JOURNAL OF MOVE AND THERAPEUTIC SCIENCE

2025; 7(1):m88

Impacto de series de apnea a diferentes volúmenes pulmonares sobre la sensibilidad al dolor: un ensayo piloto en sujetos sanos

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Conflicto de Intereses:

Los autores declaran no tener ningún conflicto de intereses.

Financiación:

Los autores declaran no haber recibido financiación/compensación para el desarrollo de esta investigación.

DOI: 10.37382/jomts.v7i1.1628

Recepción del Manuscrito:

2-Abril-2025

Aceptación del Manuscrito:

21-Julio-2025

RESUMEN

Antecedentes: La apnea es una condición caracterizada por la interrupción de la respiración, y se cree que afecta el reflejo barorreceptor en distintos volúmenes pulmonares, influyendo en las respuestas de sensibilidad al dolor.

Objetivos: El presente estudio tuvo como objetivo analizar el efecto de episodios de apnea, realizados con volúmenes pulmonares altos y bajos, sobre la hipoalgesia.

Métodos: Los participantes fueron asignados aleatoriamente a dos grupos: un grupo de apnea a volumen pulmonar alto (GA) y otro a volumen pulmonar bajo (GB). Ambas intervenciones consistieron en series intermitentes de apnea durante un periodo de 6 minutos, mientras caminaban en una cinta. La hipoalgesia se evaluó mediante umbrales de dolor a la presión (UDPs) e intensidad de dolor evocado (DE) en el pulgar, el tibial anterior y la vértebra C7. También se registraron los valores de saturación de oxígeno, frecuencia cardíaca y percepción subjetiva del esfuerzo (PSE) durante las intervenciones.

Resultados: Se incluyeron veintiocho sujetos sanos, asignados en un ratio 1:1 a los grupos GA y GB. Ambos grupos mostraron un aumento en los PPTs en el tibial anterior ($F=10,902$, $p=0.003$, $\eta^2=0.295$) y en C7 ($F=7.62$, $p=0.01$, $\eta^2=0.227$). La intensidad del DE disminuyó en ambos grupos únicamente en el tibial anterior ($F=45,455$, $p=0.043$, $\eta^2=0.149$). No se observaron interacciones significativas entre el tiempo y el grupo en ninguna de las localizaciones corporales, ni para los UDPs ni para la intensidad del DE, lo que indica que la sensibilidad al dolor se modificó de forma similar en ambos grupos.

Conclusiones: Ambas maniobras de apnea, tanto con volumen pulmonar alto como bajo, parecen modificar la sensibilidad al dolor. Sin embargo, los cambios observados fueron similares entre las intervenciones, sin diferencias marcadas entre ellas.

Palabras clave: Apnea; mantener la respiración; ejercicio; percepción del dolor; evaluación sensorial cuantitativa; umbral de dolor a la presión.

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2025; 7(1):m88

Impact of apnea bouts at different lung volumes on pain sensitivity: a pilot trial in healthy subjects.

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Conflict of Interest disclosure:

The authors declare that they have no conflict of interest.

Financial disclosure:

The authors declare that they have received no funding/compensation for the development of this research.

DOI: 10.37382/jomts.v7i1.1628

Date of reception:

2-April-2025

Date of acceptance:

21-July-2025

ABSTRACT

Background: Apnea is a conduction characterized by a cessation of breathing, which is believed to affect the baroreceptor reflex at different lung volumes, influencing the pain sensitivity responses.

Objectives: The present randomized controlled pilot trial aimed to study the effect of breath-holding bouts, with high and low lung volumes on hypoalgesia.

Methods: Subjects were randomized and allocated into a high-volume apnea group (HG), and low-volume apnea group (LG). Both interventions consisted of intermittent breath-holding bouts for a 6-min period while a walking on a treadmill. Hypoalgesia was tested with pressure pain thresholds (PPTs) and evoked pain (EP) intensity, in thumb, tibialis anterior and C7. Oxygen saturation values, heart rate, and rated perceived exertion (RPE) during the interventions were also collected.

Results: Twenty-eight healthy were included and allocated in a 1:1 ratio to HG and LG. Both groups increased PPTs in tibialis anterior (F=10,902, p-value=0.003, η2=0.295), and C7 (F=7.62, p-value=0.01, η2=0.227) locations. EP intensity was reduced in both groups only in tibialis anterior (F=45,455, p-value=0.043, η2=0.149). No time x group interactions were observed in any body location, for PPTs or EP intensity, indicating that pain sensitivity was similarly modified in both groups.

