

Eccentric-induced delayed-onset muscle soreness impairs cardiac autonomic activity in adolescent athletes: a pre-experimental study

El dolor muscular de aparición tardía inducido por contracción excéntrica afecta negativamente la actividad autonómica cardíaca en adolescentes atletas: un estudio pre-experimental

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Abstract. Objective: To investigate the impact of eccentric-induced delayed-onset muscle soreness (DOMS) on cardiac autonomic activity in adolescent athletes. Methods: A pre-experimental one-group pre-test/post-test design was carried out on fifteen competitive adolescent athletes, and the effect of DOMS on cardiac autonomic activity was assessed while controlling for body composition and anxious state/trait factors. An eccentric exercise protocol was applied to the elbow's flexor muscles to induce DOMS. Then, heart rate variability was compared before and two days after DOMS induction under resting and resisted movement conditions of the painful limb, using a t-test for paired samples. The body composition and the State-Trait Anxiety Inventory (STAI) were also measured. Results: The analysis revealed a significant effect of DOMS on autonomic response in time domain measures of root mean square of successive differences (RMSSD) (MD = -5.58, 95%CI[-9.36, -1.8], t(14) = -3.2, p = 0.007) and standard deviation of normal-to-normal intervals (SDNN) (MD = -9.43, 95%CI[-15.47, -3.39], t(13) = -3.4, p = 0.005), as well as on sympathetic nervous system (SNS) autonomic indices (MD = 0.68, 95%CI[0.07, 1.29], t(14) = 2.4, p = 0.031) and Stress index (SI) (MD = 2.72, 95%CI[0.67, 4.77], t(14) = 2.8, p = 0.013) under exercise conditions. Conclusions: DOMS changes cardiac autonomic activity compared to control conditions during mechanically evoked pain but not at rest. This study highlights the importance of considering the presence of DOMS when HRV is used in adolescent athletes for training, clinical, or research purposes.

Keywords: Sports, Acute pain, Autonomic nervous system, Mechanical hyperalgesia, Muscle damage

Resumen. Objetivo: Investigar el impacto del dolor muscular de aparición tardía inducido por ejercicios excéntricos (DOMS, por sus siglas en inglés) sobre la actividad autonómica cardíaca en atletas adolescentes. Métodos: Se llevó a cabo un diseño preexperimental de un solo grupo con preprueba y postprueba en quince atletas adolescentes competitivos, y se evaluó el efecto de DOMS en la actividad autonómica cardíaca, controlando por composición corporal y los factores de ansiedad estado/rasgo. Se aplicó un protocolo de ejercicio excéntrico a los músculos flexores del codo para inducir DOMS. Luego, se comparó la variabilidad de la frecuencia cardíaca antes y dos días después de la inducción de DOMS, tanto en condiciones de reposo como durante movimientos resistidos del miembro con dolor, utilizando la prueba t para muestras pareadas. Además, se midió la composición corporal y el Inventario de Ansiedad Estado-Rasgo (STAI, por sus siglas en inglés). Resultados: El análisis reveló un efecto significativo de DOMS en la respuesta autonómica cardíaca en el dominio de tiempo en raíz cuadrada de las diferencias sucesivas (RMSSD) (MD = -5.58, IC del 95%[-9.36, -1.8], t(14) = -3.2, p = 0.007) y desviación estándar de los intervalos normales a normales (SDNN) (MD = -9.43, IC del 95%[-15.47, -3.39], t(13) = -3.4, p = 0.005), así como en los índices autonómicos del sistema nervioso simpático (SNS, por sus siglas en inglés) (MD = 0.68, IC del 95%[0.07, 1.29], t(14) = 2.4, p = 0.031) e Índice de Estrés (SI) (MD = 2.72, IC del 95%[0.67, 4.77], t(14) = 2.8, p = 0.013) en condiciones de ejercicio. Conclusiones: El DOMS modifica la actividad autonómica cardíaca en comparación con condiciones de control durante el dolor evocado mecánicamente, pero no en reposo. Este estudio destaca la importancia de considerar la presencia de DOMS cuando se utiliza la VFC en atletas adolescentes para fines de entrenamiento, clínicos o de investigación.

Palabras clave: Deportes, Dolor agudo, Sistema nervioso autónomo, Hiperalgesia mecánica, Daño muscular

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Introduction

Delayed-onset Muscle Soreness (DOMS) is a common phenomenon, generally considered a benign and self-limiting condition, experienced by both recreational and elite athletes after strenuous physical activities that involve muscle overload and is characterized by muscle soreness and weakness, which increases substantially with movement, due to mechanical hyperalgesia (Mizumura & Taguchi, 2024; Nahon et al., 2021). DOMS onset usually occurs 6 to 12 hours after physical activity, with its greatest intensity experienced between 48 to 72 hours later. Typically, repeated eccentric contractions (i.e., a muscle action produced during muscle lengthening, where the external force overcomes the internal force exerted by the muscle) have

been associated with the apparition of DOMS, as they have been observed to cause greater damage to muscle tissue (Domínguez-Gavia et al., 2022; Douglas et al., 2017; Manetti et al., 2019; Newham et al., 1983; Tenberg et al., 2022). Therefore, previous studies have employed this modality to induce DOMS in various research scenarios (Hody et al., 2019; Nguyen et al., 2009; Nosaka et al., 2002; Ochi et al., 2020; Tenberg et al., 2022; Yoshida et al., 2022).

Numerous theories have been proposed to explain the etiology of DOMS. The mechanism for its development has been proposed to be the ultrastructural damage of muscle cells and mechanical receptors, leading to further protein degradation, apoptosis, and local inflammatory response (Hotfiel et al., 2018; Newham et al., 1983). However, unlike research on other types of pain, the effects of DOMS

outside the musculoskeletal system have not been extensively explored (Forte et al., 2022).

Regarding the autonomic nervous system (ANS), pain has been studied as a stressor agent, which can be either personal (i.e., inherent to the individual; for instance, chronic pain) or external (i.e., induced by a controlled external nociceptive source; for instance, heat or electrically induced pain). Research shows that personal and external pain can change cardiac autonomic activity, as measured typically by heart rate variability (HRV) (Bandeira et al., 2021; Forte et al., 2022).

