Received: 2 July 2021 | Revised: 23 October 2021 | Accepted: 12 November 2021

DOI: 10.1111/sms.14099

ORIGINAL ARTICLE

WILEY

Airflow restriction mask induces greater central fatigue after a non-exhaustive high-intensity interval exercise

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The airflow restriction mask (ARM) is a practical and inexpensive device for respiratory muscle training. Wearing an ARM has recently been combined with high-intensity interval exercise (HIIE), but its effect on neuromuscular fatigue is unknown. The present study investigated the effects of ARM wearing on neuromuscular fatigue after an HIIE session. Fourteen healthy men performed two HIIE sessions (4 × 4 min at 90% HR_{max}, 3 min recovery at 70% HR_{max}) with or without an ARM. Neuromuscular fatigue was quantified via pre- to post-HIIE changes in maximal voluntary contraction (MVC), voluntary activation (VA, central fatigue), and potentialized evoked twitch force at 100, 10, and 1 Hz (peripheral fatigue). Blood pH and lactate were measured before and after the HIIE session, while HR, SpO_2, dyspnea, physical sensation of effort (P-RPE), and Task Effort and Awareness (TEA) were recorded every bout. The exercise-induced decrease in MVC was higher ($p < 0.05$) in the ARM (−28 ± 12%) than in the Control condition (−20 ± 11%). The VA decreased ($p < 0.05$) in the ARM (−11 ± 11%) but not in the control condition (−4 ± 5%, $p > 0.05$). Pre- to post-HIIE declines in evoked twitch at 100, 10, and 1 Hz were similar ($p > 0.05$) between ARM and control conditions (ARM: −18 ± 10, −43 ± 11 and −38 ± 12%; Control: −18 ± 14, −43 ± 12 and −37 ± 17%). When compared with the control, the HIIE bout wearing ARM was marked by higher heart rate, plasma lactate concentration, dyspnea, P-RPE and TEA, as well as lower SpO_2 and blood pH. In conclusion, ARM increases perceptual and physiological stress during a HIIE, which may lead to a greater post-exercise central fatigue.

KEYWORDS
hypoxia, metabolic acidosis, muscle fatigue, neuromuscular function, work of breathing

1 | INTRODUCTION

High-intensity interval exercise (HIIE) is widely used as a time-efficient approach to improve endurance performance in untrained and trained individuals.[1,2] Some evidence suggest that a HIIE protocol (e.g., 4 × 4 min at 90% maximal heart rate [HR]) promotes greater gains in aerobic fitness than moderate-intensity exercise.[2] The HIIE has recently been combined with an airflow restriction mask (ARM) as a practical and efficient approach to increase respiratory muscle work by adding external breathing resistance,[3,4] and this combination can result in additional gains in specific markers of endurance performance (e.g., ventilatory threshold and respiratory compensation threshold), when compared with performing HIIE alone.[4] However, wearing an ARM during a bout of HIIE induces a greater decrease in blood pH, and a greater increase in HR and plasma lactate concentration than exercise alone.[3–5] The ARM also increases the perceived breathing effort (dyspnea) and physical sensation of effort (P-RPE) during exercise.[3,4] The increased dyspnea and P-RPE might increase the consciously aware of the magnitude of psychological and psychical sensations (Task Effort and Awareness, TEA).[6] While these alterations provoked by wearing an ARM might influence post-HIIE neuromuscular fatigue, experimental evidence supporting this assumption is, however, lacking.

Exercise-induced neuromuscular fatigue can be defined as a transient impairment in the muscle's ability to produce force or power, which can be of peripheral or central origin.[7] Peripheral fatigue involves impairment in the muscle's ability to produce force in response to neural input, while central fatigue involves the reduction of the ability of the central nervous system to activate the exercising muscles.[8] Operationally, peripheral fatigue can be quantified via pre- to post-exercise reduction in evoked twitch force,[8] while central fatigue can be measured via pre- to post-exercise reduction in voluntary activation (VA) using the superimposed twitch interpolation technique.[9] Increasing respiratory muscle work by adding external breathing resistance results in hypoventilation during intense exercise,[3] which subsequently reduces peripheral oxygen saturation (SpO_2)[7] and triggers a sympathetically-induced vasoconstriction that reduces blood flow to locomotor muscles.[10] This potential link between increased respiratory muscle work and reduced blood flow to locomotor muscles has recently been demonstrated during exercise at 90% of maximal power output,[11] an exercise intensity similar to that used during HIIE. A reduced blood flow to locomotor muscles during a high-intensity exercise might result in a greater amount of peripheral fatigue.[8,10] Supporting a link between respiratory muscle work and peripheral fatigue, a study demonstrated that addition of ~80% in inspiratory muscle work increased the amount of peripheral fatigue after an exercise performed at 90% of maximal O_2 uptake (VO_{2max}), when compared to an identical trial of equal duration without additional load on inspiratory muscles.[12] Furthermore, greater respiratory muscle work also results in greater fatigue of respiratory muscles during intense exercise.[10,13] Increased fatigue from respiratory muscles may arise sensorial feedback to central nervous system, which could result in greater central fatigue.[13–15] Thus, increased respiratory muscle work could result in exacerbation of both peripheral and central fatigue.