Conclusion: Both apnea manoeuvres, at high, and low pulmonary volume seem to modify pain sensitivity. Nevertheless, changes are similar across interventions, with an absence of marked differences between them.

Keywords: Apnoea; breath-hold; exercise; pain perception; quantitative sensory testing; pressure pain threshold.

INTRODUCTION

Dynamic apnea is defined as the voluntary interruption of breathing (Schagatay, 2010). These practices elicit characteristic physiological responses in the human body, at the level of the cardiovascular system and athletic performance. They also affect the respiratory system increasing tolerance to hypercapnia and hypoxemia (Andersson et al., 2004; Costalat et al., 2014).

During the respiratory cycle, as during exercise, changes in interpleural pressure can modify blood pressure values (Reyes del Paso et al., 2015). This interaction occurs through the stimulation of the aortic arch and carotid sinus baroreceptors, which respond to the stretching caused by these pressure changes (Koltyn & Umeda, 2006) triggering the baroreceptor reflex (Reyes del Paso et al., 2015). Therefore, any manoeuvre that alters the respiratory cycle, such as those performed during apnea bouts, could influence the stimulation of these receptors (Edwards et al., 2001; Reyes del Paso et al., 2015).

Recent literature suggests that both apnea and high-intensity exercise can independently induce hypoalgesic responses, likely through activation of overlapping autonomic and central mechanisms. The simultaneous application of these stimuli may lead to a potentiation of their individual effects. For instance, both exercise and breath-holding are associated with increased blood pressure and enhanced baroreceptor activity, which in turn are linked to pain inhibition via descending modulatory pathways (Edwards et al., 2001; Jafari et al., 2016). Moreover, the sympathetic activation during apnea may amplify the physiological stress response induced by exercise, enhancing the engagement of endogenous analgesic systems.

This relationship may stem from increased blood pressure, which has been shown to have an inverse relationship with pain intensity (Duschek et al., 2007). Baroreflex sensitivity is also modulated by lung volume during apneas, with greater sensitivity observed at low lung volumes compared to high lung volumes (Nardone et al., 2020). This phenomena may reflexively activate modulatory centres for pain and may explain the modulation of the nociceptive reflexes (Edwards et al., 2001; Suarez-Roca et al., 2019).

In addition, acute exercise bouts can produce immediate hypoalgesic responses in healthy individuals particularly at high intensities., Low to moderate intensity exercise does not appear to induce such changes (Pacheco-Barrios et al., 2020). Exercise modalities, such as aerobic exercise, present controversial findings across meta-analyses on their pain sensitivity effects (Pacheco-Barrios et al., 2020; Wewege & Jones, 2021).

Recent evidence suggests that apnea may produce hypoalgesic response (Mendoza-Arranz et al., 2024), however the effect of varying lung volumes remains unexplored as a potential factor in this effect. According to the findings mentioned before, we hypothesized that lung volume could be an influencing factor on apnea hypoalgesia, increasing the pressure pain thresholds (PPTs) and reducing the perception of evoked pain (EP).

It is suggested to conduct a pilot randomized controlled trial with the aim to compare two apnea protocols during aerobic exercise in healthy participants, between a high-volume apnea group (HG) and a low-volume apnea group (LG). Due to the intensity factor on apnea bouts, authors expect that LG will cause greater perceived intensities and, consequently a greater hypoalgesic response than HG. Authors will additionally explore heart rate (HR), oxygen saturation (SpO_2), and RPE between protocols.

METHODS

The trial was approved by the Ethics Committee for Human Research of the Centro Superior de Estudios Universitarios La Salle (CEISH-CSEULS), Madrid, Spain, with code CSEULS-PI-005/2023, and was conducted in accordance with the ethical standards of the Helsinki Declaration.

Sampling and selection criteria

A non-probabilistic sampling method was conducted. Participants should fulfil the following criteria for being eligible: 1) 18-65 years; and 2) basal $SpO_2 \geq 95$. The following exclusion criteria was applied to detect healthy subjects: 1) diabetes; 2) hypertension or hypotension: 3) frequent pain during the last month; 4) current pharmacological treatment;

5) recreational drug use; 6) self-harming behaviours; 7) cardiac and/or respiratory pathology; 8) pregnancy or possibility of being pregnant. Additionally, the following exclusion criteria was considered for avoiding an interaction with apnea or PPT responses: 9) splenectomy or spleen malformation (Shephard, 2016); 10) moderate physical activity within 24 hours before the study (Zheng et al., 2021); 11) sleep deprivation the night prior to the study (Staffe et al., 2019); and 12) alcohol consumption within 24 hours prior to participating in the study (Horn-Hofmann et al., 2019).

