Comments from the editors and reviewers:

Reviewer 0

General comments

Reviewer: This study examines changes in various factors when the 4X4 HIIT regime is performed in normoxic and hypoxic conditions. This is novel, but the authors need to make a better case for the importance of this topic, and need to better evaluate text found in the Discussion to increase the impact of these findings.

Authors' response: We thank the reviewer for their careful consideration of our work.

Specific comments

Reviewer: Please consider these comments re. your paper—thank you.

Authors' response: We have responded to the comments individually raised below.

Reviewer: If word count allows in Abstract, please list the age and VO2max of these runners; thank you.

Authors' response: We thank the reviewers for this comment and have subsequently added the age of the runners who participated in this study. An explanation regarding the absence of a VO_{2MAX} assessment is provided below.

P2 L4 – Nineteen **trained** runners **(33.4 ± 9.1 years)** completed a…

Reviewer: Line 2: HIIR is not a common abbreviation and should be deleted or revised. And because this set of text is referring to benefits of high intensity interval training, why not just use this abbreviation (HIIT) which is so well-recognized?

Authors' response: We acknowledge the reviewers comment that 'HIIT' is a more conventional acryonym that 'HIIR', and have replaced the latter with the former throughout the manuscript.

Reviewer: Line 9; be careful..this 4X4 model that you use is not time efficient vs. MICT (the bout takes 27 min not including warmup and cooldown), unless you are referring to the actual duration of interval exercise which is 16 min. Please consider revising this text.

Authors' response: We thank the reviewer for highlighting this comment and have subsequently added in further information regarding the time efficiency of HIIT compared to MICT.

P4 L5-8 – Compared to moderate-intensity continuous running, **HIIT** leads to similar improvements in cardiorespiratory fitness **that is achieved with a shorter effective exercise duration** per session (2). Due to the reduced time-commitment and **exercise** training volume…

Reviewer: Line 25: and it could be argued that these perceptually regulated bouts better mirror how exercisers actually choose to modify intensity during acute exercise.

Authors' response: We thank the author for suggesting this important point, and have subsequently added this information to the manuscript.

P5 L25-26 – … offer a viable solution**, and is perhaps more reflective of how exercisers modify intensity during acute exercise**.

Reviewer: Lines 32-34: I am not familiar with this study, but exercise at 75 %HRmax does not meet the criteria of Weston et al. (2014) designating HIIT of > 85 %HRmax.

Authors' response: We thank the reviewer for highlighting the required percentage of maximal heart rate for exercise to be considered as a high-intensity. According to Weston et al. (2014), this does not classify the exercise employed by Chacaroun et al. (2018) as high-intensity the reviewer suggests. However, Chacaroun et al. (2018) compared continuous (30 mins) and interval (1 min on, 1 min off) cycling in hypoxic (clamped SpO_2 = 75%) and normoxic conditions at a similar absolute heart rate (75% of max). The authors make reference to a position stand from the ACSM (1998), highlighting that 75% of maximal heart rate is recommended for continuous exercise. Therefore, although this intensity may not be aligned with the more recent work of Weston et al. (2014), the intensity employed and findings of Chacaroun et al. (2018) support our rationale. As such, we have not made any changes to the current manuscript.

ACSM. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. MSSE. 1998;30(6):975-991.

Chacaroun, S., Gonzalez, I. V. E., Flore, P., Doutreleau, S. and Verges, S. Physiological responses to hypoxic constant-load and high-intensity interval exercise sessions in healthy subjects. Euro J App Phys. 2018:1-12.

Weston, K. S., Wisløff, U., & Coombes, J. S. High-intensity interval training in patients with lifestyle-induced cardiometabolic disease: a systematic review and meta-analysis. Br J Sports Med. 2014;48(16):1227-1234.

Reviewer: Line 40: remember that the Bartlett et al. study that you cite here was in men with VO2max well above 55 mL/kg/min, so these results poorly generalize to the typical adult.

Authors' response: We thank the reviewer for highlighting the work we cite by Bartlett et al. (2011) includes a participant cohort with a relatively high VO_{2MAX}, which may not be representative of adults within the general population. As such, we have since replaced this reference with a study comparing HIIT and continuous exercise (Thum et al., 2017). These authors conclude that HIIT is more enjoyable in active males and females with a more representative $VO2_{MAX}$ of the general population (41.4 ± 4.1 mL/kg/min) (Thum et al., 2017).

P26 L447-449 – **Thum, J., Parsons, G., Whittle, T., & Astorino, T. (2017). High-intensity interval training elicits higher enjoyment than moderate intensity continuous exercise. PloS one. 2017;12(1):e0166299.**

Bartlett, J. D., Close, G. L., MacLaren, D. P. M., Gregson, W., Drust, B., Morton, J. P. High intensity-interval running is perceived to be more enjoyable than moderate intensity continuous exercise: implications for exercise adherence. J Sports Sci. 2011; 29:547–553.

Reviewer: Please fix the typos in lines 44-45; thank you. Also, this text does not lay a solid or clear foundation for this text referring to cognitive function, breathlessness, reaction time, etc. as currently written. This information just appears here with little transition text to relate this particular topic to the current study—please rewrite this text here to better denote the importance or relevance of cognitive function, breathlessness, motivation, etc.

Authors' response: We thank the reviewer for pointing out the spelling errors in the manuscript and these have been corrected accordingly. Cognitive function is ususally decreased when assessed in hypoxic conditions, or shortly after exercise at a relative, fixed-inensity in hypoxia, compared to normoxia (McMorris et al., 2017). Similarly, exercise-related sensations are at a premium during maximal repeated sprints in hypoxia compared to normoxia (Brocherie et al., 2017). Therefore, the importance of our work relates to attempting to incorporate a perceptually-regulated exercise intensity to compensate for the negative influence hypoxia has on fixed-intensity exercise versus normoxia, denoted via defects in cognitive function and exercise-related sensations. We have re-written the section highlighted by the reviewer to better explain the transition into exercise-related sensations and cognitive function.