In athletes, the ANS assumes a pivotal role, serving as a crucial regulator to address the heightened metabolic demands of skeletal muscle during exercise (Freeman et al., 2006; Uzawa et al., 2023). This system balances sympathetic and parasympathetic activity, ensuring optimal physiological responses to physical exertion and permitting performance (Freeman et al., 2006). The sympathetic branch of the ANS becomes increasingly active, mobilizing resources and enhancing cardiovascular capacity to deliver oxygen and nutrients to working muscles (Hargreaves & Spriet, 2020; Mongin et al., 2022). Meanwhile, the parasympathetic branch moderates this heightened state, promoting recovery and restoring homeostasis once the exercise stimulus has ceased (Peçanha et al., 2017).

HRV is a non-invasive tool used to assess the autonomic regulation of the heart by analyzing variations in the time intervals between consecutive heartbeats (Malik, 1996). It provides valuable insights into the balance between sympathetic and parasympathetic nervous system activity, with higher HRV indicating greater autonomic flexibility and adaptability (Kubota et al., 2017; Zhao et al., 2024). However, it is not only influenced by external factors (Tiwari et al., 2021): body composition and anxiety state and trait, which are relevant variables in sports performance, can also influence HRV. Therefore, it is important to control their mediating effects (Martinho et al., 2023).

Furthermore, HRV has been used in the athlete population because it is a marker of fatigue, recovery, training status, and acute physical adaptation to exercise (Manresa-Rocamora et al., 2021). HRV has been widely utilized in sports science as a reliable marker for controlling training load, allowing coaches and athletes to monitor training intensity and recovery status (Tibana et al., 2019). Therefore, training programs can be optimized to prevent overtraining, an adverse effect diminishing performance, physiological adaptations, and outcome improvements. However, if DOMS produces changes in HRV, its presence could lead to misinterpreting HRV data, providing incorrect conclusions about an athlete's physiological state, which potentially results in suboptimal training adjustments and negatively affecting performance outcomes. Thus, a comprehensive understanding of DOMS effect on HRV becomes important for coaches and athletes.

However, the specific effects of DOMS on cardiac autonomic activity, particularly in adolescent athletes, remain poorly understood. In contrast to other forms of controlled

induced pain, DOMS presents with tissue damage and inflammatory response, which could produce a different autonomic response than that observed previously (Kox et al., 2011; Newham et al., 1983). A protocol that includes the analysis of HRV both at rest and during mechanical pain reproduction could be employed to understand whether the autonomic changes are caused by pain or by other characteristics inherent to DOMS.

We hypothesize that DOMS will increase sympathetic but decrease parasympathetic activity during painful exercise but not at rest. Furthermore, body composition and anxiety state may modulate this effect. Therefore, the present study aims to investigate the impact of eccentric-induced DOMS on cardiac autonomic activity in adolescent athletes, using HRV as a sensitive measure of autonomic regulation.

Materials and methods

Experimental design

A pre-experimental one-group pre-test/post-test design was conducted. The data-collection protocol included four stages: in the first, the one maximum repetition in non-dominant elbow flexion was evaluated; in the second, body composition, anxious state/trait, and the first two measures of heart rate variability were obtained; in the third, a protocol to induce delayed-onset muscle soreness was applied; finally, anxious state and the last two measures of heart rate variability were evaluated. All stages were carried out between 18:00 to 19:00 hrs.

Participants

Athletes training in the Weights Room of the Regional Training Center of Punta Arenas, Chile, aged 16 ± 0.85 years, were selected by accidental non-probabilistic sampling.

The inclusion criteria were as follows: a) at least two years of experience in the practice of their sport; b) participation in at least one regional, national, or international tournament during the last two years; c) participation in at least three training sessions per week; and d) between 14 and 17 years of age in 2022. Exclusion criteria were: a) diagnosis of heart disease; b) consumption of analgesic and/or beta-blocker drugs; c) injury not compatible with the experimental protocol; d) consumption of tobacco, alcohol, coffee, and/or psychostimulant drugs since 72 h before the first measurement; e) presence of pain of any type during first and second HRV assessment and pain other than DOMS during third and fourth HRV assessment; and f) pregnancy. After selection, 15 adolescent athletes were recruited (male, $n=12$; female, $n=3$), practicing three sports: swimming ($n=1$), handball ($n=10$) and judo ($n=4$).

All participants and their legal representatives voluntarily signed the assent and informed consent before participating. The study was approved by the Research Ethics Committee of the University of Magallanes (N° 015/CEC-UMAG/2022) and conducted following the World Medical

Association and Helsinki Declaration concerning the ethical principles of human experimentation. Furthermore, the participants were instructed to sleep at least 7 hours the night before evaluations and avoid non-pharmacological stimulant consumption.

Instruments

Body composition

Body weight (kg), total fat mass (%), total free fat mass (kg), bone composition (kg), and water (%) were measured by bioimpedance with the Tanita BC-558 Iron-man Segmental Body Composition Monitor (Tanita Ironman, Arlington Heights, IL 60005 USA). Height (cm) was obtained by stadiometer CHARDER® HM230M hand-held measuring rod (Charder Electronics Co., Ltd. No.103, Guozhong Rd., Taiwan, R.O.C.).

Anxiety State and Trait

The 70-item State-Trait Anxiety Inventory (STAI) adaptation, Spanish version, was used, which contrasts two facets of anxiety: those related to the person (trait) and those related to external triggers in an environment close to the subject (state) (Burgos Fonseca et al., 2013).

DOMS intensity

Athletes self-reported their perception of intensity through the Numeric Rating Scale (NRS). It corresponds to the most used numeric scale in which the participants rate the pain from 0 to 10, with 0 being the absence of pain and 10 being the worst pain intensity. The NRS is an internationally validated scale, and its clinical and research use has been reported as the most preferred by professionals (Atisook et al., 2021).

Cardiovascular parameters

HRV was recorded with Polar Team2 equipment (Polar®, Finland). In the time domain, the parameters evaluated were the standard deviation of normal RR intervals (SDNN), which is understood as a marker of the total power of HRV, reflecting sympathetic and parasympathetic activity on the myocardium (BERNTSON et al., 1997a; Buchheit & Gindre, 2006); and the square root of root mean squared differences of successive RR intervals (RMSSD), which reflects parasympathetic activity on cardiac contraction (Buchheit et al., 2010).