Randomization and concealment

A randomization with 1:1 allocation ratio was conducted into LG and HG. Sex and age were considered as potential influential factors on PPT features (Vervullens et al., 2022), therefore, a cluster randomization was conducted for both factors. This process was conducted with GraphPad software (GraphPad Software Inc., La Jolla, CA, USA) prior to study start.

The evaluator assessing PPTs, and EP intensity was fully blinded to the intervention conditions, including participants' group allocation, as well as to physiological and perceptual variables such as HR, SpO_2, and RPE. Once the initial assessment was completed, the evaluator left the room to ensure they remained unaware of group allocation or any other intervention-related details. After the intervention, the evaluator was called back into the room to perform the post-intervention assessments.

Interventions

Both intervention groups performed a protocol on a treadmill at a speed of 5.5 km/h and a 5° inclination for 6 minutes. During the protocol, participants performed voluntary dynamic apneas cyclically. Each cycle consisted of a breath-hold lasting 10 seconds, immediately followed by 5 seconds of normal tidal breathing. This sequence was continuously repeated for the entire 6-minute duration of the intervention, resulting in a total of 24 apnea cycles. The only difference between the groups was the lung volume at which the apneas were performed. For the LG, each 10-second apnea was initiated following a passive expiration, similar to a relaxed sigh. In contrast, the HG performed the apneas after completing a deep inhalation to total lung capacity. The start and end times of each phase were regulated by a clock and an auditory alarm. A researcher closely supervised the participants to ensure the correct execution of both low and high pulmonary apneas, as well as the precise timing for each apnea and the subsequent periods of normal breathing.

Prior to the intervention, subjects were familiarized with the interventions and the signals emitted during the protocol.

Sociodemographic variables

The participants were characterized according to age, sex, body mass index (BMI), dominant side, resting percentage of the maximum heart rate ($\%HR_{max}$), and resting SpO_2.

Three questionnaires were provided in their validated Spanish versions, regarding the level of physical activity (Global Physical Activity Questionnaire, GPAQ) (Hoos et al., 2012), sleep quality (Pittsburgh Sleep Quality Index, PSQI) (Hita-Contreras et al., 2014), and perceived stress level (Perceived Stress Scale, PSS-14) (Remor, 2006). These three variables were assessed due to their role on pain modulation processes (Fiedler et al., 2021; Hven et al., 2017; Steinmetz et al., 2023).

Pain sensitivity assessments

The PPT, the minimum pressure to elicit the first painful sensation, was assessed using a pressure algometer (PAIN TEST™ FPX 25, Wagner Instruments, Greenwich, CT, USA) with a 1 cm^2 rubber disc measuring in kg/cm^2. Measurements were taken at three sites: the dorsal base of the distal thumb phalanx on their dominant hand, the anterior and proximal lateral aspect of the tibialis anterior muscle on their dominant leg, and the cleft between C7 and T1 vertebra's spinous process. Testing areas were marked with a pen for consistency, and three measurements were taken at each site with a 30-second rest between them, and the results were averaged for analysis. Pressure application was controlled by a metronome at a rate of 0.5 $kg/cm^2/s \pm 0.1\ kg/cm^2/s$, presenting a good inter-rater reliability (ICC=0.91) (Chesterton et al., 2007).

EP intensity refers to the severity of the pain sensation in response to a mechanical stimulus. Since there is no similar approach in the current literature using mechanical stimuli, we opted to employ the same ramp protocol until reaching a pressure of 10 kg/cm^2. The same locations were assessed on the non-dominant side (thumb, and tibialis anterior), and on the cleft between T1 and T2 vertebra's spinous process. A single trial was tested in each location, and participants reported their perceived pain intensity using a visual analogue scale (VAS) (Bijur et al., 2001).

Both PPTs and EP intensity were tested before and 2-min immediately after the completion of the protocols. To mitigate potential interactions influencing pain sensitivity assessments, PPTs were always evaluated prior to EP. Furthermore, the order of PPTs assessment locations was randomized for each participant, while the order of EP assessment locations would remain the same with that of PPTs. The sequence for assessing locations was determined with GraphPad prior to study start.