P5 L47-P6 L51 – … to **maintain** exercise-related sensations **contributing** to RPE (16) in hypoxia and normoxia. **Cyling continuously for 10 min at a fixed-intensity (corresponding**

to 50% VO_{2Max}) in hypoxia *versus* normoxia negatively impacts cognitive function (17). Slower self-selected running velocities may assist **with mitigating** hypoxic-induced negative cognitive function compared to normoxia (18).

Brocherie, F., Millet, G. P., & Girard, O. (2017). Psychophysiological responses to repeated-sprint training in normobaric hypoxia and normoxia. International Journal of Sports Physiology and Performance, 12(1), 115-123.

McMorris, T., Hale, B. J., Barwood, M., Costello, J., & Corbett, J. (2017). Effect of acute hypoxia on cognition: A systematic review and meta-regression analysis. Neuroscience & Biobehavioral Reviews, 74, 225-232.

Reviewer: Please list a rationale for this study aim—why does this really matter or to whom do these data apply? Is this for training purposes or something else?

Authors' response: We thank the reviewer for suggesting to list a short rationale after the aim of the study. We have subsequently added this into the manuscript which can also be found below.

P6 L59-61 – **Decreasing external load with matched internal load during perceptually-regulated HIIT in hypoxia compared to normoxia may benefit athletes during heavy training blocks prior to competition.**

Reviewer: Is it wise to have only 3 women in the study? Please comment.

Authors' response: In response to the reviewers comment, our aim was not to investigate the effect of gender in response to perceptually-regulated interval running in hypoxia and normoxia. Rather our intention was to investigate the effect of perceptually-regulated interval running in hypoxia and normoxia on adjustments in running velocity and aoociated exercise-related sensations of trained runners. During our recruitment period, three eligible females volunteered for the study who matched the inclusion criteria (P6 L67-69). We have calculated groups means ± SD and re-analysed the primary outcomes of our study (velocity, heart rate, SpO_2 and exercise-related sensations) only with the 16 male participants (excluding the three females). As shown at the bottom of this response document, this analysis indicates that including only three females does not lead to different groups means ± SD, probability values and effect sizes compared to a dataset of 16 males. Consequently, including the 3 female participants in our final sample of 19 participants does not change the overall message of the study. Therefore, we believe that keeping the three females within the current participant total (n = 19) is warranted since our power calculation indicated 21 participants are requied to yield sufficient power in the statistical tests carried out (P6 L73-P7 L76).This would not be achieved if the data from the three females were removed (n = 16).

Reviewer: Is there a reason why a VO2max test was not undertaken?

Authors' response: We thank the reviewer for raising this comment. Although identifying and presenting VO_{2MAX} values of the participants in our study would have been informative, we didn't feel it was necessary. This is because we used a modified, and validated, method (Martin et al., 1992) to determine the individual velocity required for each individual to run at an RPE of 16, which is presented (P17 L268-269) and the main purpose of our work. As such, of the ceiling value (VO_{2MAX}) did not need to be identified in the current study.

Martin, P. E., Rothstein, D. E., Larish, D. D. Effects of age and physical activity status on the speed-aerobic demand relationship of walking. J Appl Phys 1992;73:200–206.

Reviewer: Were participants informed about the study aim e.g. to test changes in your measures in hypoxia vs. normoxia?

Authors' response: We appreciate the reviewer raising this important comment. Prior to enrolling onto the study, participants were informed that they will perform two HIIT protocols, randomly in hypoxic and normoxic conditions. We explained the measures that we would be performing, but did not directly outline that we would be looking at the comparison between hypoxic and normoxic conditions to the participants. Naturally, this may have impacted their perceptions or lead to social desirability bias in response to perceptual scales and assessment of attention and executive function. Further, as outlined in the manuscript (P9 L132-135), participants were blinded to the environmental condition during the HIIT protocol as we removed the hypoxic generator from their view, and simulated 100 m (machine switched on) during normoxia. We have subsequently added in some further information regarding this comment to the manuscript as outlined below.

P7 L86-88 – **To minimise the impact of social desirability bias, participants were made aware of the purpose of the study but were naïve to experimental hypotheses.**

Adams, S. A., Matthews, C. E., Ebbeling, C. B., Moore, C. G., Cunningham, J. E., Fulton, J., & Hebert, J. R. The effect of social desirability and social approval on self-reports of physical activity. Am J Epidem, 2005;161(4):389-398.

Reviewer: I think the Results would be better structured by describing the fidelity of HIIT first, by denoting the HR and velocity data. This confirms that these bouts actually represent HIIT based on 85 %HRmax. Then, follow this with your other outcomes.

Authors' response: We acknowledge and agree with the reviewer that the results structure would be better when beginning the first section with velocity and heart rate data. The heading of this section has been renamed, and only includes velocity and heart rate data.

P12 L190 – ***Changes in velocity and HR***

Reviewer: I also think that the Results text needs better subheadings to clarify its organization e.g. change in HR and running velocity in response to..; change in muscle deoxygenation in response to, etc.

Authors' response: We appreciate the reviewer suggesting better subheadings within the results section. These have subsequently been renamed as below.

P12 L196 – ***Changes in SpO_2 and muscle oxygenation***

P12 L201 – ***Changes in exercise-related sensations***

P13 L222 – ***Changes in $[La^+]$ and attention and executive function***

Reviewer: Line 186 needs a clearer subheading e.g. change in recovery and .. in response to..

Authors' response: Please see response above regarding this comment.

Reviewer: Line 244, Discussion; so what is the importance of these findings to the athlete, coach, clinician, etc.? Please cite this here.

Authors' response: We acknowledge the reviewers comment that the importance of our findings should be stated here for those in an applied setting. We have subsequently added this information in to the manuscript, which can also be found below.

P17 L261-266 – **A matched internal workload for a decreased external workload during perceptually-regulated HIIT in hypoxia *versus* normoxia may assist athletes to reach intended session goals with minimal over-induced physiological stress. However, perceptually-regulated HIIT exacerbates exercise-related sensations and blood lactate concentrations in hypoxia compared to normoxia. This may then have negative carry-over effects on training responsiveness in the following days.**

Reviewer: Line 269; so what is the importance or application of this particular finding?