In the frequency domain, three components were evaluated: the high-frequency (HF) power band at 0.15 to 0.40 Hz (Akselrod et al., 1981) and the low-frequency (LF) power band at 0.04 to 0.15 Hz, which is considered a marker of parasympathetic and sympathetic activity over the heart (Goldstein et al., 2011). The very low frequency (VLF) band is between 0.0033 and 0.04 Hz (Fisher et al., 2014; Mccraty & Shaffer, 2015).

In addition, the parasympathetic nervous system index (PNS), sympathetic nervous system index (SNS), and Stress Index (SI) were calculated. The PNS reflects the total vagal stimulation and is calculated from the time average of the

R-R intervals, RMSSD, and the index derived from Poincaré's graph corresponding to the width of the ellipse (SD1) in normalized units (related to RMSSD) and indicates the standard deviations above or below the averages obtained in the normal population (Tulppo et al., 1996). The SNS index, reflecting the total sympathetic stimulation, is calculated from the time-averaged R-R intervals, the Baevsky SI (a value positively correlated with cardiovascular system stress and cardiac sympathetic activity), and the Poincaré graph-derived index of ellipse length (SD2) in normalized units (related to SDNN) (Tulppo et al., 1996). The SI indicates the degree of load on the autonomic nervous system; it is normalized using the square root of the Baevsky SI (BERNTSON et al., 1997b; Rajendra Acharya et al., 2006).

The data obtained on HRV were digitized and analyzed using Kubios HRV® software.

Artifacts and ectopic heartbeats, which did not exceed 3% of the recorded data, were excluded ("Heart Rate Variability: Standards of Measurement, Physiological Interpretation, and Clinical Use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology.," 1996).

Procedure

Measurements were conducted in the Regional Training Centre of the Punta Arenas Fiscal Gymnasium (National Sports Institute) in a quiet room illuminated by cold-spectrum lighting between 18:00 and 20:00 hours. Temperature and relative humidity were not controlled. The participants were instructed to sleep adequately for at least 7 hours from the night before the assessments start until the protocol's end. Additionally, they were asked to refrain from eating 1 hour before each session, avoid strenuous physical activity, and consume sufficient water. The assessment protocol consisted of measuring HRV on four occasions: two before the induction of delayed-onset muscle soreness, at rest and during a protocol consisting of isotonic bicep curls, and two after induction, at rest and during the execution of the same bicep curls. The study was performed in four stages, detailed below:

Stage 1: The subjects' one repetition maximum (1RM) was recorded in elbow flexion exercise of the non-dominant arm with a kettlebell in a supine grip (bicep curl). This joint is little used in comparison to others in everyday life.

The 1RM measurement was performed according to an adaptation of Lavender and Nosaka's protocol. For the warm-up and the measurement, the subjects were seated, with the trunk tilted anteriorly and the forearm of the non-dominant arm in supination, resting on the ipsilateral thigh. The warm-up consisted of a three-minute self-regulated continuous elbow flexion and extension. Then, for the 1RM measurement, they were given a progressively heavier Russian weight with an increase of 5 lbs and asked to perform a full elbow flexion. Each repetition was separated by 2 minutes of rest. The test ended if the subject could not lift the same weight with the correct technique in 3 consecutive

attempts. The 1RM was considered the last weight effectively lifted. At the end of the session, the subjects were instructed to have optimal rest during the week, especially before starting the subsequent stages. In addition, they were asked to consume sufficient water, avoid consuming drugs (e.g., coffee, alcohol, tobacco), and limit strenuous physical activity.

Stage 2: 7 days after Stage 1, the subject's body composition was measured by bio-impedance analysis. Then, they were instructed to answer the STAI autonomously but with the assistance of the evaluators to attend questions. Finally, baseline measures of HRV were measured as follows: (i) subjects were placed seated in a quiet and calm environment for 6 minutes, keeping feet, hands, and back supported (HRV 1); (ii) immediately afterward, subjects were asked to perform a 3-minutes series of elbow flexions controlled by an online metronome at six bpm (every 10 seconds), the concentric and eccentric phases were performed in 1 second each, verified by the evaluators with a digital stopwatch (HRV2). The technique used for the exercise was the same as that for obtaining the RM with 50% of this weight.

Stage 3: Induction of DOMS: 24 hours after the previous stage, the subjects participated in a standardized and individualized protocol in intensity. For this, the protocol proposed by Lavender and Nosaka was adopted (Lavender & Nosaka, 2008).

A protocol of eccentric muscle actions was used to elicit DOMS in the elbow's flexor muscles. Athletes were positioned seated in a chair, with the performing elbow on the ipsilateral thigh. They performed non-dominant eccentric bicep curls with a Russian dumbbell at 90% of 1RM, using the dominant hand to aid the concentric phase. Six sets of 5 repetitions were performed, with 2 minutes rest between each set. The athlete started with a flexion of approximately 120° and extended the elbow in a controlled and uniform manner for 5 seconds until reaching maximum elbow extension. Two evaluators monitored correct execution. The protocol was terminated early if the athlete could not control elbow extension for 5 seconds twice in a row in two consecutive sets. The subject was verbally motivated to deliver their maximum effort when a failure occurred. Full elbow mobility was checked before the protocol.

The elbow flexor muscles have been extensively used to elicit muscle pain (Agten et al., 2017; Lavender & Nosaka, 2008; Nguyen et al., 2009; Nosaka et al., 2002; Stennett et al., 2021; Yoshida et al., 2022).

Stage 4: 48 hours after DOMS induction, subjects completed the Anxious State questionnaire from the STAI. Then, the Stage 2 protocol was repeated, obtaining measurements at rest (HRV3) and during the 3-minute bicep curls with DOMS (HRV4). Finally, the NRS was used to quantify pain intensity during bicep curls.

A visual summary of the protocol can be seen in Figure 1.



Figure 1. Protocol Flowchart.

Statistical analysis

The mean and standard deviation were used to describe the numerical variables ($M \pm SD$), and for categorical variables, relative (%) and absolute (n) frequency were used. The variables' normality was evaluated using parametric statistics with the Shapiro-Wilk test and graphical exploration of the data.

