respect to each of the electrical stimuli.

During the breath-holding task, the experimenter monitored the participants’ performance on the breath-holding tasks and administered 18 electrical stimuli. Six stimuli for each type of breath-hold were administered. Thus, for each type of breath-hold, four randomly chosen breath-holds were without any pain stimulation (see Fig. 3).

During spontaneous breathing, participants received no breathing instructions and could not see their own respiratory signal on the monitor in the participant’s room. In the experimenter room, the experimenter monitored the participants’ spontaneous breathing pattern.

---

**Fig. 1.** Spinal nociceptive flexion reflex (NFR) electrode placement. The recording electrodes were placed over the left biceps femoris muscle 10 cm above the popliteal fossa, with a reference electrode attached over the antero-lateral aspect of tibial bone plateau. To elicit NFR activity, repeated electro-cutaneous stimulation was applied over the sural nerve at the back of the lateral malleolus of the same side leg.
and triggered the electrical stimulation manually. Every participant received 20 electrical stimuli with a 15–25 s interstimulus time interval.

During breath-holding task the experimenter monitored the participants' performance on the breath-holding tasks and administered the electrical stimuli at the targeted breath-holds. The NFR and pain ratings were recorded with respect to each of the electrical stimuli.

2.4. Data reduction and analysis

Respiratory and EMG recordings were synchronized using AcqKnowledge software (V4.2, BIOPAC Systems Inc., USA), allowing to check the exact location of the electrical stimulation within the respiratory cycle. The raw EMG signal rectified by a root-mean-square transformation per 5 ms bin. The integral of the rectified EMG was calculated for the 85–180 ms time interval following the onset of the electrocutaneous stimulus, as a measure of NFR amplitude (see Fig. 4).

For the spontaneous breathing task, the on- and offset of each respiratory cycle were visually determined using AcqKnowledge software. The peak within each respiratory cycle was determined automatically by the software as the time of the highest value of respiration amplitude between onset and end times. To determine whether an electrocutaneous stimulus occurred during in- or exhalation, and when it occurred relative to inspiratory peak, a stimulus-to-peak time ratio (SP time ratio) was calculated for each electrical stimulus. For example, if the inspiratory peak (indicating the switch from inspiration to expiration) occurred at 2 s, and the electrical stimulus was delivered at 1.7 s, then the SP ratio is 1.7/2 = 0.85. Thus, SP time ratios smaller than 1 indicate that the electrical stimulus occurred during inspiration.

Fig. 2. The overall design of study comprised two breathing tasks of spontaneous breathing and breath holding. Each task consisted of different phases.

Fig. 3. A sample of experimental diagram for 30 breath-holds and 18 electro-cutaneous stimuli in one participant. A computerized analogue visual biofeedback of the respiratory signal allowed the participants to perform the instructed breath-holds. The amplitudes representing full-inhalation, mid-inhalation and exhalation breath holding were displayed with horizontal lines on a monitor. The programme instructed the participants to perform in random order 10 breath-holds at mid-inhalation, full-inhalation and exhalation.
whereas SP time ratios bigger than 1 indicate that the stimulus occurred during expiration (see Fig. 5).

Because instructed breath-holds could impact on the leg’s muscle tone, particularly during the full-inspiration task, we checked whether baseline EMG activity during the 150 ms interval prior to the electrocutaneous stimulation differed among the three types of instructed breath-holds (exhalation, mid inhalation and full inhalation) (see Fig. 4). To this end, and as the assumption of sphericity (Mauchly’s

**Fig. 4.** The scatterplot of electro-cutaneous stimuli relative to the inspiratory peak time during spontaneous breathing for 32 participants. The respiration curve is only a symbolic cycle for a better representation. Each dot represents one stimulation. Stimulations which occurred at a SP-ratio smaller than 1 occurred during inspiration, those at a SP-ratio bigger than 1 are occurred during expiration.

**Fig. 5.** An illustration of the time windows for electromyography processing for (A) Baseline activity prior to electro-cutaneous stimuli, and (B) NFR 85 ms after electro-cutaneous stimuli. This graph represents six random trials of NFR after root-mean-squared processing for one of the subjects.
The coefﬁcent on inspiration. For each of models the unstandardized coefﬁcient was dummy coded into two phases of inspiration and expiration, phase model (alternative model) that also included a phase variable, respiratory phase during spontaneous breathing. For formation in three distinct phases, testing the effects of (1) an instructed hood) for each model was computed and tested using one-sided Chi

dimensional multilevel model was designed such that the repeated measure ANOVA with an alpha threshold of .05 was used for the data analysis of the baseline EMG recording (SPSS Statistics version 21).