Authors' response: We understand the reviewers comment that this take home message can be further developed for importance and application. We have subsequently added this information in to the manuscript, which can also be found below.

P18 L291-294 – **This finding may be of benefit to athletes who are unable or advised by their coach not to be training at a full intensity. Completing perceptually-regulated HIIT in hypoxia that requires slower running velocities compared to normoxia may in turn minimise mechanical constraints and eventually injury risk.**

Reviewer: Line 302: what do you mean by 'metabolic by product?' this is blood lactate so just represent this as is to be most clear. And why does this excess accumulation of BLa matter to the scientist or athlete/practitioner?

Authors' response: We thank the reviewer for suggesting more clarity regarding the take home message of this paragraph in the discussion, and have replaced '*metabolic by-product*' with '$[La^+]$'. We have also added in a sentence regarding the implications of this finding in an applied setting.

P19 L327 – … to increased **$[La^+]$** at slower…

P19 L328-P20 L332 – **Practitioners should be aware that perceptually-regulated HIIT in hypoxia is a viable method for matching indices of physiological stress to normoxia. However, the blood lactate concentration increases after exercise were larger in hypoxia compared to normoxia. This may have negative implications on the muscle fatigue recovery process.**

Reviewer: Lines 307-15: are there any data showing that hypoxia reduces O2 delivery to the brain which then may alter perceptions of exercise which are regulated by various brain centers? Please comment on this.

Authors' response: We thank the reviewer for raising this interesting point. Accordingly, we have added some information from the work of Subudhi et al. (2007 & 2009) relating to the negative implication hypoxia has on oxygen delivery to the brain, potentially altering perceptions of exercise. We also believe that this point should be of consideration for further research investigations, attempting to capture further measurements in response to HIIT in hypoxia at a perceptually-regulated intensity compared to normoxia.

P20 L342-348 – **Further, it could be postulated that cerebral deoxygenation was greater during HIIT in hypoxia *versus* normoxia, as demonstrated by Subudhi et al. during**

incremental cycling (40, 41). Accordingly, cerebral deoxygenation during HIIT may contribute to an integrative decision regarding negative perceptions, in which hypoxia hastens this effect (41). Given that the perceptually-regulated exercise model is governed centrally, this may provide a potential explanation as to why exercise-related sensations were more elevated in the hypoxic trial.

P28 L522-524 – **Subudhi, A. W., Dimmen, A. C., & Roach, R. C. Effects of acute hypoxia on cerebral and muscle oxygenation during incremental exercise. J App Phys. 2007;103(1):177-183.**

P28 L525-527 – **Subudhi, A. W., Miramon, B. R., Granger, M. E., & Roach, R. C. Frontal and motor cortex oxygenation during maximal exercise in normoxia and hypoxia. J App Phys. 2009;106(4):1153-1158**.

Reviewer: This text seems to be way too much of a 'stretch' from your particular study and should be removed, as it is not relevant; thank you. *Athletes and clinical patients awaiting or shortly proceeding surgery may exercise in hypoxia to increase the internal workload similar to that achieved in normoxia for a lower external workload. This could decrease joint pain of the lower extremities during ambulation.*

Authors' response: We understand the reviewers concern regarding some of the statements presented in the limitations and perspectives section. We have since removed the points raised by the reviewer.

Reviewer 2

Reviewer: This study was primarily aimed at investigating potential differences in running velocities between perceptually-regulated high-intensity intervals in hypoxia and normoxia. It has been demonstrated that running velocity progressively decreased from interval 1 to 4, more pronounced in hypoxic conditions. Negative exercise-related sensations increased over time, again more pronounced in hypoxia.

The authors deal with an interesting topic especially from a training-practical point of view however, findings are not really unexpected and novelty of this study should be more highlighted. Methods are well and reproducible described and results are nicely presented. Nevertheless, the authors may respond to the following comments:

Authors' response: We thank the reviewer for their careful consideration of our work. We have responded to the comments individually raised below.

Reviewer: In the introduction session, you may refer to studies demonstrating differences between RPE and cardiorespiratory responses in hypoxia/altitude compared to normoxia.

Authors' response: We thank the reviewer for raising our attention to this point and have added in this information to the introduction section as outlined below.

P5 L36-38 – **Although HR was similar between conditions, RPE has been reported to be higher in hypoxia compared to normoxia during fixed-intensity interval runs (5) and repeated-sprint cycling (12).**

P26 L443-445 – **Brocherie, F., Millet, G. P., & Girard, O. Psychophysiological responses to repeated-sprint training in normobaric hypoxia and normoxia. International J of Sports Phys Perform. 2017;12(1):115-123.**

Reviewer: Nineteen experienced runners have been recruited. As you might expect, I am not happy with the inclusion of only 3 females. Such a sex distribution may reduce the conclusiveness of the findings and does not allow to analyse potential sex differences.

Authors' response: We understand the reviewers concern regarding the small population of females within our participant cohort. We would like to highlight that within the literature, it is inconclusive as to whether gender distributions impact on acute responses to hypoxia – with some confirming (Lombardi et al., 2013; Mortola & Saiki, 1996) and others rejecting (Loeppky et al., 2001; Sandoval & Matt, 2002) this hypothesis.

In response to the reviewers comment, our aim was not to investigate the effect of gender in response to perceptually-regulated interval running in hypoxia and normoxia. Our aim was to investigate the effect of perceptually-regulated interval running in hypoxia and normoxia on trained runners. During our recruitment period, three eligible females volunteered for the study who matched the inclusion criteria (P6 L67-69). We have calculated groups means ± SD and re-analysed the main findings of our study (velocity, heart rate, SpO_2 and exercise-related sensations) without the presence of the three females (located at the bottom of this response document) which does not change the overall message of the study. Therefore, we believe that keeping the three females within the current participant total (n = 19) is warranted since our power calculation indicated 21 participants are requied to yield suffificent power in the statistical tests carried out (P6 L73-P7 L76), which would not be achieved if the data from the three females were removed (n = 16).