Cardiorespiratory evaluation

HR and SpO_2 values were explored while resting in supine position for a period of 2 min. The last value along this period was considered as the resting basal value. Additionally, HR and SpO_2 were assessed through the intervention protocol (6 min) and after its completion for a 2-minute period. These values were video-taped and extracted second by second for analysis. Both measures were analysed with a pulse-oximeter placed on the index finger of the dominant hand (NONIN Medical Inc., Model 9843, USA) (Basaranoglu et al., 2015).

HR response

SpO_2 was analysed at rest (baseline), and during the 6-min intervention protocols. Time expended in exercise-induced hypoxemia zones were analysed between groups, for Normal saturation zone (≥95% SpO_2), Mild hypoxemia zone (93-94% SpO_2), Moderate hypoxemia zone (88-92% SpO_2), and Severe hypoxemia zone (≤87% SpO_2) (Dempsey, 1999).

Rated perceived exertion

RPE was assessed immediately after the completion of the protocol using the Borg CR-10 scale (Shariat et al., 2018).

Statistical analysis

The results were expressed as means and standard deviations (SD). To confirm the normality of the data, the Shapiro-Wilk test was used.

All continuous variables were assessed for normal distribution with the Shapiro-Wilk test (confirming normality if p-value > 0.05). Baseline differences between groups were analysed with Student's t-test, or Mann-Whitney U-test, based on the presence of normal or non-normal distribution in the explored variables, respectively. A chi-squared test was employed to detect differences between groups in categorical variables.

A mixed ANOVA with Group factor (HG and LG), and Time factor (baseline, and 2-min immediately after treatment completion), employing individual analyses for every PPTs and EP locations. Time and Group main effects, and Time x Group interaction were extracted and reported. Post-hoc analyses with Bonferroni correction were conducted if significancy was obtained in any main effect, or interaction. Authors would confirm differences within or between groups if both, main or interaction effects, and Bonferroni correction reached significancy.

Differences between groups in time between $\%HR_{max}$ zones, time in SpO_2 zones, and RPE were compared pair-wisely with Student's t-test, or Mann-Whitney U-test, based on the presence of normal or non-normal distribution in the explored variables, respectively. The mean difference (MD) or median difference (MdnD) will be reported for each variable tested with Student's t-test, or Mann-Whitney U-test respectively.

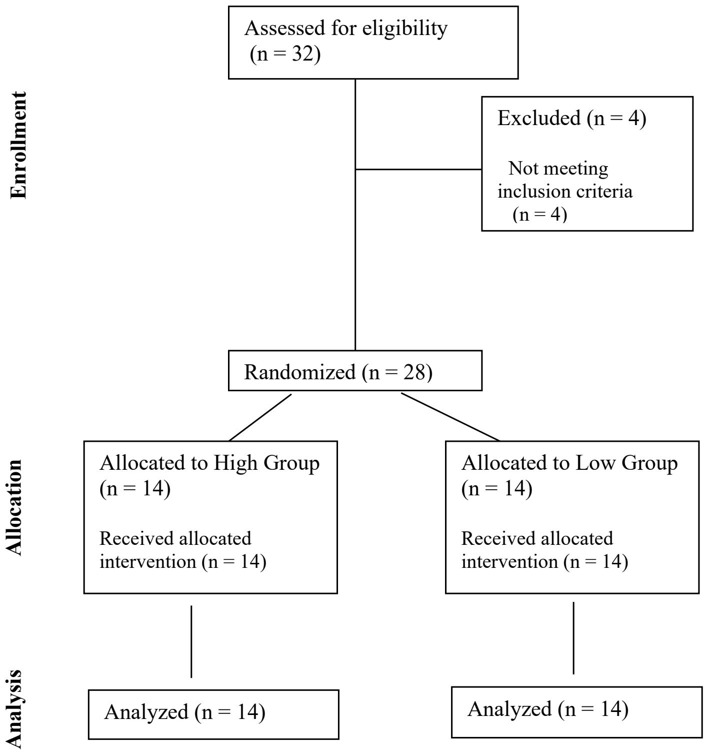
All statistical analyses were performed with the software *"The jamovi project (2023). jamovi (Version 2.3.17) [Computer Software]. Retrieved from https://www.jamovi.org"*, with a 95%CI, and considering statistical significancy when p-value < 0.05.