Although there is a potential link between respiratory muscle work and peripheral and central fatigue, it is currently unknown whether performing an HIIE bout wearing an ARM increasing respiratory muscle work results in greater peripheral and/or central fatigue. To our knowledge, studies investigating the influence of increasing respiratory muscle work on peripheral and central fatigue have been conducted using time-to-exhaustion trials, which is adequate to assess endurance performance, but is rarely used in a training program. Thus, a study using HIIE could provide insights about the influence of respiratory muscle work on peripheral and central fatigue during a more applicable exercise model. In addition, as ARM can be used in different environments, this device might be more useful for training respiratory muscles in a typical training program,[3,4] in comparison with devices exclusively used in laboratory (e.g., two-way low-resistance non-rebreathing valve). As alterations in the development of peripheral and central fatigue explain part of the gains in endurance capacity after high-intensity interval training,[16] understanding the consequences of ARM wearing during an HIIE on neuromuscular fatigue and its link with perceptual and physiological alterations might assist trainers and exercisers to determine the utility of wearing an ARM during an HIIE session. In addition, a better understanding of the contributions of peripheral and central mechanisms to neuromuscular fatigue during HIIE and ARM wearing combined might also assist in interpreting previous findings showing additional gains in endurance performance when high-intensity interval training is performed wearing an ARM, in comparison with training without an ARM.[4]

Therefore, the effect of wearing an ARM during an HIIE bout on end-exercise peripheral and central fatigue was investigated in the present study. To provide a broader view of the overall consequences of ARM wearing during HIIE and its potential connections with central and peripheral fatigue development, we also explored the alterations in SpO_2, HR, blood pH, plasma lactate concentration, dyspnea, P-RPE, and TEA. We hypothesized that wearing an ARM would cause a greater

reduction in the SpO_2 and blood pH, and a greater increase in the HR, plasma lactate concentration, dyspnea, P-RPE, TEA, and greater end-exercise peripheral and central fatigue.

2 | MATERIALS AND METHODS

2.1 | Participants

Fourteen healthy men (age 24.1 ± 6.5 years, height 1.72 ± 0.06 m, body mass 70.1 ± 8.7 kg, VO_{2max} 41.2 ± 7.0 mL. kg^{-1}. min^{-1}, and peak power output 226 ± 35 W) participated in this study. Participants signed a written consent form after receiving verbal and written information about the risks and procedures of the experimental trials. This study was approved by the Human Research Ethics Committee of the Federal University of Pernambuco.

2.2 | Study design

Participants visited the laboratory on four different occasions. On the first visit, participants performed a familiarization with the neuromuscular function assessment and a maximal incremental exercise test to determine their peak power output and VO_{2max}. Thirty minutes after the maximal incremental exercise test, participants were familiarized with exercising wearing an ARM and again with the neuromuscular function assessment. On the second visit, at least 72 h after the first visit, participants returned to the laboratory and were familiarized with full experimental procedures (i.e., HIIE, ARM wearing, and neuromuscular function assessment). Participants also practiced how to move as quickly as possible from the cycle ergometer to the chair for the neuromuscular function assessment. This practice permitted the assessment of post-HIIE neuromuscular function 30 s after the HIIE during the experimental trials.

In the third and fourth visits (at least 72 h apart), participants performed the experimental trials, which consisted of either a HIIE wearing the ARM or a HIIE without wearing the ARM (i.e., control). The experimental trials were performed in a randomized, counterbalanced, and crossover design. Randomization and balance of the participants were performed using the website: http://www.jerrydallal.com/random/permute.htm. The experimental trials were performed at least 7 days apart for washout of any residual fatigue from the previous trial. Participants completed a 24-h dietary record on the day preceding the first experimental trial and replicated the recorded diet on the day preceding the second experimental trial. Participants also completed a 24-h dietary record on the day preceding the second experimental trial to check compliance with the recommendations. Participants were asked to refrain from exercise, and alcohol and caffeine intake for 24 h before each experimental trial. The experimental trials were performed in a postprandial state (~2 h after the last meal) and at the same time of the day to avoid any effect of the circadian rhythm.

2.3 | Procedures

2.3.1 | Maximal incremental exercise test

Participants underwent a maximal incremental exercise test on an electromagnetically-braked cycle ergometer (Ergo-Fit 167). The maximal incremental exercise test started with a 5-min warm-up at 70 W, followed by increments of 30 W every 3 min until exhaustion. Pedal cadence was maintained between 70 and 80 revolutions per minute throughout the exercise, with exhaustion defined as an inability to maintain the pedal cadence above 70 revolutions per minute or by voluntary disengagement. Pulmonary gas exchange was measured breath-by-breath using a metabolic cart (Cortex Metalizer 3B). The metabolic cart was calibrated before each test according to the manufacturer's recommendations, using a 3-L syringe and a standard gas of established O_2 and CO_2 concentrations (12% and 5%, respectively). The HR was measured using a HR monitor (Polar) connected to the metabolic cart. The HR_{max} was defined as the highest 5-s mean values recorded at the end of the test. The VO_{2max} was confirmed when at least two of the following criteria were met: (1) an increase of less than 150 mL. min^{-1} with an increase in power; (2) HR_{max} values of ±10 bpm of predicted HR_{max} (i.e., 220—age) and; (3) respiratory exchange rate ≥1.15 units.[17] Peak power output was the highest power reached during the test; when the last stage was incomplete, the peak power output was the fractional time completed in the last stage multiplied by the increment rate (i.e., 30 W).

2.3.2 | Experimental trials

The timeline of the experimental trial is illustrated in Supplementary Figure 1. Initially, blood samples were collected from the antecubital vein and earlobe to measure blood pH and plasma lactate concentration, respectively. Thereafter, pre-HIIE neuromuscular function was assessed. Participants then performed an HIIE consisting of a 10-min warm-up at a power corresponding to 70% of HR_{max}, followed by four bouts of 4 min at a power