We do believe that the reviewer raises an important comment, and have since highlighted this in the limitations and perspectives section of the paper for future investigations.

P22 L384-387 – **In addition, whether there are gender differences in response to hypoxic exposure during perceptually-regulated HIIT should be investigated, given that our final sample size (n = 19) included only three females.**

Loeppky, J. A., Scotto, P., Charlton, G. C., Gates, L., Icenogle, M., & Roach, R. C. (2001). Ventilation is greater in women than men, but the increase during acute altitude hypoxia is the same. Respiration physiology, 125(3), 225-237.

Lombardi, C., Meriggi, P., Agostoni, P., Faini, A., Bilo, G., Revera, M., ... & Gregorini, F. (2013). High-altitude hypoxia and periodic breathing during sleep: gender-related differences. Journal of sleep research, 22(3), 322-330.

Mortola, J. P., & Saiki, C. (1996). Ventilatory response to hypoxia in rats: gender differences. Respiration physiology, 106(1), 21-34.

Sandoval, D. A., & Matt, K. S. (2002). Gender differences in the endocrine and metabolic responses to hypoxic exercise. Journal of Applied Physiology, 92(2), 504-512.

Reviewer: Did you perform some type of power calculation? (at least a-posteriori).

Authors' response: We thank the reviewer for raising this comment. We did indeed carry out a power analysis to determine the number of participants required for sufficient power in our results. Information regarding this has been added to the manuscript, as found below.

P6 L72-P7 L78 – **A-priori sample size was calculated using G*Power (Version 3.1.9.3). This was determined using published power output data by Jeffries et al. (19), whereby**

healthy individuals cycled at a perceptually-regulated intensity (RPE = 16) in hypoxic (FiO_2 = 15.0%) and normoxic conditions. Twenty-one participants were deemed sufficient to yield a power of 0.8 at an α probability of 0.05. Two individuals dropped out due to injuries sustained during their time enrolled onto the study, not associated with the HIIT protocols we employed.

P26 L467-469 – **Jeffries, O., Patterson, S. D., & Waldron, M. The effect of severe and moderate hypoxia on exercise at a fixed level of perceived exertion. Euro J App Phys. 2019;1-12.**

Reviewer: What means experienced runners? Can you report race times, VO2max, etc.?

Authors' response: We appreciate the reviewers comment regarding our use of the term 'experienced runners'. As we did not collect information regarding race times and race history nor did we assess VO_{2MAX}, we have replaced this term with 'trained runners' throughout the manuscript. Further, the runners we recruited included those with middle and long distance backgrounds. As such, it would be difficult to estimate or predict one particular race distance (i.e., 10 km) for all participants if they had not competed in this distance previously. We believe the term 'trained' better reflects the demographic of individuals recruited for the study, whom may have a knowledge of different race times and race history, but we have no quantifiable data to present.

Reviewer: Please, provide a table depicting more characteristics of study participants, beside anthropometric data, e.g. also performance parameters, regular physical sports/exercise activity, medical history, coffee and/or alcohol drinking, smoking, medications, etc.

Authors' response: We appreciate the reviewer suggesting to add further characteristics of the participants who completed the study protocol. Prior to enrolling onto the study, we screened volunteers (using a health questionnaire) for their medical history. As described in the methods section (P6 L66-69), we only included individuals who were free of clinical signs of disease, orthopedic, neurological, cardiovascular or respiratory problems. Further, runners were recruited who trained for ≥6 h/wk. Therefore, we are unable to provide any further information regarding the characteristics of participants as this was not collected, but re-assure the reviewer that they were of a healthy status.

Reviewer: The limitation section should be extended and the statements that "athletes and clinical patients awaiting or shortly proceeding surgery may exercise in hypoxia to increase the internal workload similar to that achieved in normoxia for a lower external workload" and "this could decrease joint pain of the lower extremities during ambulation" are in my opinion not justified based on the presented findings and should rather be deleted.

Authors' response: We understand the reviewers concern regarding some of the statements presented in the limitations and perspectives section. We have since removed the points raised by the reviewer, and added in sentences regarding the need to investigate gender differences in response to perceptually-regulated HIIT in hypoxia.

P22 L384-387 – **In addition, whether there are gender differences in response to hypoxic exposure during perceptually-regulated HIIT should be investigated, given that our final sample size (n = 19) included only three females.**

Reviewer: The conclusion might a bit more focus on the training-practical importance of the findings.

Authors' response: We thank the reviewer for raising this important point, and have subsequently added a sentence within the conclusion section of our manuscript highlighting the practical considerations of our findings.

P22 L396-401 – **Our results suggest that athletes under the influence of hypoxia require lower external workloads to reach a perceptually-regulated target during HIIT than normoxia. If employed in a practical setting, coaches should consider the potential of negatively implicated exercise-related sensations and blood lactate concentrations which may have further negative carry-over effects on training responsiveness in the following days.**

Primary outcome measures processed and analysed with males and females (n = 19) and males only (n = 16).

Statistical analysis presented here used the methods presented in the manuscript. A two-way ANOVA investigated the main effect of condition, time and interaction. Group means ± SD, *p* values and effects sizes are presented for velocity, heart rate, SpO_2 and exercise-related sensations.