MLWin software version 2.30 was used for the multilevel modelling of subjective pain ratings and the NFR. The likelihood ratio test was used for parameter estimation, and for the testing of two competing models (null model versus alternative model; Rashbash et al., 2005). The longitudinal multilevel model was designed such that the repeated measurements of painful stimuli (level 1) were nested within participants (level 2). To allow for the comparison of the models’ coefﬁcients, we used a full information maximum likelihood approach. To compare the relative ﬁt of two competing models, the deviance (−2Log-likelihood) for each model was computed and tested using one-sided Chi square test with a threshold of .05. The multilevel modelling was performed in three distinct phases, testing the effects of (1) an instructed breath-holding task, (2) different types of breath-holding, and (3) respiratory phase during spontaneous breathing. For the effect of the instructed breath-holding task, we compared the null model (unconditional model) including all observations within all participants with the task model (alternative model). The alternative model included ‘breathing task’ as a variable, dummy coded for spontaneous breathing versus instructed breath-holding, and centred on spontaneous breathing. To test the effect of the type of breath-holding, the null model comprising all data of the breath holding task within all participants was compared with a depth model (alternative model) that included three categories of breath-holding: exhalation, mid-inhalation and full-inhalation, with the ﬁrst category as a reference. Finally, to test the effect of respiratory phase during spontaneous breathing, we compared the null model including all observations during spontaneous breathing with a phase model (alternative model) that also included a phase variable, which was dummy coded into two phases of inspiration and expiration, centred on inspiration. For each of models the unstandardized coefﬁcient, deviance and Chi-square probability level were reported. The unstandardized coefﬁcients can be interpreted as the grand mean in the null model, the mean in centred category of alternative model, and the mean difference from centred category in other condition(s).

3. Results

3.1. Baseline EMG activity

The muscle’s baseline activity prior to the presentation of the electrocutaneous stimulus did not differ between the three types of breath-holding (main effect: p = .992).

3.2. Instructed breath-holding task

Performing instructed breath-holds signiﬁcantly altered self-reported pain (Chi² = 157.75, p < .0001) and NFR (Chi² = 5.6, p = .17) compared to the null model (unconditional intercept). In this model, self-reported pain was lower (9.6 points on the NRS scale) during breath-holding compared to spontaneous breathing. The NFR increased 0.5 mV·s from spontaneous breathing to breath-holding, but this effect was not signiﬁcant (see Table 1).

3.3. Spontaneous breathing

The phase model of spontaneous breathing did not improve the prediction of subjective pain levels (Chi² = 3.9, p = .34) or the NFR (Chi² = 5.6, p = .45) above the null model. The decreases in pain (B = −.76 points on the NRS) and the NFR (B = −.21 mV·s) during expiration relative to inspiration were not signiﬁcant (see Table 1).

3.4. Breath-holding model

The breath-holding model did not add to the null model for self-reported pain (Chi² = 1.12, p = .57), whereas it did for the NFR (Chi² = 9.1, p = .01). Pairwise comparisons of the three different types of breath-holds showed a signiﬁcant decrease in the NFR amplitude after full-inhalation (B = −1.04 mV·s, Chi² = 8.72, p = .003) and exhalation (B = −0.71 mV·s, Chi² = 3.86, p = .049) compared to mid-inhalation.

4. Discussion

The objectives of the present study were three-fold: To explore whether self-reported pain and nociception as measured by the NFR (1) vary between spontaneous breathing versus instructed breath-holding, (2) are reduced by post-inspiratory breath-holds, and (3) differ between the inspiratory versus expiratory phase during spontaneous breathing.