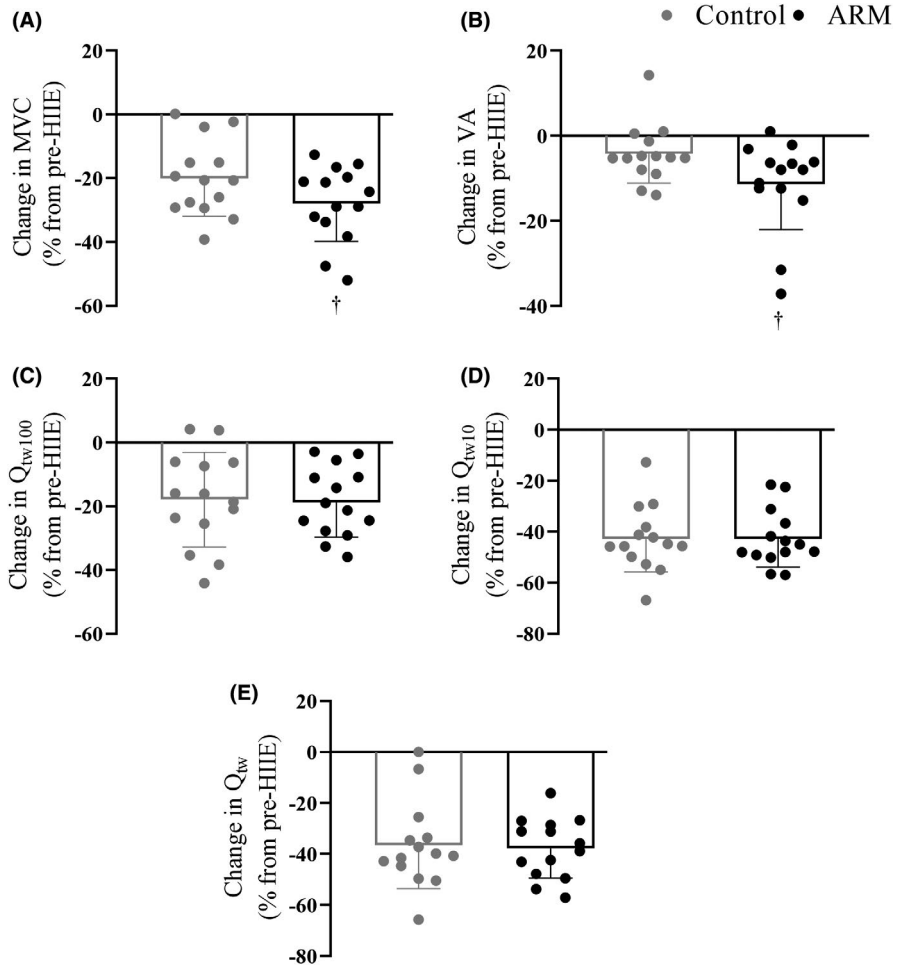

FIGURE 1 Changes in maximal voluntary contraction (A), voluntary activation (B), and quadriceps twitch force evoked by paired-pulse at 100 Hz (C) and 10 Hz (D), and by single pulse at 1 Hz (E), after performing a high-intensity interval exercise wearing (ARM) or without wearing (Control) an airflow restriction mask. †Significantly greater reduction than Control ($p < 0.05$). Data are mean ± SD, $n = 14$

corresponding to 90% of HR_{max}. The bouts were interspaced by a 3-min recovery at a power corresponding to 70% of HR_{max}. Power and VO_2 at 90% and 70% of HR_{max} were obtained using individual linear regression by plotting HR as a function of power during the incremental test (HR mean during the last 5 s of each stage).[18] The mean power output at 90% and 70% of HR_{max} was 182 ± 31 W (80.0 ± 3.4% PPO) and 103 ± 25 W (45.2 ± 6.4% PPO). The mean VO_2 at 90% and 70% of HR_{max} was 33.3 ± 6.0 mL. kg^{-1} .min^{-1} (80.9 ± 6.0% $\dot{V}O_{2max}$) and 21.3 ± 5.0 mL .kg^{-1} .min^{-1} (51.5 ± 7.8% VO_{2max}).

The SaO_2, HR, dyspnea, P-RPE, and TEA were collected throughout HIIE. Neuromuscular function was reevaluated 30 s after the HIIE (post-HIIE), while blood samples from the antecubital vein and earlobe were obtained 2 min after the HIIE. In the ARM condition, the openings and flow valves of the ARM were adjusted to simulate 3000 ft (Training Mask LLC), which corresponds to an expiratory resistance pressure of ~10 cmH_2O.[19] We chose 3000 ft (10 cmH_2O) because this resistance pressure imposes tolerable increase in respiratory muscle work in individuals unaccustomed to ARM wearing and a significant decrease in the SpO_2 and blood pH.[3,4,20]

2.4 | Measures and analysis

2.4.1 | Neuromuscular function assessment

Participants sat on a custom-made bench chair, with their hip joint angle set at 120° and knee joint angle set at 90°. A non-compliant cuff was attached to their right ankle, just superior to the malleoli, and connected to a calibrated force transducer with measurement range from 0 to 1,960 N (EMG System of Brazil). Safety belts were strapped across their chest, hips, and thighs to minimize the body movement and recruitment of additional muscles. A monopolar diameter cathode electrode was placed above the right femoral nerve around the femoral triangle and an anode on the gluteal fold opposite the cathode (Ambu® Neuroline 715). The optimal electrical stimulus intensity for neuromuscular function assessment was identified in the familiarization session by delivery paired doublet pulses of 100 Hz (80 μs duration) on the femoral nerve using a constant current electrical stimulator (Neuro-TES; Neurosoft). Electrical stimulus was delivered starting at 100 V, increasing 30 V every 30 s until attainment of a plateau in quadriceps twitch force (Q_{tw100}). The plateau in the Q_{tw100} was determined when the increase in