		Males & females					Males only				
	Measure	Condition				*p* value (effect size)	Condition				*p* value (effect size)
Physiology	Velocity (km/h-1)	HYP		NOR		Condition: *p* < 0.01 (0.91)	HYP		NOR		Condition: *p* < 0.01 (0.92)
		13.9 ± 0.6		14.7 ± 0.3		Time: *p* < 0.01 (0.65)	14.1 ± 0.7		14.9 ± 0.3		Time: *p* < 0.01 (0.66)
		Interval				Interaction: *p* < 0.01 (0.42)	Interval				Interaction: *p* < 0.01 (0.45)
		1	2	3	4		1	2	3	4	
		14.8 ± 0.2	14.4 ± 0.5	14.1 ± 0.7	13.8 ± 0.8		15.1 ± 0.2	14.6 ± 0.4	14.2 ± 0.6	14.0 ± 0.8	
	Heart rate (bpm)	HYP		NOR		Condition: *p* = 0.65 (0.01)	HYP		NOR		Condition: *p* = 0.53 (0.03)
		170 ± 3		169 ± 4		Time: *p* < 0.01 (0.62)	169 ± 3		168 ±4		Time: *p* < 0.01 (0.66)
		Interval				Interaction: *p* = 0.28 (0.07)	Interval				Interaction: *p* = 0.23 (0.09)
		1	2	3	4		1	2	3	4	
		165 ± 1	169 ± 0	171 ± 0	173 ±1		164 ± 1	168 ± 1	170 ± 0	173 ± 1	
	SpO2 (%)	HYP		NOR		Condition: *p* < 0.01 (0.99)	HYP		NOR		Condition: *p* < 0.01 (0.99)
		86 ± 0		95 ± 0		Time: *p* = 0.37 (0.06)	86 ± 0		95 ± 0		Time: *p* = 0.51 (0.50)
		Interval				Interaction: *p* = 0.17 (0.09)	Interval				Interaction: *p* = 0.14 (0.12)
		1	2	3	4		1	2	3	4	
		90 ± 6	91 ± 6	90 ± 6	90 ± 7		90 ± 5	91 ± 6	90 ± 6	90 ± 7	
Exercise-related sensations	Recovery (au)	HYP		NOR		Condition: *p* < 0.01 (0.61)	HYP		NOR		Condition: *p* < 0.01 (0.61)
		6 ± 2		7 ± 1		Time: *p* < 0.01 (0.81)	6 ± 2		7 ± 1		Time: *p* < 0.01 (0.80)
		Interval				Interaction: *p* < 0.01 (0.24)	Interval				Interaction: *p* < 0.01 (0.35)
		1	2	3	4		1	2	3	4	
		9 ± 0	7 ± 0	6 ± 1	5 ± 1		9 ± 0	7 ± 0	6 ± 1	5 ± 1	
	Motivation (au)	HYP		NOR		Condition: *p* < 0.01 (0.65)	HYP		NOR		Condition: *p* < 0.01 (0.71)
		13 ± 2		14 ± 1		Time: *p* < 0.01 (0.50)	12 ± 3		14 ± 1		Time: *p* < 0.01 (0.52)
		Interval				Interaction: *p* < 0.01 (0.25)	Interval				Interaction: *p* < 0.01 (0.28)
		1	2	3	4		1	2	3	4	
		15 ± 0	14 ± 1	12 ± 2	12 ± 2		15 ± 0	14 ± 1	12 ± 2	12 ± 2	
	Breathlessness (au)	HYP		NOR		Condition: *p* < 0.01 (0.56)	HYP		NOR		Condition: *p* < 0.01 (0.61)
		9 ± 1		7 ± 1		Time: *p* < 0.01 (0.55)	9 ± 1		7 ± 1		Time: *p* < 0.01 (0.61)
		Interval				Interaction: *p* = 0.80 (0.02)	Interval				Interaction: *p* = 0.58 (0.04)
		1	2	3	4		1	2	3	4	
		7 ± 1	8 ± 1	8 ± 1	8 ± 1		7 ± 1	8 ± 1	8 ± 1	8 ± 1	
	Limb discomfort (au)	HYP		NOR		Condition: *p* = 0.02 (0.30)	HYP		NOR		Condition: *p* = 0.04 (0.26)
		6 ± 1		5 ± 1		Time: *p* < 0.01 (0.59)	6 ± 1		5 ± 1		Time: *p* < 0.01 (0.59)
		Interval				Interaction: *p* = 0.78 (0.02)	Interval				Interaction: *p* = 0.66 (0.59)
		1	2	3	4		1	2	3	4	
		5 ± 1	6 ± 0	6 ± 1	7 ± 0		4 ± 0	6 ± 0	6 ± 1	7 ± 1	
	Pleasure (au)	HYP		NOR		Condition: *p* < 0.01 (0.59)	HYP		NOR		Condition: *p* < 0.01 (0.63)
		7 ± 2		10 ± 1		Time: *p* < 0.01 (0.60)	7 ± 2		10 ± 1		Time: *p* < 0.01 (0.68)
		Interval				Interaction: *p* = 0.07 (0.12)	Interval				Interaction: *p* = 0.02 (0.19)
		1	2	3	4		1	2	3	4	
		10 ± 1	9 ± 2	8 ± 3	7 ± 3		10 ± 2	9 ± 2	8 ± 3	7 ± 3	

Title

Psycho-physiological responses to perceptually-regulated interval runs in hypoxia and normoxia

Author names and affiliations

Hobbins L[a], Gaoua N[a], Hunter S[a], Girard O[bc]

[a]Sport and Exercise Science Research Centre (SESRC), London South Bank University, London, United Kingdom

[b]Murdoch Applied Sports Science (MASS) Laboratory, Murdoch University, Perth, Australia

[c]Athlete Health and Performance Research Center, ASPETAR, Qatar Orthopedic and Sports Medicine Hospital, Doha, QATAR