Compared to non-manipulated, spontaneous breathing, the breathing manipulation applied in the present study (breath-holding) signiﬁcantly reduced self-reported pain, whereas it increased the NFR. The decrease in self-reported pain can likely be understood from a higher attentional involvement and predictability in the breath-holding compared to the spontaneous breathing task. As participants had to comply with the instructed depths and timings of the breath-holds, it
is plausible to assume that the task required substantial attentional resources. Several studies have shown that distraction results in lower pain ratings (Roy et al., 2011; Van Damme et al., 2008; Verhoeven et al., 2011). More generally, any guided breathing task is likely capable of drawing attention away from the subjective pain experience and dampening the pain experience, especially when the instructed breathing pattern is still relatively untrained and attentional demands are high. Besides having been distracted, participants may also have experienced the painful stimulus as relatively more predictable during the breath-hold compared to the spontaneous breathing task, resulting in overall lower levels of anxiety during instructed compared to spontaneous breathing (Carlsson et al., 2006). Both phenomena could produce opposite effects for nociception as studies have shown that the nociceptive withdrawal reflex is higher when participants concentrate on the stimuli, and prediction or distraction usually do not decrease the reflex (Bjerre et al., 2011). Thus, the present findings highlight a potentially important influence of attention and distraction on pain in any instructed breathing task, particularly in studies that aim to investigate mechanisms underlying respiratory hypoalgesia.

An alternative explanation for an increased NFR during instructed breath-holds relates to a potential subthreshold facilitation of alpha motoneurons. For example, contractions of upper limb muscles are known to facilitate reflexes elicited in lower limb muscles without changes in baseline EMG activity in these muscles (Delwaide and Toulouse, 1981). Likewise, muscle contractions associated with instructed, voluntary breath-holds may facilitate the NFR (Bishop et al., 1970; Schmidt-Vanderheyden and Koepchen, 1970; Schmidt-Vanderheyden et al., 1970).

As pain has been described to concurrently increase tidal volume, mean inspiratory flow and the occurrence of spontaneous breath-holds (Boiten, 1998), it is plausible that breath-holding after a deep inhalation could be functional in reducing the impact of painful stimulation. We hypothesised that breath-holds at different levels of MITE (full-inhalation vs. mid-inhalation vs. exhalation) would impact on self-reported pain and the nociceptive reflex. More specifically, we expected a decrease in the nociceptive reflex when the breath-hold occurred at a high level of inspiratory capacity compared to lower levels. This hypothesis was only partially confirmed, as full-inhalation breath-holds were associated with a reduced nociceptive reflex compared to a breath-hold at 50% of MITE, but not compared to breath-holds following exhalation. Potentially, participants may have generated an expiratory pressure against a closed glottis during the full-inhalation breath-hold, very much like the Valsalva Manoeuvre. This would yield a sudden and high intrathoracic pressure following the end of inspiration, resulting in a higher stroke volume and blood pressure (Ghione, 1996; Novak, 2011; Vogel et al., 2005), and in concomitant baroreceptor stimulation producing antinociceptive effects (Edwards et al., 2002; Edwards et al., 2001). To further explore this possible mechanism, future studies could consider investigating whether participants close their glottis during an instructed breath-hold at full-inspiration as applied in the present study. Post-expiratory pauses may have anti-nociceptive effects due to higher activation of baroreceptors. This is conceivable as blood pressure is typically maximal towards the end of inspiration, and/or lower anxiety during breath-holding task. Pain ratings and the NFR were not affected by respiratory phase during spontaneous breathing in the present study. Also, pain ratings were not affected by different types of breath-holding manoeuvres.

4.1. Limitations

Some limitations of the present study should be acknowledged. First, the findings may not be generalized to other types of pain and other populations. Second, as the low pass filter applied on the EMG recording equalized the sampling frequency of the signal (1000 Hz), a potential risk of aliasing is present in the EMG recordings. Finally, as the present study did not include beat-to-beat blood pressure, and intrathoracic pressure recordings, any interpretation in terms of antinociceptive effects of baroreceptor activation remains speculative at this stage.

5. Conclusion

Both self-reported pain and the NFR are affected by an instructed breath-holding task. Compared to spontaneous breathing, instructed breath-holds were associated with lower pain ratings, but with a relatively potentiated NFR. Both effects could be due to distraction from pain and/or lower anxiety during breath-holding task.

Our findings further confirm that the depth of breath-holding affects spinal nociceptive processes: NFR activity was significantly less during breath-holds at full-range inhalation and following exhalation, compared to breath-holds at mid-range inhalation. However, further research should investigate the different processes that may underlie these effects.

Pain ratings and the NFR were not affected by respiratory phase during spontaneous breathing in the present study. Also, pain ratings were not affected by different types of breath-holding manoeuvres.

Conflict of interest statement

None of the authors have any conflicts of interests related to this manuscript.