RESULTS

Sample characteristics

A total of 32 subjects were assessed for eligibility, excluding 4 individuals for not meeting the inclusion criteria. The remaining 28 subjects were randomly assigned to HG and LG, with all receiving the allocated intervention and completing it. See Figure 1.

Figure 1. Flow chart showing the eligibility process for the participants included in the study.



These amount of subjects was selected with an exploratory purpose due to the pilot aim of the trail. The results of this pilot trail will serve for future trials to conduct a proper sample size calculation for an extensive randomized controlled trial.

Groups presented similar values across sociodemographic variables (p-value > 0.05). Additionally, groups presented similar values for physical activity level, sleep quality, perceived stress level, and baseline PPTs, and EP intensity in all the explored locations (p-value > 0.05). Baseline values of HG and LG are presented in Table 1.

Pressure pain threshold - Thumb

No significant differences were detected through time, between groups, nor an interaction between time and group.

Pressure pain threshold – Tibialis

A significant increase in PPT was detected through time (F=10,902, p-value=0.003, η^2=0.295). However, no differences were detected between groups, nor an interaction between groups and time.

Pressure pain threshold – C7

A significant increase in PPT was detected through time (F=7.62, p-value=0.01, η^2=0.227). However, no differences were detected between groups, nor an interaction between groups and time. The data from PPT measurements in the three regions are summarized Table 2.

Evoked pain intensity - Thumb

No significant changes were detected in EP intensity through time, across groups neither an interaction between time and group.

Evoked pain intensity - Tibialis

A significant reduction in EP intensity was detected through time (F=4.5455, p-value=0.043, η^2=0.149). However, no relevant changes were detected across groups, neither an interaction between time and group.

Evoked pain intensity – T1

No significant changes were detected in EP intensity through time, across groups neither an interaction between time and group.

The values of EP intensity measurements are summarized in Table 2.

HR response

HG and LG spent similar times in Zones 1 (MD [HG-LG]: 15.7 s, p=0.749), Zone 2 (MdnD [HG-LG]: 13 s, p=0.52) and Zone 3 (MdnD [HG-LG]: -18 s, p=0.883). Subjects of LG and HG did not reach Zone 4 or Zone 5. See Figure 2, and Table 3.

Oxygen saturation

HG and LG spent similar times in Normal saturation zone (MdnD [HG-LG]: 34 s, p-value=0.26), Mild hypoxemia zone (MD [HG-LG]: 29 s, p-value=0.23), Moderate hypoxemia zone (MD [HG-

LG]: -42.5 s, *p*-value=0.22), and Severe hypoxemia zone (MdnD [HG-LG]: -12 s, *p*-value=0.42). See Figure 3, and Table 3.

Table 1. Sociodemographic and baseline clinical data of participants.

	HG (n=14)	LG (n=14)	Pair-wise comparisons (*p*-value)
Age (years)	30±11	30±13	0.799§
Sex (n Male/n Female)	8/6	9/5	0.699$
BMI (kg/m^2)	23.24±2.79	23.44±2.49	0.843‡
GPAQ (METs)	81.54±51.97	85.71±50.86	0.832‡
PSS-14	16.57±7.68	19.36±8.33	0.366‡
PSQI	5.01±2.68	7.29±3.26	0.054‡
Rest SpO_2 (%)	97±0.84	97±1.08	0.884§
Rest $\%HR_{max}$	37.04±3.91	34.69±6.26	0.245‡
PPT Thumb (kg/cm^2)	4.97±1.76	5.21±1.86	0.541§
PPT Tibialis (kg/cm^2)	5.13±1.38	5.92±2.59	0.325‡
PPT C7 (kg/cm^2)	3.71±1.61	4.29±1.84	0.376‡
EP Thumb	57.21±26.11	55.07±22.94	0.783§
EP Tibialis	46.07±22.07	50.43±22.51	0.609‡
EP T1	64.57±19.97	59.01±20.91	0.477‡

Mean ± SD were presented in the table.

‡. T-Student Test was applied; §. Mann U-Withney test was applied; $. Chi-squared test was applied;

*. $p<0.05$.

$\%HR_{max}$, Percentage of theoretical maximum heart rate; AG, Apnoea group; CG, Control group; BMI, Body mass index; CPM, Conditioned pain modulation; EP, Evoked pain; GPAQ, Global physical activity questionnaire; HG, High lung volume apnoea group; LG, Low lung volume apnoea group; METs, Metabolic equivalent of task; PPT, Pressure pain threshold; PSQI, Pittsburgh sleep quality index; PSS-14, Perceived stress scale; SpO_2, Oxygen saturation.