Corresponding author

Mr. Liam Hobbins

hobbinsl@lsbu.ac.uk

Sport and Exercise Science Research Centre

London South Bank University

103 Borough Road

London

SE1 0AA

Abstract

We investigated whether perceptually-regulated high-intensity intervals in hypoxia are associated with slower running velocities *versus* normoxia, when physiological responses and exercise-related sensations remain the same. Nineteen **trained** runners **(33.4 ± 9.1 years)** completed a high-intensity interval running protocol (4 × 4-min intervals at a clamped perceived rating exertion of 16 on the 6–20 Borg scale, 3-min passive recoveries) in either hypoxic (HYP; FiO_2 15.0%) or normoxic (NOR; FiO_2 20.9%) conditions. Participants adjusted to a progressively slower running velocity from interval 1–4 (-7.0%), and more so in HYP *vs.* NOR for intervals 2, 3 and 4 (-4.6%, -6.4% and -7.9%, respectively; $p < 0.01$). Heart rate increased from interval 1–4 (+4.8%; $p < 0.01$), independent of condition. Arterial oxygen saturation was lower in HYP *vs.* NOR (86.0% *vs*. 94.8%; $p < 0.01$). Oxyhemoglobin (-23.7%) and total hemoglobin (-77.0%) decreased, whilst deoxyhemoglobin increased (+44.9%) from interval 1–4 ($p < 0.01$), independent of condition. Perceived recovery (-41.6%) and motivation (-21.8%) were progressively lower from interval 1–4, and more so in HYP *vs.* NOR for intervals 2, 3 and 4 (recovery: -8.8%, -24.2% and -29.3%; motivation: -5.3%, -20.3% and -22.4%, respectively; $p < 0.01$). Perceived breathlessness (+18.6%), limb discomfort (+44.0%) and pleasure (-32.2%) changed from interval 1–4, with significant differences (+21.8%, +11.3% and -31.3%, respectively) between HYP and NOR ($p < 0.01$). Slower interval running velocities in hypoxia achieve similar heart rate and muscle oxygenation responses to those observed in normoxia when perceptually-regulated, yet at the expense of less favourable exercise-related sensations.

Key words

High-intensity intermittent running; normobaric hypoxia; perceptually-regulated exercise; ratings of perceived exertion; near-infrared spectroscopy; effort perception.

Introduction

High-intensity interval training (HIIT) is a popular exercise format in athletic and clinical populations (1,2). HIIT includes repeated short-to-long (2–5 min) intense exercise bouts (80–90% of the velocity associated with maximal oxygen uptake or vVO_{2Max}) interspersed with shorter (1–3 min) recoveries (3). Compared to moderate-intensity continuous running, HIIT leads to similar improvements in cardiorespiratory fitness that is achieved with a shorter effective exercise duration per session (2). Due to the reduced time-commitment and exercise training volume, investigations surrounding the potential physiological and performance benefits of HIIT have surged (4).

HIIT in normobaric hypoxia (a lower inspired oxygen fraction or FiO_2) is receiving attention for its potential in further advancing athletic performance compared to HIIT in normoxia. Buchheit et al. (5) employed a HIIT protocol (3 × 5-min, 90-s recovery) carried out in hypoxia (vVO_{2Max} = 84%; FiO_2 = 15.4%) and normoxia (vVO_{2MAX} = 90%) at a fixed-intensity (determined in normoxia) in highly-trained runners. A reduced physiological stress (i.e., lower heart rate or HR) was observed during hypoxia compared to normoxia, likely due to a lower vVO_{2Max} in hypoxia *versus* normoxia. However, fixed exercise intensities, regardless of environmental conditions, do not permit adjustments (i.e., increases or decreases of workload) during exercise to match the intensity target (i.e., vVO_{2MAX}). In turn, over-induced physiological stress may be counter-productive (i.e., greater deoxygenated muscle heamoglobin, lower oxygenated haemoglobin) for intended session goals (6). Furthermore, matched absolute fixed exercise intensities (i.e., a similar percentage of vVO_{2MAX}) lead to greater physiological stress (i.e., compensatory increase in HR) in hypoxia compared to normoxia due to reduced FiO_2 (7). Perceptually-regulated exercise intensities, that allow velocity adjustments based upon exercise-related sensations in order to maintain a target effort

level, may offer a viable solution**, and is perhaps more reflective of how exercisers modify intensity during acute exercise**.

Perceptually-regulated exercise permits the individual exercising to self-regulate external workload (i.e., running velocity/cycling power production) based upon Borg's rating of perceived exertion (RPE) scale (8). The validity and usefulness of using RPE for perceptually-regulating exercise has been described (9). The reduced oxygen availability in hypoxia makes the expectation tenable that there would be a slower self-selected running velocity in hypoxia for a given RPE, while velocity in normoxia would be more preserved, as evidenced previously (10). Chacaroun et al. (11) demonstrated for a lower power output (-15%), *vastus lateralis* muscle deoxyhemoglobin was higher and oxyhemoglobin lower in hypoxia (FiO_2 = 13.5%) compared to normoxia during a single interval session (15 × 1-min at 75% of maximal HR, 1-min recoveries). **Although HR was similar between conditions, RPE has been reported to be higher in hypoxia compared to normoxia during fixed-intensity interval runs (5) and repeated-sprint cycling (12).** Employing self-paced exercise, in replace of fixed-intensity exercise, may assist in overcoming the over-excessive physiological stress observed when exercising in hypoxia *versus* normoxia, due to the likelihood of greater velocity preservations in the latter than the former.

In normoxia at pre-determined fixed intensities, **HIIT** is perceived as more enjoyable compared to moderate-intensity continuous running (13). However, during **HIIT** at fixed-intensities, exercise-related sensations decrease when the exercise intensity rises above threshold preference (14). Further, **HIIT** in hypoxia at fixed-intensities typically surpasses the preferred threshold in normoxia (15). Implementing a self-paced exercise model may permit modifications required (i.e., slower running velocities) to **maintain** exercise-related sensations **contributing** to RPE (16) in hypoxia and normoxia. **Cyling continuously for 10 min at a fixed-intensity (corresponding to 50% VO_{2Max}) in hypoxia *versus* normoxia negatively**

impacts cognitive function (17). Slower self-selected running velocities may assist with mitigating hypoxic-induced negative cognitive function compared to normoxia (18). These potential findings may benefit athletes exercising intensely in hypoxia, shortly followed by skills requiring attention and accuracy.

Therefore, the aim of this study was to investigate the effect of HIIT at a clamped RPE of 16 (typically used by athletes during HIIT) (19) in hypoxia and normoxia on adjustments in running velocity and associated exercise-related sensations of trained runners. We hypothesized that running velocity would be progressively slower in hypoxia compared to normoxia across intervals, whilst physiological and cognitive responses, and exercise-related sensations would not differ between conditions. Decreasing external load with matched internal load during perceptually-regulated HIIT in hypoxia compared to normoxia may benefit athletes during heavy training blocks prior to competition.