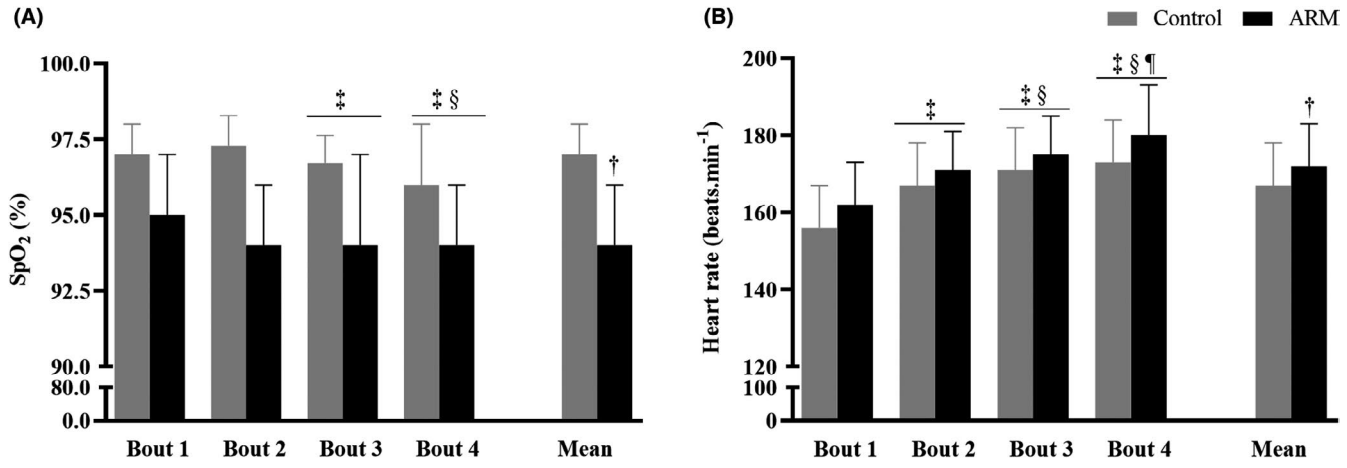

FIGURE 2 Peripheral O_2 saturation (A) and heart rate (B) during a high-intensity interval exercise wearing (ARM) or without wearing (Control) an airflow restriction mask. ‡Significantly different from bout 1, $p < 0.05$. §Significantly different from bout 2. ¶Significantly different from bout 3. †Significantly different from Control, $p < 0.05$. Data are mean ± SD, $n = 14$

force was lower than 5% with an increase in the electrical stimulus intensity. The plateau in the Q_{tw100} was double-checked before each experimental trial. The optimal electrical stimulus intensity for neuromuscular function assessment during the experimental trial was set at 120% of the plateau in the Q_{tw100}.

The pre-HIIE neuromuscular function assessment was preceded by a warm-up composed of four 5-s quadriceps isometric contractions (50%, 60%, 70%, and 80% of the MVC recorded in the familiarization session), interspaced with a 30-s rest between contractions. Subsequently, participants performed three MVCs of knee extensors (i.e., quadriceps muscle), with knee joint angle fixed at 90° and 1-min rest between contractions. During each MVC, participants were instructed to produce maximal force and maintain it for 5 s. Instantaneous force was displayed on a screen positioned in front of the participants to assist in maintenance of maximal force. During each MVC, a paired doublet pulse stimulus (100 Hz) was manually delivered as soon as the plateau in isometric force was visually identified by the experimenter (superimposed Q_{tw100}). In addition, paired doublet pulse stimulus at 100 and 10 Hz and single pulse stimulus at 1 Hz were delivered 2, 4, and 6 s after each MVC. Post-HIIE neuromuscular function was assessed 30 s after the HIIE using the same procedure, except that no warm-up was provided and only one MVC was performed.

The highest force generated during the MVC[21] and the peak force evoked by paired and single pulses in relaxed muscle (Q_{tw100}, $Q_{tw10,}$ and Q_{tw}) were recorded. Voluntary activation was determined via the superimposed twitch interpolation technique using the following equation[22]:

$$\text{VA}\,(\%) = \left[1 - \left(\text{superimposed } Q_{tw100}/Q_{tw100} \text{ at rest}\right)\right] \times 100, \quad (1)$$

where superimposed Q_{tw100} is the force evoked during the maximal voluntary contraction (MVC) by the paired doublet stimulus at 100 Hz and Q_{tw100} at rest is the post-MVC evoked force by the paired doublet stimulus at 100 Hz.

The highest MVC at pre-HIIE (and related Q_{tw100}, $Q_{tw10,}$ Q_{tw}, and VA) were used as pre-HIIE measurements.[18,23] The pre- to post-HIIE reduction in MVC was used as a marker of neuromuscular fatigue.[23] The pre- to post-HIIE reduction in VA was used as a marker of central fatigue,[23] while the reductions in Q_{tw100}, $Q_{tw10,}$ and Q_{tw} were used as markers of peripheral fatigue.[23]

The between-day coefficient of variation (CV) and intraclass correlation coefficient (ICC) for pre-HIIE measurements were: MVC (CV = 5.8 ± 8.2%, ICC = 0.72, $p = 0.001$), VA (CV = 3.6 ± 3.8%, ICC = 0.67, $p = 0.003$), Q_{tw100} (CV = 6.3 ± 4.0%, ICC = 0.70, $p = 0.002$), Q_{tw10} (CV = 3.6 ± 3.1%, ICC=0.95, $p < 0.001$), and Q_{tw} (CV = 5.1 ± 5.6%, ICC = 0.73, $p = 0.001$).

2.4.2 | Electromyography muscle activity recording

During neuromuscular function assessment, EMG activity for the right *vastus lateralis* was recorded using monitoring electrodes with full-surface solid adhesive hydrogel. The skin was shaved, abraded with emery paper, and cleaned with alcohol to reduce skin impedance. Electrodes were placed according to the Surface Electromyography for the Non-Invasive Assessment of Muscles Standards,[24] with electrodes position marked with indelible ink to ensure identical placement at subsequent visit. The EMG signal was recorded with a sample rate of 2000 Hz via a 16-bit A/D converter, with input impedance = 10^9 Ohms, common

mode rejection ratio = >100 dB, and gain = 2,000 (EMG System of Brazil). The raw EMG signal was filtered with second-order Butterworth band-pass filters (cutoff frequencies set at 20 and 500 Hz) to remove external interference noise and movement artifacts.