Rated perceived exertion

HG and LG presented similar perceived exertion at the end of the apnea protocols (MD (HG-LG): -0.93, p=0.159), see Table 3.

DISCUSSION

No relevant differences were observed between groups, and therefore, with current data we cannot assume any relevant difference between groups on hypoalgesia. However, a significant time effect was observed for PPT in tibialis and C7, as for evoked pain intensity in tibialis, indicating that both apnea maouvers are able to produce hypoalgesic responses.

The initial hypothesis was that the LG protocol would generate a more pronounced hypoalgesic response. This idea is supported by evidence available in the study of Nardone (Nardone et al., 2020), which reported a greater antinociceptive effect at low lung volumes, likely due to increased chemoreceptor

Table 2. Mixed ANOVAs of pain sensitivity.

Measures		Groups	Time-point Pre	Time-point Post	Mixed ANOVA (F, *p*-value, η_p^2) Time	Group	Time x Group
PPT	Thumb	HG	4.97±0.48	5.72±0.49	4.08, 0.054, 0.136	0.014, 0.907, 0.001	2.25, 0.146, 0.08
		LG	5.21±0.48	5.32±0.49			
	Tibialis anterior	HG	5.13±0.55	5.91±0.56	**10.902, 0.003*, 0.295** **0.003†**	0.697, 0.411, 0.026	0.576, 0.455,0.022
		LG	5.92±0.55	6.4±0.56			
	C7	HG	3.7±0.46	4.56±0.45	**7.62, 0.01*, 0.227** **0.01†**	0.315, 0.58, 0.012	1.29, 0.267, 0.047
		LG	4.29±0.46	4.65±0.45			
EP	Thumb	HG	57.2±6.57	49.9±6.84	2.14, 0.155, 0.076	0.0257, 0.874, 0.001	2.06, 0.163, 0.073
		LG	55.1±6.57	55±6.84			
	Tibialis anterior	HG	46.1±5.96	38.6±5.59	**4.545, *0.043, 0.149** **0.043†**	0.277, 0.603, 0.011	0.0206, 0.887, 0.001
		LG	50.4±5.96	41.9±5.59			
	T1	HG	64.6±5.47	54.8±5.65	3.42, 0.076, 0.116	0.0186, 0.893, 0.001	2.63, 0.117, 0.092
		LG	59±5.47	58.4±5.65			

Estimated Marginal Mean ± Standard Error, were presented in the table.

*, $p<0.05$.

†, Bonferroni post-hoc analysis *p*-value. This post-hoc analysis revealed significant reduction among groups between basal CPM and EP after intervention.

AG, Apnea group; CG, Control group; PPT, Pressure pain threshold; CPM, Conditioned pain modulation.; HG: High lung volume apnoea group; LG: Low lung volume apnoea group; EP Evoked pain.

stimulation. However, their intervention focused exclusively on respiratory maneuvers, while our protocol combined voluntary breath-holding with aerobic activity (walking). This concurrent motor task may have modulated or overridden the respiratory-induced effects observed in Nardone's study, potentially attenuating the influence of lung volume alone. Additionally, the absence of significant group differences in our results could reflect an insufficient stimulus intensity to trigger distinct pain sensitivity responses based solely on pulmonary volume.

Several physiological pathways may be involved in the observed hypoalgesic effects. The baroreflex, which is activated by cardiovascular changes during apnea and exercise, has been shown to inhibit nociceptive transmission through descending modulation (Reyes del Paso et al., 2015). Additionally, cortical areas such as the periaqueductal gray (PAG) and the rostral ventromedial medulla (RVM) may be engaged, contributing to descending inhibition. Furthermore, increased blood pressure and oxygen desaturation might stimulate the release of

Figure 2. % of heart rate (HR) means of each group during the intervention.