Methods

Participants

Nineteen trained runners (3 females, 16 males; age: 33.4 ± 9.1 years; height: 176 ± 88 cm; weight: 76.3 ± 10.9 kg) provided written informed consent to participate. Participants had no musculoskeletal injuries and met the following eligibility criteria: a training volume ≥6 h/wk, free of clinical signs of disease, orthopedic, neurological, cardiovascular or respiratory problems, and no hypoxic exposure >2000 m for >48 h 6 months before the study. The study was carried out in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Anti-Doping Lab Qatar institutional review board (Agreement SCH-ADL-170). A-priori sample size was calculated using G*Power (Version 3.1.9.3). This was

determined using published power output data by Jeffries et al. (20), whereby healthy individuals cycled at a perceptually-regulated intensity (RPE = 16) in hypoxic (FiO_2 = 15.0%) and normoxic conditions. Twenty-one participants were deemed sufficient to yield a power of 0.8 at an α probability of 0.05. Two individuals dropped out due to injuries sustained during their time enrolled onto the study, not associated with the HIIT protocols we employed.

Experimental design

Participants reported to the laboratory on three occasions, each separated by ≥48 h. The first session included study familiarisation. The second and third visits included completing a **HIIT** protocol in either hypoxia or normoxia in a randomized, conterbalanced order. Physiological, perceptual and cognitive responses were assessed continuously, immediately before and after each interval, and before and after the **HIIT** protocol, respectively. Participants were instructed to refrain from any intense exercise 48 h prior to each visit and consume their last meal at least 2 h prior to the **HIIT** sessions. **To minimise the impact of social desirability bias, participants were made aware of the purpose of the study but were naïve to experimental hypotheses.** Laboratory conditions were similar throughout all sessions (mean temperature ~22˚C, relative humidity ~50%) and time of day was standardized for each participant.

Familiarization session

At the preliminary visit to the laboratory, participants were familiarised with the perceptual scales and cognitive test. Preferred running velocity (PRV) was determined for each participant in normoxia using a modified version of identifying preferred walking speed (21). After a 5-min warm up at 10 km/h^{-1}, participants completed four ramped treadmill runs (increasing and decreasing velocities) on an instrumented treadmill (ADAL3D-WR, Medical Development–HEF Tecmachine, France). After every 20 s per ramp, participants rated their RPE of the

current velocity (controlled by the investigator and out of sight of the participant) in accordance with Borg's (20) 6 ("*no exertion at all*") – 20 ("*maximal exertion*") numeric scale. Ramp one started at 10 km/h^{-1}, increasing by 0.8 km/h^{-1} every 20 s until the velocity was considered as RPE ≥18; ramp two started at +1.5 km/h^{-1} the previous end velocity, decreasing by 0.8 km/h^{-1} until the velocity was considerd as RPE ≤12; ramp three started at the velocity considered as an RPE of 14 in ramp two, increasing by 0.5 km/h^{-1} until the velocity was considerd as RPE ≥18; and ramp four started at +1.0 km/h^{-1} the previous end velocity, decreasing by 0.5 km/h^{-1} until the velocity was considered as RPE ≤12. Ramps two, three and four began once the participants declared their perceived recovery level as a 7 out of 10 following the previous ramp (23). HR was recorded every 20-s through each ramp. PRV corresponded to the velocity participants considered as a RPE of 16 (between "*hard*" and "*very hard*") or closest to a HR of 160 bpm. After 10 min of rest, participants completed one 4-min interval composing the **HIIT** protocol (see below) for habituation.

Experimental trials

Participants completed two experimental trials in normoxia (NOR; FiO_2 = 20.9%) and hypoxia (HYP; FiO_2 = 15.0%, equivalent to ~2700 m above sea level). After a standardised warm up (5-min at 10 km/h^{-1}), a facemask connected to a portable hypoxic generator (See *Hypoxic simulation* section) was attached. Participants rested for 1-min (quiet standing) before a 1-min run at their PRV (RPE = 16). Participants then rested for 3 min before completing the **HIIT** protocol. The **HIIT** protocol was based upon aerobic interval-training (2). Participants completed four, 4-min intervals, interspersed with 3-min recoveries (quiet standing). The first 30 s of each 4-min interval began at participants' PRV; participants were then free to decide if or how treadmill velocity needed to be adjusted (manually by one experimenter) to ensure maintenance of a RPE of 16 every 30 s. Participants hand-signalled in response to the current

velocity (finger up to increase, finger down to decrease, and circle using index finger and thumb to maintain); and signalled again to inform how much of an increase/decrease in velocity is required [1, 2 or 3 fingers up (faster) or down (slower) for 0.5, 1.0 or 1.5 km/h^{-1} changes, respectively]. Signals were trialled during familiarisation. Mild verbal encouragement to keep running at an RPE of 16 was used throughout **HIIT**. Total hypoxic exposure corresponded to exactly 28 min.

Hypoxic simulation

Participants were fitted with a facemask fastened with a Velcro headset connected via plastic tubing to a hypoxic generator (Altitrainer, SMTec SA, Nyon, Switzerland) to simulate hypoxia. The gas mixing system enriches inspired air by adding a fixed quantity of nitrogen via a 30-L mixing chamber, with the dilution being constantly controlled by a PO_2 probe (precision = T0.82 torr, safety FiO_2 = 9.7%). The hypoxic generator was hidden from participant viewing to ensure condition blinding. When breathing 'normal air' during normoxia, the hypoxic generator was on (for background noise) and set at a simulated altitude of 100 m to increase the strength of blinding.

Measures

Exercise intervals

HR was monitored telemetrically with a Polar transmitter-receiver (Polar S810, Kempele, Finland) and recorded 20 s before and every 30 s during each interval. Arterial oxygen saturation (SpO_2) was assessed via finger pulse oximetery (Palmsat 2500, NONIN Medical Inc., Plymouth, MI, USA) at the same time intervals. HR and SpO_2 were obtained before (i.e., after a 2-min seated period) and at the end of the warm-up procedure (i.e., prior to **HIIT**). Both

the HR watch (RS400, Polar) and oximeter receiver were attached on the handrails of the treadmill outside of the participants' view.