M-wave peak-to-peak amplitude (M_{wave_ampl}) and area (M_{wave_area}) were calculated for each 1 Hz stimulus (i.e., Q_{tw}). The beginning of the M-wave was considered as an increase of two standard deviation above the baseline values, while the ending as a reduction to values lower than two standard deviation of the baseline. The M-wave and the corresponding mechanical force trace are shown in Supplementary Figure 2. The root mean square (RMS) of the EMG signal around the highest force during each MVC (250 ms signal) was also calculated (EMG_{MVC}).

2.4.3 | Peripheral oxygen saturation and heart rate

The SpO_2 was continuously monitored during the HIIE via a pulse oximeter attached to the right forefinger (Contec Medical Systems). The HR was monitored beat-by-beat throughout the HIIE using a HR monitor (Polar Electro Oy). Data of SpO_2 and HR during the final 5 s of each bout were averaged and used for comparison between experimental conditions.

2.4.4 | Blood pH and plasma lactate concentration

Venous blood samples were collected from the antecubital vein (10 mL) and immediately analyzed for blood pH using a portable pH meter (Hanna, HI 8424). Capillary blood samples were collected from the earlobe (40 μL), immediately transferred to tubes containing 10 μL of EDTA, and centrifuged for 10 min at 1000 x *g* (4°C). Plasma lactate concentration was enzymatically determined using commercial kits (Bioclin), with the resultant reaction reading performed in a spectrophotometer (Genesys 10 SUV-vis; Thermo Electron Scientific Instruments).

2.4.5 | Dyspnea, physical sensation of effort and task effort and awareness

To measure perceived dyspnea, volunteers were asked to inform "what is your sensation of dyspnea now?" using a modified 10-point scale, where "0" is normal breathing and "10" is extremely breathless.[25] To measure P-RPE, volunteers were asked to inform "what is your perceived sensation of physical effort now?" using a 15-point Borg scale, where "6" is without effort and "20" is maximum effort.[6] The TEA was obtained using a scale that quantify the extent by which participants were consciously of the magnitude of their psychological effort.[6] The TEA scale ranged from −4 to 10 points, where "−4" means that participant is without psychological effort and "10" means that participant is constantly aware of severe psychological effort. The Dyspnea, P-RPE, and TEA were collected during the last 15 s of each bout.

2.5 | Statistical analysis

The Shapiro Wilk test was used to test data distribution. The $M_{wave\cdot ampl}$ was not normally distributed even after logarithmic transformation and was therefore compared between conditions using Friedman test. The EMG_{MVC} was normally distributed after logarithmic transformation and the remaining variables were normally distributed. Parameters of neuromuscular function, blood pH, and plasma lactate were compared using a two-factor general linear model, with repeated measures in both factors [condition (ARM and Control) and moment (pre- and post-HIIE)]. The effect of condition (ARM and Control) and bouts (1–4) on SpO_2, HR, Dyspnea, P-RPE, and TEA were determined using a two-factor general linear model, with repeated measures in both factors. Duncan's *post hoc* test was used to locate differences when necessary. The level of significance was set at $p < 0.05$. Due to technical problems, data from M-wave and EMG_{mvc} at some time points were missed and therefore the final sample size (n) is reported throughout the results section.

3 | RESULTS

3.1 | Neuromuscular fatigue

Parameters related to neuromuscular fatigue are reported in Supplementary Table 1 and Figure 1. There was a condition-moment interaction ($F_{[1,13]} = 9.2$, $p = 0.01$) for MVC. The MVC decreased from pre- to post-HIIE in both Control and ARM conditions (all, $p < 0.001$); however, the degree of MVC reduction was greater ($p = 0.01$) in the ARM (−28 ± 12%) than in the Control condition (−20 ± 11%). Accompanying the greater MVC reduction, there was also a condition-moment interaction ($F_{[1,13]} = 4.8$, $p = 0.048$) for VA, with a greater pre- to post-HIIE decline in the ARM (−11 ± 11%, $p < 0.001$) but not in the Control (−4 ± 7%, $p = 0.06$). There was only a main effect of time (all, $F_{[1,13]} > 41.3$, $p < 0.001$), without a main effect of condition (all, $F_{[1,13]} < 1.7$, $p > 0.22$) or a condition-moment interaction (all, $F_{[1,13]} < 0.67$, $p > 0.43$), for Q_{tw100}, Q_{tw10}, and Q_{tw}. The Q_{tw100}, $Q_{tw10,}$ and Q_{tw} reduced from pre- to post-HIIE similarly in both conditions. The M_{wave}

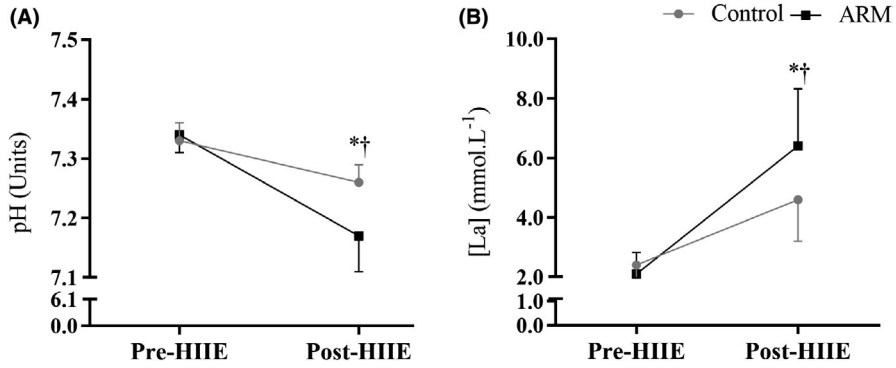

FIGURE 3 Blood pH (A) and plasma lactate concentration (B) pre and post a high-intensity interval exercise wearing (ARM) or without wearing (Control) an airflow restriction mask. *Significantly different from pre-HIIE, $p < 0.05$. †Significantly different from Control at post-HIIE, $p < 0.05$. Data are mean ± SD, $n = 14$

amplitude and area were similar between Control and ARM conditions and were not altered from pre- to post-HIIE ($p > 0.05$). The averaged EMG_{MVC} reduced from pre- to post-HIIE (main effect of time, $F_{[1,9]} = 34.0$, $p < 0.001$) and was similar between conditions (main effect of condition, $F_{[1,9]} = 0.45$, $p = 0.52$).