To analyze the effect of DOMS on cardiac autonomic regulation, an analysis of covariance (ANCOVA) was used to determine within-subjects differences in HRV indices, controlling for the residual effect of age and sex differences. This allowed the evaluation of the variation in HRV indices between DOMS and basal conditions during exercise and at rest to establish if the observed effect was attributable to the residual impact of the exercise performed in the basal period and the exercise performed in DOMS conditions.

To assess whether body composition or anxious state exerted a significant influence on HRV indices in response to DOMS, it was performed 10,000 bootstrap resampling-based simulations of a linear model with least-squares optimization, using as dependent variable the observed difference between the experimental condition concerning basal (Δ : DOMS - Control), as a measure of autonomic response in response to DOMS during exercise, and as independent variable the body composition or anxious state variables sequentially. Estimating the p-values of the linear model's simulations were obtained from the transformation of the maximum likelihood of the effect, expressed as follows: $2 \times (1 - \max(pd, 1 - pd))$, where pd represents the probability of direction.

To describe the relationship between body composition and anxious state parameters, Pearson's correlation coefficient was used to characterize their relationship with the main effects.

For statistical significance, it was considered a probability of committing a type I error (α) of less than 5% (i.e., $p < 0.05$). All analyses were performed with the statistical programming language R in version 4.2.2 (R Core Team, 2021)

Results

The characteristics of the sample can be seen in Table 1.

Autonomic response to DOMS

DOMS mean intensity and standard deviation assessed by NRS were 5.1 ± 2.1 , which shows that the induction protocol was sufficient to cause moderate muscle pain while isotonic bicep curls were performed. When assessing autonomic response to DOMS, a significant effect was observed

for RMSSD in the time domains, as well as for the autonomic indices SNS and SI under exercise conditions (see Table 2) but not at rest (see Table 3).

Table 1. Sociodemographic, sports, and body composition characteristics of the study sample.

Characteristic	Descriptive statistics				
	Mean	SD	N	%	
Age (years)	16.00	0.85	-	-	
Years of sports practice	4.27	2.34	-	-	
Sport	Handball	-	-	10	67%
	Judo	-	-	4	27%
	Swimming	-	-	1	6.7%
Gender	Female	-	-	3	20%
	Male	-	-	12	80%
Body composition	Weight (kg)	69	9	-	-
	Height (cm)	172	10	-	-
Body fat	Total	16	8	-	-
	LUL ¹	14	7	-	-
	RUL ²	12.8	6.9	-	-
	RLL ³	17	10	-	-
	LLL ⁴	16	10	-	-
	Torso	15.5	6.9	-	-
Muscle mass	Total	55	9	-	-
	LUL ¹	3.19	0.73	-	-
	RUL ²	3.23	0.71	-	-
	RLL ³	9.51	1.54	-	-
	LLL ⁴	9.61	1.51	-	-
	Torso	29.3	4.4	-	-
Body water (%)	61.3	4.6	-	-	
Bone mass	2.88	0.44	-	-	

¹ LUL = Left upper limb.

² RUL = Right upper limb.

³ RLL = Right lower limb.

⁴ LLL = Left lower limb.

Table 2. Comparisons of paired exercise condition HRV measurements (HRV 4 - 2) separated by domain evaluated.

Domain	Parameter	IC _{95%}		Statistic ³			
		η^2_p	Low	High	F	df	p-value
Time	RMSSD	0.402	0	0.698	6.722	1, 10	0.027
	SDNN	0.101	0	0.481	1.12	1, 10	0.315
	Mean R-R interval	0.153	0	0.530	1.801	1, 10	0.209
Frequency	HF	0.117	0	0.498	1.328	1, 10	0.276
	LF	0.229	0	0.589	2.969	1, 10	0.116
	LF/HF	0.030	0	0.383	0.305	1, 10	0.593
	VLF	0.004	0	0.267	0.042	1, 10	0.843
Autonomic Activity indices	SNS	0.442	0.015	0.720	7.922	1, 10	0.018
	PNS	0.210	0	0.575	2.653	1, 10	0.575
	Stress	0.541	0.078	0.773	11.809	1, 10	0.006

Table 3. Comparisons of paired resting condition HRV measurements (HRV 3 - 1) separated by domain evaluated.

Domain	Parameter	IC _{95%}		Statistic ³			
		η^2_p	Low	High	F	df	p-value
Time	RMSSD	0.000	0	0.105	0.003	1, 10	0.955
	SDNN	0.010	0	0.321	0.102	1, 10	0.756
	Mean R-R interval	0.043	0	0.409	0.455	1, 10	0.515
Frequency	HF	0.001	0	0.172	0.008	1, 10	0.930
	LF	0.033	0	0.390	0.343	1, 10	0.571
	LF/HF	0.001	0	0.158	0.007	1, 10	0.936
	VLF	0.000	0	0.000	0.000	1, 10	0.992
Autonomic activity indices	SNS	0.004	0	0.265	0.036	1, 10	0.854
	PNS	0.002	0	0.215	0.016	1, 10	0.903
	Stress	0.021	0	0.361	0.212	1, 10	0.655

¹ η^2_p = Partial Eta squared from ANCOVA.

² IC_{95%} = 95% Confidence interval.

³ Test statistics from ANCOVA, including sex and age as covariates.

Effect of anxiety and body composition on HRV

Of the estimated effects, the anxious state seemed to moderate the effect of DOMS on the SI proportionally to

the increase of this ($\beta = 0.12$, 95%CI [-0.02, 0.20]). Despite the above, this effect was not statistically significant ($p = 0.07$).

Concerning body composition, it was observed that body fat seemed to affect the VLF response in DOMS conditions. In contrast, fat assessed by body segments seemed to suggest a moderating effect that increases the VLF response in exercise conditions versus DOMS compared to the control condition (RUL, $\beta = 3.76$, 95%CI[0, 10.64], $p = 0.05$; RLL, $\beta = 2.37$, 95%CI[0.13, 6.34], $p = 0.033$; LLL, $\beta = 2.38$, 95%CI[0.08, 6.71], $p = 0.04$).

No moderating effect of the other anxious state or body composition variables assessed on the DOMS response on HRV parameters was observed.

Body composition and anxiety

The significant correlations between body composition and anxious state parameters can be seen in Figure 3.