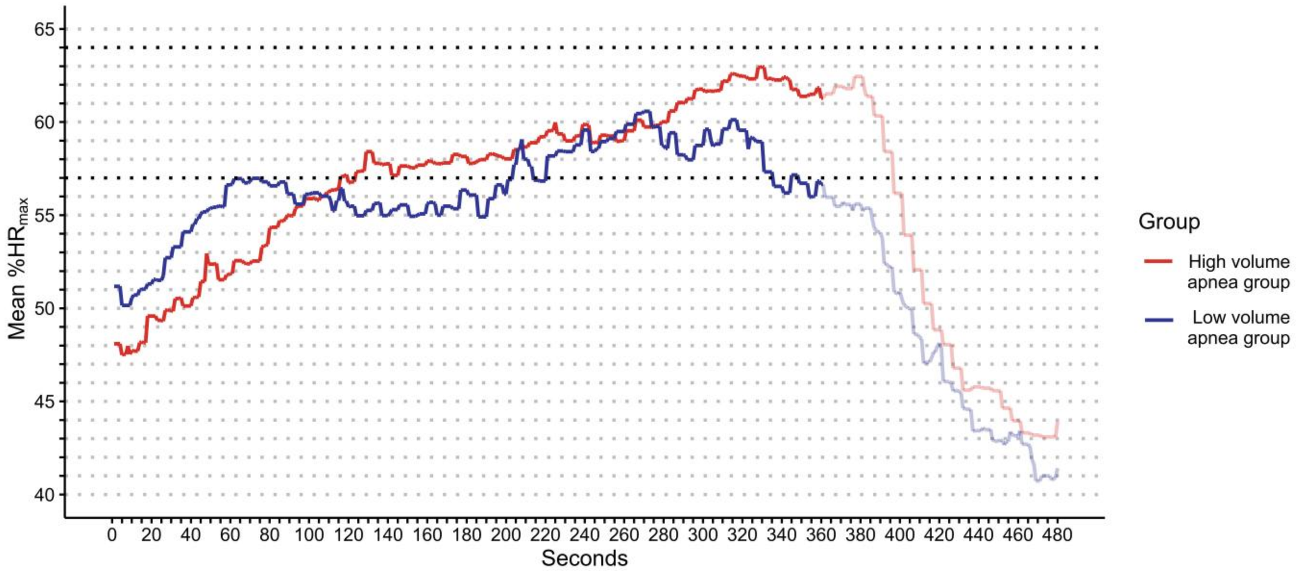


Figure 3. % of oxygen saturation (SpO_2) means of each group during the intervention.

endogenous opioids, such as beta-endorphins, enhancing pain threshold (Hughes & Patterson, 2020).

The cardiovascular changes that occur during aerobic exercise in apnea may activate the baroreceptor reflex, which in turn can trigger a hypoalgesic response by stimulating the centers of the central nervous system responsible for pain inhibition. These results could generate an improvement in pain sensitivity. Previous studies have also demonstrated this increase in pain thresholds in response to different apnea manoeuvres (Reyes del Paso et al., 2015). It has been shown that aerobic exercise alone is effective in producing a hypoalgesic response by increasing PPT, influencing pain modulation mechanisms and nociceptive processing (Vaegter & Jones, 2020). In this sense, by simultaneously implementing both interventions, two treatment alternatives that are capable of generating this type of effect are combined.

Table 3. Time in %HRmax zones and induced-hypoxemia zones during the interventions and rated perceived exertion.

	HG (n=14)	LG (n=14)	Pair-wise comparisons (*p*-value)
HR data			
Time in $\%HR_{max}$ Zone 1 (s)	168.3±122.65	152.6±133.94	0.749‡
Time in $\%HR_{max}$ Zone 2 (s)	120.9±99.87	111±109.32	0.52§
Time in $\%HR_{max}$ Zone 3 (s)	66.5±100.37	77±98.03	0.883§
Time in $\%HR_{max}$ Zone 4 (s)	0	0	-
Time in $\%HR_{max}$ Zone 5 (s)	0	0	-
SpO_2 data			
Time in Normal saturation zone (s)	133.6±130.01	76.6±73.01	0.26§
Time in Mild hypoxemia zone (s)	94±75.85	65±45.02	0.23‡
Time in Moderate hypoxemia zone (s)	101.9±81.65	144.4±96.49	0.22‡
Time in Severe hypoxemia zone (s)	29.71±49.25	66.1±112.40	0.418§
RPE			
Borg CR-10	4.43±1.79	5.36±1.6	0.159‡

Mean ± SD were presented in the table.

‡. T-Student Test was applied; §. Mann U-Withney test was applied.

*. $p<0.05$.

$\%HR_{max}$, Percentage of theoretical maximum heart rate; Borg CR-10, Borg Category Rating 10 point scale; HG, High lung volume apnea group; LG, low lung volume apnea group; HR, Heart rate; SpO_2, Oxygen saturation; Min, Minimum.