3.2 | Peripheral O_2 saturation and heart rate

Resting SpO_2 was 99.6 ± 1.0%. The SpO_2 reduced during HIIE in both conditions (main effect of bout, $F_{[3,39]} = 4.2$, $p = 0.01$, Figure 2A), but mean values were lower in the ARM than in the Control condition (main effect of condition, $F_{[1,39]} = 36.8$, $p < 0.001$, Figure 2A). Similarly, HR progressively increased during HIIE in both conditions (main effect of bout, $F_{[3,39]} = 41.2$, $p < 0.001$, Figure 2B), but mean HR was higher in the ARM than in the Control condition (main effect of condition, $F_{[1,13]} = 6.5$, $p = 0.02$).

3.3 | Blood pH and lactate

Blood pH decreased from pre- to post-HIIE in both Control and ARM conditions ($p < 0.05$); however, the reduction was greater in the ARM than in the Control condition (condition-moment interaction, $F_{[1,10]} = 27.0$, $p < 0.001$, Figure 3A). Plasma lactate concentration increased from pre- to post-HIIE in both Control and ARM conditions ($p < 0.05$), but the increase was more pronounced in the ARM than in the Control condition (condition-moment interaction, $F_{[1,13]} = 28.4$, $p < 0.001$, Figure 3B).

3.4 | Dyspnea, physical sensation of effort, and task effort and awareness

There was a condition-bout interaction for dyspnea ($F_{[3,39]} = 3.8$, $p = 0.02$, Figure 4A). While dyspnea slightly increased over the bouts in the Control condition, with higher values at the third and fourth bouts compared with the first and second bouts ($p < 0.05$), in the ARM condition dyspnea progressively increased and was always higher than in the Control condition ($p < 0.05$). The P-RPE increased during HIIE in both conditions (main effect of bout, $F_{[3,39]} = 36.8$, $p < 0.001$, Figure 4B), but mean values were higher in the ARM than in the Control condition (main effect of condition, $F_{[1,13]} = 23.7$, $p < 0.001$, Figure 4B). There was a condition-bout interaction for TEA ($F_{[3,39]} = 3.6$, $p = 0.02$, Figure 4C). The TEA slightly increased over the bouts in the Control condition, with higher values at the third and fourth bouts compared with the first bout ($p < 0.05$). In the ARM condition, however, the TEA progressively increased throughout exercise and values at second and third bouts were higher than in the Control condition ($p < 0.05$).

4 | DISCUSSION

We found in the present study that central fatigue (i.e., reduction in VA) was exacerbated after an HIIE with ARM wearing. Peripheral fatigue (i.e., reduction in Q_{tw100}, $Q_{tw10,}$ and Q_{tw}), however, was of the same magnitude after HIIE with or without ARM wearing. ARM wearing also provoked greater peripheral O_2 desaturation, cardiovascular stress, metabolic acidosis, dyspnea, physical sensation of effort, and sense of effort, when compared with Control. Together, these findings suggest that ARM wearing results in greater perceptual and physiological disturbance, with substantial consequences in central fatigue.

A novel finding of the present study was that ARM wearing caused a greater pre- to post-HIIE reduction in MVC when compared with the Control condition (~28% vs. ~20%). This greater reduction in MVC was accompanied by a ~2.5 times greater reduction in VA (~11% vs. ~4%). The reduction in Q_{tw100}, $Q_{tw10,}$ and Q_{tw} was similar between ARM (~18%, 43%, and 38%) and control (~18%, 43%, and 37%). No previous studies have investigated the effect of increase respiratory muscle work via ARM wearing during an HIIE on neuromuscular fatigue development, but a previous study showed that MVC and VA decreased similarly after a high-intensity exercise (>90% $\cdot VO_{2max}$) with

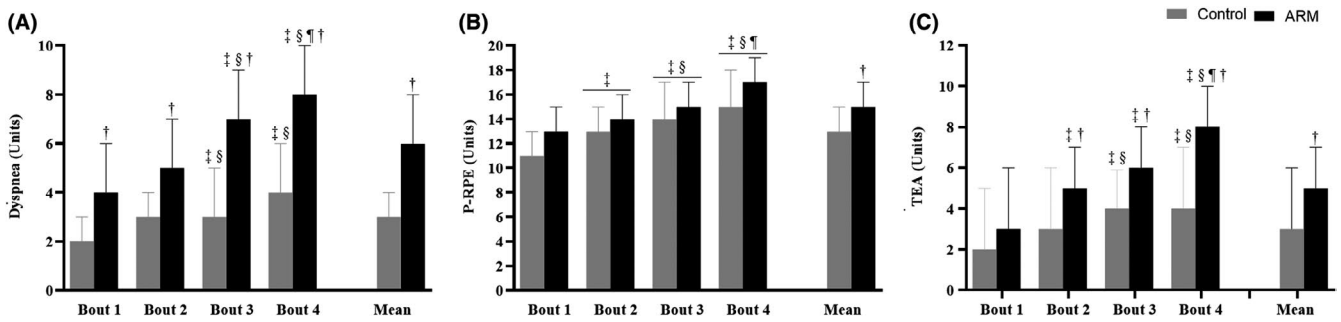

FIGURE 4 Dyspnea (A), physical sensation of effort (B), and Task of effort and awareness (C) during a high-intensity interval exercise wearing (ARM) or without wearing (Control) an airflow restriction mask. ‡Significantly different from bout 1, $p < 0.05$. §Significantly different from bout 2. ¶Significantly different from bout 3. †Significantly different from Control, $p < 0.05$. Data are mean ± SD, $n = 14$