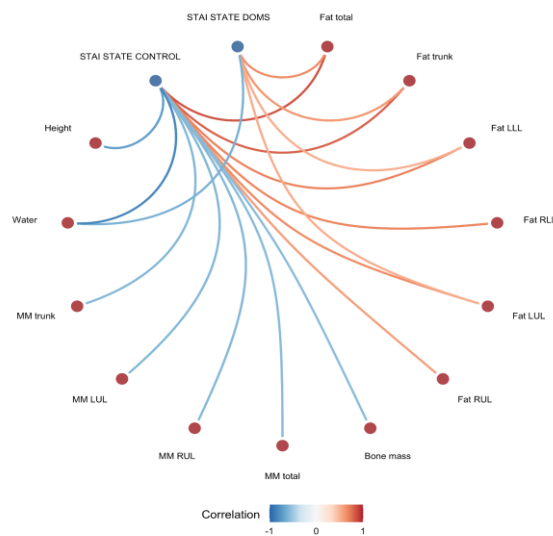


Figure 3. Correlogram of the relationship between the variables of body composition and anxious state. Note: The color of the lines represents the correlation between the variables with a significance level of less than 5% (i.e., $p < 0.05$). MM: Muscle mass. LLL: left lower limb. RLL: Right lower limb. LUL: left upper limb. RUL: Right upper limb

Discussion

This study aimed to investigate the effects of DOMS on cardiac autonomic activity in adolescent athletes while controlling the impact of body composition and anxiety state and trait. To our knowledge, this is the first study to investigate the effect of DOMS on cardiac autonomic modulation through assessment of HRV in rest and exercise conditions in this population. Previous research has studied the effect of various types of pain on cardiac autonomic activity, finding HRV analysis to be a reliable method and reporting significant changes in sympathetic and parasympathetic autonomic activity in response to different types of induced pain (Forte et al., 2022; Koenig et al., 2014). Although

these findings have been mostly reported in healthy adults and not adolescents, the observations were hypothesized to be similar.

During the execution of standardized isotonic bicep curls, the analysis of HRV showed higher sympathetic activity parameters when comparing DOMS to the control condition, as evidenced by decreased RMSSD and SDNN, increased SNS index, and SI. These results suggest that mechanical hyperalgesia associated with DOMS could be the primary cause of the observed changes in autonomic function. Earlier research has shown that nociceptive inputs could activate sympathetic pathways, contributing to the prevalence of sympathetic activity instead of vagal tone (Forte et al., 2022). However, other variables, such as pain intensity and subjective pain experience, may also modulate autonomic response to pain, highlighting the need for further research in this area (Hohenschurz-Schmidt et al., 2020; Kocsel et al., 2023).

On the other hand, the results obtained at rest did not show evidence of significant changes in the markers of cardiac autonomic activity in this sample of adolescent athletes. This could suggest that the effects of DOMS are primarily attributable to pain rather than other characteristics, such as muscle damage or inflammation. However, it is important to note that the induction of DOMS was performed on a small and unilateral muscle group (elbow flexors), being hypothesized that this may limit its effect on global autonomic activity. Thus, while our findings do not evidence significant changes, we cannot rule out the possibility that muscle damage and local inflammation induced by DOMS may have some effect on cardiac autonomic activity. A previous study reported the impact of acute inflammation on HRV, but DOMS-associated inflammation has not been explored (Kox et al., 2011). Further investigation is necessary to explore the effects of DOMS on broader muscle groups for a more precise understanding of the effects of muscle damage and inflammation on cardiac autonomic activity.

Concerning the relationship between morphological and physiological measures, positive correlations were observed between total body fat percentage and the anxious state score obtained by the athletes before and after DOMS induction. This agrees with the results reported by Martínez-Rodríguez et al. in young soccer players, where they found higher anxiety scores in athletes with higher body fat percentages in a sample of similar ages to our adolescent athletes (Martínez-Rodríguez et al. 2022). Since body fat percentage is a relevant parameter for athlete performance, those with higher body fat percentages might feel more pressure regarding their performance in the measurements or their ability to respond to the demands of the protocol, which may explain why anxious state scores were higher in those with higher body fat percentages (Esco et al., 2018).

Nevertheless, this pre-experimental study is not exempt from limitations. First, these results are not generalizable to other populations of adolescent athletes due to the small sample size and the non-probabilistic accidental sampling.

Secondly, the protocol was executed in the regional training center in calm and quiet conditions; however, other factors, such as relative humidity and temperature, were not controlled. Finally, this study did not consider a control group without DOMS induction, which would have allowed us to consider the aforementioned confounding factors in the analysis but requires a much larger sample size to avoid the effects of measuring as dependent on personal circumstances as HRV.

Future research should consider more homogeneous and representative samples of athletes and include a control group, ideally separated by type of sport and years of practice. In addition, the protocols should be carried out in a controlled laboratory setting to avoid the influence of other factors outside the study and to consider longitudinal designs to measure the evolution of the effect. Moreover, additional research is necessary to ascertain the significance of the spread of DOMS and the muscle damage and inflammation it causes. It is also relevant to investigate how practicing various types of exercise affects cardiac autonomic activity in the presence of DOMS. This can be achieved through sport-specific protocols.

Implications in sports practice

The present study provides valuable insights into the autonomic response to DOMS in adolescent athletes. The finding of increased sympathetic activity in response to exercise-induced DOMS suggests that athletes may experience altered autonomic control during the recovery phase of their training (Michael et al., 2017). These findings have potential implications for adolescent athletes' training and load control strategies. Coaches and trainers should consider incorporating measures to monitor and regulate autonomic activity in athletes during the recovery phase after intense or new exercise. However, caution should be exercised when extrapolating these findings to different protocols since exercise intensity could mediate autonomic response (Kaufmann et al., 2023; Michael et al., 2017). Overall, these results highlight the importance of considering DOMS when using HRV as an instrument during athletes' recovery.

Finally, this study's findings provide additional background information to the current understanding of the relationship between DOMS, exercise, and cardiac autonomic activity. However, further investigation using the previously mentioned recommendations is relevant to providing a more comprehensive understanding of this complex interaction and its potential implications for athletic health and performance.