Regarding the decrease in EP intensity, only finding a time effect was observed in tibialis anterior. The latest studies addressing the effects of blood flow restriction on exercise-induced hypoalgesia suggest that both intensity and volume are the variables to consider, as they determine whether the hypoalgesic effect is greater or not compared to interventions without blood flow restriction (Karanasios et al., 2023). According to the latest literature review conducted by Karanasios et al. (Karanasios et al., 2023), several articles have shown that restrictions of blood flow at an occlusive arterial pressure of 80% have achieved greater effects than restrictions at 40%. Considering that some mechanisms for inducing hypoalgesia are similar between this type of intervention and the one conducted in our study (Hughes & Patterson, 2020), this could suggest that a higher intensity and greater oxygen desaturation are necessary for different mechanisms such as the baroreceptor reflex, increased blood pressure, and overexpression of biomarkers (beta-endorphins, etc.) to be activated. On the other hand, in cases where the intensity is not sufficient, the effects produced by this type of intervention could be due to other alternative explanations such as the impact of attentional factors on the hypoalgesic response (Silvestrini & Corradi-Dell'Acqua, 2023). It can be considered that the performance of voluntary breath-holding at specific intervals while conducting a 6-minute walk test represents a higher distraction and cognitive load than our body is accustomed to. Therefore, these factors could be predominantly involved in generating hypoalgesia at low intensities. In this case, there were no significant differences in the perceived exertion between groups, potentially explaining the similar pain sensitivity response.

Limitations

The study has certain limitations that are important to highlight. Firstly, there was a small data loss of HR and SpO_2 due to issues with the pulse oximeter. However, this loss occurred in a small number of subjects and for a short period of time during the intervention. Secondly, it is important to note that blood pressure was not measured in our study, which is a relevant variable to consider in hypoalgesia generation. For future research designs, it is recommended to include blood pressure measurement to have a more comprehensive understanding of the mechanisms involved in the hypoalgesic response. This would allow for a better assessment of the relationship between cardiovascular changes and pain modulation during the intervention protocol. Additionally, it is important to mention that the sample size used in our study was 28 subjects in total. While this sample size can provide valuable information, it is important to consider that larger sample sizes are often recommended for detecting with a higher precision the potential differences between interventions.

Clinical implications

These results can be advantageous for clinical practice. By working with high lung volume apnea, a lower internal workload is generated, leading to an effortless intervention. This makes it a better-tolerated option for patients. When transferring these results to clinical practice, it will be an option that promotes greater treatment adherence among patients, as it does not generate as much fatigue as the LG protocol. Additionally, subjecting deconditioned patients, those with cardiorespiratory diseases to the low-volume protocol could be a contraindication that can be overcome by training with high volume. In contrast, the LG protocol should involve more time spent at low oxygen saturations, potentially posing a risk of dizziness or adverse effects in this type of high-risk population. On the other hand, another clinical advantage of apnea is that it can be used to address patients with hypervigilance or kinesiophobia, as it generates a distracting stimulus. However, future studies must conclude its effectiveness and safety in healthy subjects in order to be tested in clinical populations.

CONCLUSION

The results offered by this research suggest that apnea training, regardless of the volumes used, may have immediate hypoalgesic effects upon completing the intervention in healthy subjects. No significant differences between protocols can be concluded from the present study. Future studies are needed to ensure the effects produced by this type of training protocol.

FRASES DESTACADAS

- Tanto el protocolo de apnea a bajo como a alto volumen pulmonar generaron efectos hipoalgésicos inmediatos.
- Las apneas realizadas a diferentes volúmenes pulmonares produjeron efectos similares sobre la sensibilidad al dolor.
- Las apneas a alto volumen pulmonar podrían ser un protocolo más viable.

HIGHLIGHTS

- Both low and high lung volume apnea protocols led to immediate hypoalgesic effects
- High and low lung volume apneas produced similar effects on pain sensitivity.
- High lung volume apnea may be a more viable protocol

DATA AVAILABILITY STATEMENT

The study presents original contributions shown in the article. For any further inquiries, please direct them to the corresponding author.

AUTHOR CONTRIBUTIONS

VGS: research, data curation, data visualization, writing - original draft, writing - review and editing. AMR, and JALV: research, data curation, data visualization, writing - original draft. JFM and FDAF: conceptualization, methodology development, formal analysis, funding acquisition, data visualization, writing - review and editing.

CONFLICT OF INTEREST

The authors declare not having any commercial or financial conflicts of interest.

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