increased inspiratory muscle work via inspiratory resistive loads.[12] The reasons for these differences are speculative, but some methodological approaches might explain these different results. First, in the present study we assessed the VA 30 s after exercise, while the time until assessment was longer (2.5 min) in the previously mentioned study.[12] It has been reported that a delay (~2 min) in the post-HIIE neuromuscular assessment permits partial recovery of both MVC and VA,[21,26] suggesting that any difference between conditions may be missed after this time window.[17] Second, due to the brief period of recovery between bouts of HIIE, exercise duration in the present study was double (16 vs. ~7.9 min).[12] An increase in exercise duration exacerbates reduction in VA[27]; thus, a prolonged time with increased respiratory muscle work may be necessary to induce a great reduction in VA. Third, in the present study, the resistance pressure imposed by wearing ARM was higher than in that study (~10 vs. 3–7 cmH_2O),[12] which may have exacerbated reductions in the VA. Fourth, exercise model (HIIE vs. continuous) might also explain these discrepancies.

In relation to the model of exercise, some studies suggest that a typical HIIE session may induce a modest or even absent central fatigue.[18,28] In the present study, the magnitude of central fatigue was of lower magnitude than that reported for continuous, high-intensity exercise.[29] Also, the magnitude of central fatigue was higher when wearing the ARM (~11%), but this magnitude of reduction was also lower than that reported after continuous, high-intensity exercise with additional load on inspiratory muscles (~19%).[29] Interestingly, the magnitude of central fatigue was not significantly different from Control (~12%) in the mentioned study.[29] These findings suggest that an increase of respiratory muscle work has more potential to influence central fatigue during HIIE than during continuous exercise. Our findings provide therefore the first evidence that a substantial amount of central fatigue can be provoked by ARM wearing during HIIE. Our findings also suggest that exacerbated neuromuscular fatigue after HIIE when wearing an ARM is primarily of central origin. Although we cannot ascertain from our data the mechanism by which central fatigue is increased during a HIIE when wearing an ARM, during exercise cardiorespiratory system and locomotor muscles trigger sensory feedback from group III/IV afferent toward the central nervous system.[12,30] Increased input from afferent signals due to increased metabolic and respiratory disturbance might inhibit central motor drive, ultimately reducing muscle activation.[15,31] In fact, wearing an ARM caused significant physiological stress, as demonstrated by the reduced blood pH and SpO_2, and increased plasma lactate and HR. Although it remains speculative, these physiological alterations might act as signaling to central nervous system and might have contributed to the increased central fatigue when performing HIIE wearing an ARM.

Another potential explanation for the greater central fatigue when wearing an ARM during a HIIE resides within the central nervous system. In the present study, wearing an ARM during HIIE increased dyspnea, P-RPE, and TEA, probably due to the increased ventilatory resistance to inspiratory and respiratory flow (i.e., higher respiratory muscle work) provoked by ARM wearing.[3,20] During intense exercise, central command (the activity of motor and premotor areas of the brain relating to voluntary muscle contraction) might be a putative regulator of respiratory muscle work.[32] Neural drive from central command to the respiratory muscles might also cause a corollary discharge to somatosensory areas.[33] Thus, greater dyspnea, P-RPE, and TEA when wearing an ARM might be the result of an increased central command to attend the greater respiratory muscle work. On the other hand, an increase in respiratory muscle work increasing dyspnea might carry to a reduction in the central motor command over the time.[14,15] The reduction of central command, and consequently the increase of central fatigue, might be proportional to the dyspnea caused by the imposed respiratory muscle work.[7] In the present study, wearing an ARM doubled the dyspnea

throughout the HIIE (mean of eight units) in relation to the control (mean of four units). Thus, the increased dyspnea might have contributed to a greater central fatigue when performing the HIIE wearing an ARM.

Different from central fatigue, wearing an ARM did not provoke greater end-exercise peripheral fatigue compared with Control. The similarly in $Q_{tw100,}$ Q_{tw10}, and Q_{tw} values following ARM and Control trials suggests no influence of wearing an ARM on peripheral fatigue. This result is in contrast with a previous study demonstrating that additional respiratory muscle work provoked a greater pre- to post-exercise decrease in quadriceps twitch force in comparison with Control.[12] The quadriceps twitch force in that study, however, was obtained at exhaustion when exercising with additional respiratory work, but prior to exhaustion (iso-time trial) in the Control. Using this experimental design, these findings suggest that peripheral fatigue development is accelerated with the addition of respiratory muscle work.[12] In the present study, HIIE was not performed until exhaustion and, therefore, peripheral fatigue was not assessed at exhaustion in the ARM or Control conditions. It could be speculated that HIIE duration might not have been sufficiently long to detect a difference in peripheral fatigue between conditions. However, whether performing HIIE with ARM wearing until exhaustion would result in detectable differences in peripheral fatigue throughout the bouts deserves further investigation.