Conclusions

These findings suggest that the autonomic nervous system responds to DOMS when it is reproduced by muscle contraction in adolescent athletes, showing a greater prevalence of sympathetic activity compared with the condition

without DOMS. This study highlights the importance of considering the presence of DOMS when HRV is used in adolescent athletes for training, clinical, or research purposes. It also opens the door to investigate further the possible moderation effect of HRV in DOMS and specific sports performance.

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Data availability statement

The original contributions presented in the study are included in the article. Further inquiries can be directed to the corresponding author.

Disclosure of interest

The authors report that there are no competing interests to declare.

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All the authors have intellectually contributed to the development of the study, assume responsibility for its content, and agree with the definitive version of the article.

References

- Agten, C. A., Buck, F. M., Dyer, L., Flück, M., Pfirrmann, C. W. A., & Roskopf, A. B. (2017). Delayed-Onset Muscle Soreness: Temporal Assessment With Quantitative MRI and Shear-Wave Ultrasound Elastography. *American Journal of Roentgenology*, *208*(2), 402–412. <https://doi.org/10.2214/AJR.16.16617>
- Akselrod, S., Gordon, D., Ubel, F. A., Shannon, D. C., Berger, A. C., & Cohen, R. J. (1981). Power Spectrum Analysis of Heart Rate Fluctuation: A Quantitative Probe of Beat-to-Beat Cardiovascular Control. *Science*, *213*(4504), 220–222. <https://doi.org/10.1126/science.6166045>
- Atisook, R., Euasobhon, P., Saengsanon, A., & Jensen, M. P. (2021). Validity and Utility of Four Pain Intensity Measures for Use in International Research. *Journal of Pain Research*, *Volume 14*, 1129–1139. <https://doi.org/10.2147/JPR.S303305>
- Bandeira, P. M., Reis, F. J. J., Sequeira, V. C. C., Chaves, A. C. S., Fernandes, O., & Arruda-Sanchez, T. (2021). Heart rate variability in patients with low back pain: a systematic review. *Scandinavian Journal of Pain*, *21*(3), 426–433. <https://doi.org/10.1515/sjpain-2021-0006>
- BERNTSON, G. G., THOMAS BIGGER, J., ECKBERG, D. L., GROSSMAN, P., KAUFMANN, P. G., MALIK, M., NAGARAJA, H. N., PORGES, S. W., SAUL, J. P., STONE, P. H., & VAN DER MOLEN, M. W. (1997a). Heart rate variability: Origins, methods, and interpretive caveats. *Psychophysiology*, *34*(6), 623–648. <https://doi.org/10.1111/j.1469-8986.1997.tb02140.x>
- BERNTSON, G. G., THOMAS BIGGER, J., ECKBERG, D. L., GROSSMAN, P., KAUFMANN, P. G., MALIK, M., NAGARAJA, H. N., PORGES, S. W., SAUL, J. P., STONE, P. H., & VAN DER MOLEN, M. W. (1997b). Heart rate variability: Origins, methods, and interpretive caveats. *Psychophysiology*, *34*(6), 623–648. <https://doi.org/10.1111/j.1469-8986.1997.tb02140.x>
- Buchheit, M., Chivot, A., Parouty, J., Mercier, D., Al Haddad, H., Laursen, P. B., & Ahmaidi, S. (2010). Monitoring endurance running performance using cardiac parasympathetic function. *European Journal of Applied Physiology*, *108*(6), 1153–1167. <https://doi.org/10.1007/s00421-009-1317-x>
- Buchheit, M., & Gindre, C. (2006). Cardiac parasympathetic regulation: respective associations with cardiorespiratory fitness and training load. *American Journal of Physiology-Heart and Circulatory Physiology*, *291*(1), H451–H458. <https://doi.org/10.1152/ajpheart.00008.2006>
- Burgos Fonseca, P., Gutiérrez Sepúlveda, A., & Pino Muñoz, M. (2013). *Adaptación y validación del Inventario Ansiedad Estado - Rasgo (STAI) Población Universitaria de la Provincia de Ñuble*. Universidad de Bío-Bío.

- Domínguez-Gavia, N. I., Candia-Luján, R., De León Fierro, L. G., Ortiz-Rodríguez, B., & Carrasco-Legleu, C. E. (2022). La hidroterapia y sus efectos sobre el dolor muscular tardío en deportistas: una revisión sistemática (Hydrotherapy and its effects on delayed onset muscle soreness in athletes: a systematic review). *Retos*, *46*, 733–738. <https://doi.org/10.47197/retos.v46.93960>
- Douglas, J., Pearson, S., Ross, A., & McGuigan, M. (2017). Eccentric Exercise: Physiological Characteristics and Acute Responses. *Sports Medicine*, *47*(4), 663–675. <https://doi.org/10.1007/s40279-016-0624-8>
- Esco, M., Fedewa, M., Cicone, Z., Sinelnikov, O., Sekulic, D., & Holmes, C. (2018). Field-Based Performance Tests Are Related to Body Fat Percentage and Fat-Free Mass, But Not Body Mass Index, in Youth Soccer Players. *Sports*, *6*(4), 105. <https://doi.org/10.3390/sports6040105>
- Fisher, A. C., Groves, D., Eleuteri, A., Mesum, P., Patterson, D., & Taggart, P. (2014). Heart rate variability at limiting stationarity: evidence of neuro-cardiac control mechanisms operating at ultra-low frequencies. *Physiological Measurement*, *35*(2), 309–322. <https://doi.org/10.1088/0967-3334/35/2/309>
- Forte, G., Troisi, G., Pazzaglia, M., Pascalis, V. De, & Casagrande, M. (2022). Heart Rate Variability and Pain: A Systematic Review. *Brain Sciences*, *12*(2), 153. <https://doi.org/10.3390/brainsci12020153>
- Freeman, J. V., Dewey, F. E., Hadley, D. M., Myers, J., & Froelicher, V. F. (2006). Autonomic Nervous System Interaction With the Cardiovascular System During Exercise. *Progress in Cardiovascular Diseases*, *48*(5), 342–362. <https://doi.org/10.1016/j.pcad.2005.11.003>
- Goldstein, D. S., Benthó, O., Park, M.-Y., & Sharabi, Y. (2011). Low-frequency power of heart rate variability is not a measure of cardiac sympathetic tone but may be a measure of modulation of cardiac autonomic outflows by baroreflexes. *Experimental Physiology*, *96*(12), 1255–1261. <https://doi.org/10.1113/expphysiol.2010.056259>
- Hargreaves, M., & Spriet, L. L. (2020). Skeletal muscle energy metabolism during exercise. *Nature Metabolism*, *2*(9), 817–828. <https://doi.org/10.1038/s42255-020-0251-4>
- Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. (1996). *Circulation*, *93*(5), 1043–1065.
- Hody, S., Croisier, J.-L., Bury, T., Rogister, B., & Leprince, P. (2019). Eccentric Muscle Contractions: Risks and Benefits. *Frontiers in Physiology*, *10*. <https://doi.org/10.3389/fphys.2019.00536>
- Hohenschurz-Schmidt, D. J., Calcagnini, G., Dipasquale, O., Jackson, J. B., Medina, S., O'Daly, O., O'Muircheartaigh, J., de Lara Rubio, A., Williams, S. C. R., McMahon, S. B., Makovac, E., & Howard, M. A. (2020). Linking Pain Sensation to the Autonomic Nervous System: The Role of the Anterior Cingulate and Periaqueductal Gray Resting-State Networks. *Frontiers in Neuroscience*, *14*. <https://doi.org/10.3389/fnins.2020.00147>
- Hotfiel, T., Freiwald, J., Hoppe, M. W., Lutter, C., Forst, R., Grim, C., Bloch, W., Hüttel, M., & Heiss, R. (2018). Advances in Delayed-Onset Muscle Soreness (DOMS): Part I: Pathogenesis and Diagnostics. *Sportverletzung Sportschaden : Organ Der Gesellschaft Fur Orthopadisch-Traumatologische Sportmedizin*, *32*(4), 243–250. <https://doi.org/10.1055/a-0753-1884>
- Kaufmann, S., Gronwald, T., Herold, F., & Hoos, O. (2023). Heart Rate Variability-Derived Thresholds for Exercise Intensity Prescription in Endurance Sports: A Systematic Review of Interrelations and Agreement with Different Ventilatory and Blood Lactate Thresholds. *Sports Medicine - Open*, *9*(1), 59. <https://doi.org/10.1186/s40798-023-00607-2>
- Kocsel, N., Galambos, A., Szőke, J., & Kökönyei, G. (2023). The moderating effect of resting heart rate variability on the relationship between pain catastrophizing and depressed mood: an empirical study. *Biologia Futura*. <https://doi.org/10.1007/s42977-023-00190-3>
- Koenig, J., Jarczok, M. N., Ellis, R. J., Hillecke, T. K., & Thayer, J. F. (2014). Heart rate variability and experimentally induced pain in healthy adults: A systematic review. *European Journal of Pain*, *18*(3), 301–314. <https://doi.org/10.1002/j.1532-2149.2013.00379.x>
- Kox, M., Ramakers, B. P., Pompe, J. C., van der Hoeven, J. G., Hoedemaekers, C. W., & Pickkers, P. (2011). Interplay Between the Acute Inflammatory Response and Heart Rate Variability in Healthy Human Volunteers. *Shock*, *36*(2), 115–120. <https://doi.org/10.1097/SHK.0b013e31821c2330>
- Kubota, Y., Chen, L. Y., Whitsel, E. A., & Folsom, A. R. (2017). Heart rate variability and lifetime risk of cardiovascular disease: the Atherosclerosis Risk in Communities Study. *Annals of Epidemiology*, *27*(10), 619–625.e2. <https://doi.org/10.1016/j.annepidem.2017.08.024>
- Lavender, A. P., & Nosaka, K. (2008). Changes in markers of muscle damage of middle-aged and young men following eccentric exercise of the elbow flexors. *Journal of Science and Medicine in Sport*, *11*(2), 124–131. <https://doi.org/10.1016/j.jsams.2006.11.004>
- Malik, M. (1996). Heart Rate Variability. *Annals of Noninvasive Electrocardiology*, *1*(2), 151–181. <https://doi.org/10.1111/j.1542-474X.1996.tb00275.x>
- Manetti, M., Tani, A., Rosa, I., Chellini, F., Squecco, R., Idrizaj, E., Zecchi-Orlandini, S., Ibba-Manneschi, L., & Sassoli, C. (2019). Morphological evidence for telocytes as stromal cells supporting satellite cell activation in eccentric contraction-induced skeletal muscle injury. *Scientific Reports*, *9*(1), 14515. <https://doi.org/10.1038/s41598-019-51078-z>