Surprisingly, peripheral fatigue was not increased even with ARM wearing causing a greater decrease in blood pH and a greater increase in plasma lactate, which are markers associated with peripheral fatigue.[31,34] The more pronounced decrease of blood pH and increase of plasma lactate suggest that the contribution of anaerobic glycolysis was greater during exercise with ARM than during exercise without ARM. These findings might indicate that exercise with ARM would promote the recruitment of fast glycolytic muscle fibers that is generally fast fatigable.[35] This assumption is reasonable because SpO_2 was lower, which could have probably affected O_2 supply to the locomotor muscles.[10] If this would be the case, however, peripheral fatigue should have been greater after ARM wearing than after Control. It is difficult to ascertain from our data which muscle(s) was(were) responsible for the increased plasma lactate when wearing an ARM. The greater resistance imposed on respiratory muscle work[3,20] when wearing an ARM might increase the anaerobic metabolism within the respiratory muscles, which contributes to a systemic increase in plasma lactate and consequently blood pH reduction.[7] Thus, the higher plasma lactate concentration in the ARM condition suggests that anaerobic metabolism within the respiratory muscles may have been increased, which may also have contributed to the blood pH reduction.

Furthermore, a greater reduction in blood pH may also have been due to a higher accumulation of arterial CO_2[36] caused by the inadequate ventilation when wearing an ARM.[13] Wearing an ARM impairs CO_2 expiration and causes greater CO_2 reuptake and CO_2 concentrations in dead space.[3] Furthermore, wearing an ARM during exercise increases both partial pressures of end-tidal CO_2 and arterial partial CO_2 pressure.[20] As a result of elevated arterial CO_2 tension, CO_2 reacts with water to produce HCO_3^- and H^+ ions, causing acidosis.[13] Although we have not measured the gas exchange and pulmonary ventilation, previous studies have consistently demonstrated that ARM wearing causes a reduction in pulmonary ventilation and respiratory frequency[3,20] and an increase in arterial partial pressure CO_2,[20] partial pressure of end-tidal CO_2,[3,20] and volume of expired CO_2.[3,20] Furthermore, inadequate ventilation when wearing an ARM could also have contributed to the greater SpO_2 drop in the ARM than in the Control.[3,20] The greater SpO_2 drop could also be a consequence of a right shift in the oxyhemoglobin dissociation curve caused by the reduction in blood pH.[7] Arterial O_2 desaturation sensitizes central and peripheral chemoreceptors to hypoxia and HR is upregulated to increase cardiac output and maintain O_2 supply to both locomotor and respiratory muscles.[37] Thus, our findings suggest that wearing an ARM alters acid-balance equilibrium and induces peripheral deoxygenation and exacerbated heart stress during an HIIE. These alterations, however, might have influenced central but not peripheral fatigue.

Some limitations of the present study should be highlighted. We chose an HIIE protocol to investigate the effects of wearing an ARM on locomotor muscle fatigue and associated physiological responses; therefore, our results are restricted to this mode of exercise. We also used femoral nervous stimulus to assess central fatigue. Thus, the inclusion of transcranial magnetic stimulus in further studies will improve our understanding about central fatigue when wearing an ARM. Nevertheless, twitch interpolation technique using femoral nervous stimulus is a validity technique to assess the central component of muscle fatigue[9]; thus, our findings provide important insights in relation to the effect of ARM wearing on central fatigue. Furthermore, we identified values of VA at baseline of ~89%, indicating a lower muscle activation. Nevertheless, quadriceps muscles are less completely activated than lower mass muscles (e.g., ankle plantar flexors).[9] In fact, VA measured at quadriceps muscles ranges from 85% to 95%, while VA measured at muscles of lower mass range from 90% to 99%.[9] In addition, there was a natural delay for assessing central and peripheral fatigue. Nevertheless, the time elapsed from the end of exercise to the neuromuscular function assessment was very short (30 s), and much

shorter than those reported in the literature for studies in cycle ergometer.[12,27,28,31] Although some fatigue recovery might still occur within this short time window,[21,26] the magnitude of recovery is small.[9] Further, the strength and respiratory muscle work of expiratory and inspiratory muscles were not quantified in the present study. Thus, we cannot quantify how much additional work was imposed on the respiratory muscles during the HIIE wearing the ARM. Previous studies, however, demonstrated that wearing an ARM set at 3000 ft restrains airflow and cause expiratory resistance pressure of ~10 cmH_2O,[19] which considerably increase respiratory work.[3,20] Finally, we were unable to measure gas exchange and pulmonary ventilation during exercise. However, the effect of wearing an ARM on pulmonary gas exchange during HIIE has been well established,[3,20] which allowed us to anticipate the expected ventilatory and gas exchange responses.

5 | PERSPECTIVE

Airflow restriction mask wearing by exercise practitioners and enthusiasts has increased in recent years; thus, better understanding of the physiological and central and peripheral aspects of neuromuscular fatigue might assist this population in determining the additional benefits of ARM wearing during HIIE sessions. Our finding of increased central fatigue when wearing an ARM indicates that training with an ARM might enhance tolerance to central fatigue with consequent improvements in endurance performance. Thus, further studies should explore the chronic effects of ARM wearing during an HIIE training program on central fatigue and gains in endurance performance.

In conclusion, wearing an ARM exacerbated perceptual and physiological disturbance during an HIIE. This increased perceptual and physiological disturbance was accompanied by a greater central fatigue with ARM wearing. Wearing an ARM during a HIIE has, however, no effect on peripheral fatigue. These results suggest that wearing an ARM during an HIIE exacerbates central but not peripheral fatigue.

ACKNOWLEDGEMENTS

This study was financed in part by the Foundation for Science and Technology of Pernambuco (FACEPE). Adriano E Lima-Silva received a scholarship from the National Council for Scientific and Technological Development (grant 301340/2019-6). Paulo Franco-Alvarenga is grateful for the scholarship from the UNESA Productivity Research Program. This research was partially funded by Coordination for the Improvement of Higher Education Personnel—Brazil (CAPES), Finance Code 001.

CONFLICT OF INTEREST

No conflicts of interest, financial or otherwise, are declared by the authors.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Da Silva KJ, Silva LC, Felippe LC, et al. Airflow restriction mask induces greater central fatigue after a non-exhaustive high-intensity interval exercise. *Scand J Med Sci Sports*. 2022;32:487–497. doi:10.1111/sms.14099