- Manresa-Rocamora, A., Flatt, A. A., Casanova-Lizón, A., Ballester-Ferrer, J. A., Sarabia, J. M., Vera-García, F. J., & Moya-Ramón, M. (2021). Heart rate-based indices to detect parasympathetic hyperactivity in functionally overreached athletes. A meta-analysis. *Scandinavian Journal of Medicine & Science in Sports*, *31*(6), 1164–1182. <https://doi.org/10.1111/sms.13932>
- Martínez-Rodríguez, A., Peñaranda-Moraga, M., Vicente-Martínez, M., Martínez-Moreno, M., Cuestas-Calero, B. J., Soler-Durá, J., Yáñez-Sepúlveda, R., & Muñoz-Villena, A. J. (2022). Relationship between Anthropometric Measures and Anxiety Perception in Soccer Players. *International Journal of Environmental Research and Public Health*, *19*(15), 8898. <https://doi.org/10.3390/ijerph19158898>
- Martinho, D. V., Field, A., Rebelo, A., Gouveia, É. R., & Sarmiento, H. (2023). A Systematic Review of the Physical, Physiological, Nutritional and Anthropometric Profiles of Soccer Referees. *Sports Medicine - Open*, *9*(1), 72. <https://doi.org/10.1186/s40798-023-00610-7>
- Mccraty, R., & Shaffer, F. (2015). Heart Rate Variability: New Perspectives on Physiological Mechanisms, Assessment of Self-regulatory Capacity, and Health Risk. *Global Advances in Health and Medicine*, *4*(1), 46–61. <https://doi.org/10.7453/gahmj.2014.073>
- Michael, S., Graham, K. S., & Davis, G. M. (2017). Cardiac Autonomic Responses during Exercise and Post-exercise Recovery Using Heart Rate Variability and Systolic Time Intervals—A Review. *Frontiers in Physiology*, *8*. <https://doi.org/10.3389/fphys.2017.00301>
- Mizumura, K., & Taguchi, T. (2024). Neurochemical mechanism of muscular pain: Insight from the study on delayed onset muscle soreness. *The Journal of Physiological Sciences*, *74*(1), 4. <https://doi.org/10.1186/s12576-023-00896-y>
- Mongin, D., Chabert, C., Extremera, M. G., Hue, O., Courvoisier, D. S., Carpena, P., & Galvan, P. A. B. (2022). Decrease of heart rate variability during exercise: An index of cardiorespiratory fitness. *PLOS ONE*, *17*(9), e0273981. <https://doi.org/10.1371/journal.pone.0273981>
- Nahon, R. L., Silva Lopes, J. S., & Monteiro de Magalhães Neto, A. (2021). Physical therapy interventions for the treatment of delayed onset muscle soreness (DOMS): Systematic review and meta-analysis. *Physical Therapy in Sport*, *52*, 1–12. <https://doi.org/10.1016/j.ptsp.2021.07.005>
- Extramuscular Connective Tissue Thickness and Delayed Onset Muscle Soreness in Healthy Participants: A Randomized Controlled Crossover Trial. *Sports Medicine - Open*, *8*(1), 57. <https://doi.org/10.1186/s40798-022-00446-7>
- Tiwari, R., Kumar, R., Malik, S., Raj, T., & Kumar, P. (2021). Analysis of Heart Rate Variability and Implication of Different Factors on Heart Rate Variability. *Current Cardiology Reviews*, *17*(5). <https://doi.org/10.2174/1573403X16999201231203854>
- Newham, D. J., McPhail, G., Mills, K. R., & Edwards, R. H. T. (1983). Ultrastructural changes after concentric and eccentric contractions of human muscle. *Journal of the Neurological Sciences*, *61*(1), 109–122. [https://doi.org/10.1016/0022-510X\(83\)90058-8](https://doi.org/10.1016/0022-510X(83)90058-8)
- Nguyen, D., Brown, L. E., Coburn, J. W., Judelson, D. A., Eurich, A. D., Khamoui, A. V., & Uribe, B. P. (2009). Effect of Delayed-Onset Muscle Soreness on Elbow Flexion Strength and Rate of Velocity Development. *Journal of Strength and Conditioning Research*, *23*(4), 1282–1286. <https://doi.org/10.1519/JSC.0b013e3181970017>
- Nosaka, K., Newton, M., & Sacco, P. (2002). Delayed-onset muscle soreness does not reflect the magnitude of eccentric exercise-induced muscle damage. *Scandinavian Journal of Medicine & Science in Sports*, *12*(6), 337–346. <https://doi.org/10.1034/j.1600-0838.2002.10178.x>
- Ochi, E., Ueda, H., Tsuchiya, Y., Kouzaki, K., & Nakazato, K. (2020). Eccentric contraction-induced muscle damage in human flexor pollicis brevis is accompanied by impairment of motor nerve. *Scandinavian Journal of Medicine & Science in Sports*, *30*(3), 462–471. <https://doi.org/10.1111/sms.13589>
- Peçanha, T., Bartels, R., Brito, L. C., Paula-Ribeiro, M., Oliveira, R. S., & Goldberger, J. J. (2017). Methods of assessment of the post-exercise cardiac autonomic recovery: A methodological review. *International Journal of Cardiology*, *227*, 795–802. <https://doi.org/10.1016/j.ijcard.2016.10.057>
- R Core Team. (2021). R: a Language and Environment for Statistical Computing. *R Foundation for Statistical Computing: Vienna, Austria*.
- Rajendra Acharya, U., Paul Joseph, K., Kannathal, N., Lim, C. M., & Suri, J. S. (2006). Heart rate variability: a review. *Medical & Biological Engineering & Computing*, *44*(12), 1031–1051. <https://doi.org/10.1007/s11517-006-0119-0>
- Stennett, B., Anderson, M. B., Vitus, D., Ferguson, E., Dallery, J., Alappattu, M., Robinson, M., & Boissoneault, J. (2021). Sex moderates the effects of experimentally induced musculoskeletal pain on alcohol demand in healthy drinkers. *Drug and Alcohol Dependence*, *219*, 108475. <https://doi.org/10.1016/j.drugalcdep.2020.108475>
- Tenberg, S., Nosaka, K., & Wilke, J. (2022). The Relationship Between Acute Exercise-Induced Changes in
- Tibana, R. A., Sousa, N. M. F. de, Prestes, J., Feito, Y., Ferreira, C. E., & Voltarelli, F. A. (2019). Monitoring Training Load, Well-Being, Heart Rate Variability, and Competitive Performance of a Functional-Fitness Female Athlete: A Case Study. *Sports*, *7*(2), 35. <https://doi.org/10.3390/sports7020035>
- Tulppo, M. P., Makikallio, T. H., Takala, T. E., Seppanen, T., & Huikuri, H. V. (1996). Quantitative beat-to-beat

- analysis of heart rate dynamics during exercise. *American Journal of Physiology-Heart and Circulatory Physiology*, 271(1), H244–H252. <https://doi.org/10.1152/ajpheart.1996.271.1.H244>
- Uzawa, H., Akiyama, K., Furuyama, H., Takeuchi, S., & Nishida, Y. (2023). Autonomic responses to aerobic and resistance exercise in patients with chronic musculoskeletal pain: A systematic review. *PLOS ONE*, 18(8), e0290061. <https://doi.org/10.1371/journal.pone.0290061>
- Yoshida, R., Nakamura, M., & Ikegami, R. (2022). The Effect of Single Bout Treatment of Heat or Cold Intervention on Delayed Onset Muscle Soreness Induced by Eccentric Contraction. *Healthcare*, 10(12), 2556. <https://doi.org/10.3390/healthcare10122556>
- Zhao, Y., Yu, H., Gong, A., Zhang, S., & Xiao, B. (2024). Heart rate variability and cardiovascular diseases: A Mendelian randomization study. *European Journal of Clinical Investigation*, 54(1). <https://doi.org/10.1111/eci.14085>

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