Muscle oxygenation trends of the right *vastus lateralis* muscle were recorded using near-infrared spectroscopy (NIRS; Portalite, Artinis, Netherlands) in real-time. A wireless bi-polar optode sensor was attached (~10 cm above the proximal patella border) and secured to skin via adhesive tape. Sampling frequency was set at 10 Hz (11) following a 'zero set' of all signals. Bandages were fastened around the lower limb and optode to prevent external light distorting readings. Oxy- (Δ; [O_2Hb]), deoxy- (Δ; [HHb]) and total haemoglobin (μmol; [tHb]) were exported (1 Hz). For analysis, each interval was averaged and normalized to a 10 s sample prior to interval one (reference value) for each respective condition and presented as percentage change.

During recovery

Perceived recovery and motivation to exercise were assessed 30 s before each interval. Perceived recovery was assessed by answering '*how recovered do you feel currently?*' via a numeric scale, ranging from 0 ("*very poorly recovered*") to 10 ("*very well recovered*") (23). Recovery was assessed before interval one to determine perceptions following the warm up. Perceived motivation to exercise was assessed via a 20-cm visual analog scale (24). Participants were asked '*how motivated do you feel to exercise right now?*' and answered by adjusting the level on the scale between 0 ("*extremely low*"; white colored) and 20 ("*extremely high*"; black colored). Immediately after each interval, ratings of perceived breathlessness, limb discomfort and pleasure were assessed. Perceived breathlessness was assessed by answering '*how does your breathing feel currently?*' via a numeric scale, ranging from 0 ("*nothing at all*") to 10 ("*very, very severe*") (25). Using the same scale, perceived limb discomfort was assessed by answering '*how do your legs feel currently?*'. A 20-cm visual analog scale (same

as motivation above) was used to assess '*how pleasant was that run?*' ranging from 0 ("*extremely unpleasant*") and 20 ("*extremely pleasant*").

Pre- and post-exercise

A capillary blood sample taken from the fingertip was analyzed for blood lactate concentration ($[La^+]$) with the Lactate Pro (LT-1710, Arkray, Japan) portable analyzer before the warm-up and 2 min after **HIIT**. An offline Stroop colour-word test (26) assessed attention and executive function. Using one hand and as quickly as possible, participants selected the colored key on the keyboard representing the color of the text appearing on the screen (red, yellow, green or blue). The cognitive test lasted for 3 min, and took place in a silent environment before the warm up and 3 min after **HIIT**. Reaction time (ms; time taken to select a color) and accuracy (%; correct color selected) were averaged over each test for analysis.

Statistical analysis

Data distribution was assessed via a Shapiro-Wilk test. A parametric within-subject two-way analysis of variance was used to investigate the main effect of condition (NOR *vs*. HYP), time (interval 1, 2, 3 *vs*. 4 or pre *vs*. post) and the condition × time interaction for normally distributed data. Partial eta-squared (η^2) was calculated as a measure of effect size. Values of 0.01, 0.06 and above 0.14 were considered as small, medium and large, respectively (27). A related samples Friedman's non-parametric test was used for data not normally distributed. Bonferroni post-hoc pairwise comparisons were used to identify locations of significant effects. Statistical testing was carried out in SPSS (v21; CED, Cambridge, United Kingdom). Data was considered significant if $p \leq 0.05$. All data are presented as group means ± SD.

Results

Changes in velocity and HR

Compared to interval 1, participants adjusted to a progressively slower running velocity during intervals 2, 3 and 4 (-2.8%, -5.2% and -7.0%, respectively; $p < 0.01$), and more so in HYP *vs.* NOR for intervals 2, 3 and 4 (-4.6%, -6.4% and -7.9%, respectively; $p < 0.01$; Figure 1A). Compared to interval 1, HR increased during intervals 2, 3 and 4 (+2.3%, +3.6% and 4.8%, respectively; $p < 0.01$; Figure 1B), independently of condition ($p = 0.65$).

Changes in SpO_2 and muscle oxygenation

SpO_2 was globally lower in HYP *vs.* NOR (-9.3% average across intervals; $p < 0.01$; Figure 1C), independently of time ($p = 0.37$). From interval 1 to 4, [O_2Hb] and [tHb] decreased (-23.7% and -77.0%, respectively) whilst [HHb] increased (+44.9%; $p < 0.01$; Figures 2A–C), independently of condition ($p > 0.08$).

Changes in exercise-related sensations

Perceived recovery decreased progressively from interval 1 to 4 (-41.6%; $p < 0.01$), and more so in HYP *vs.* NOR before intervals 2, 3 and 4 (-8.8%, -24.2% and -29.3%, respectively; $p = 0.02$; Figure 3A). Perceived motivation decreased progressively from interval 1 to 4 (-21.8%; $p < 0.01$), and more so in HYP *vs.* NOR before intervals 3 and 4 (-20.3% and -22.4%, respectively; $p < 0.01$; Figure 3B). Compared to interval 1, perceived breathlessness increased following intervals 2, 3 and 4 (+14.0%, +13.6% and +18.6%, respectively; $p < 0.01$; Figure 3C), independently of condition. Breathlessness was rated globally higher in HYP *vs.* NOR (+21.8%; $p < 0.05$), irrespective of time. Compared to interval 1, perceived limb discomfort increased following intervals 2, 3 and 4 (+23.3%, +35.3% and +44.0%, respectively; $p < 0.01$; Figure 3D), independently of condition. Limb discomfort was rated globally higher in HYP *vs.* NOR (+11.3%; $p = 0.01$), irrespective of time. The time-dependent decreases in perceived

pleasure across intervals (-14.7%, -25.4% and -32.3%, intervals 2, 3 and 4 *vs.* 1, respectively; $p < 0.01$; Figure 3E) tended to be larger in HYP *vs.* NOR (-31.3%, $p = 0.06$).

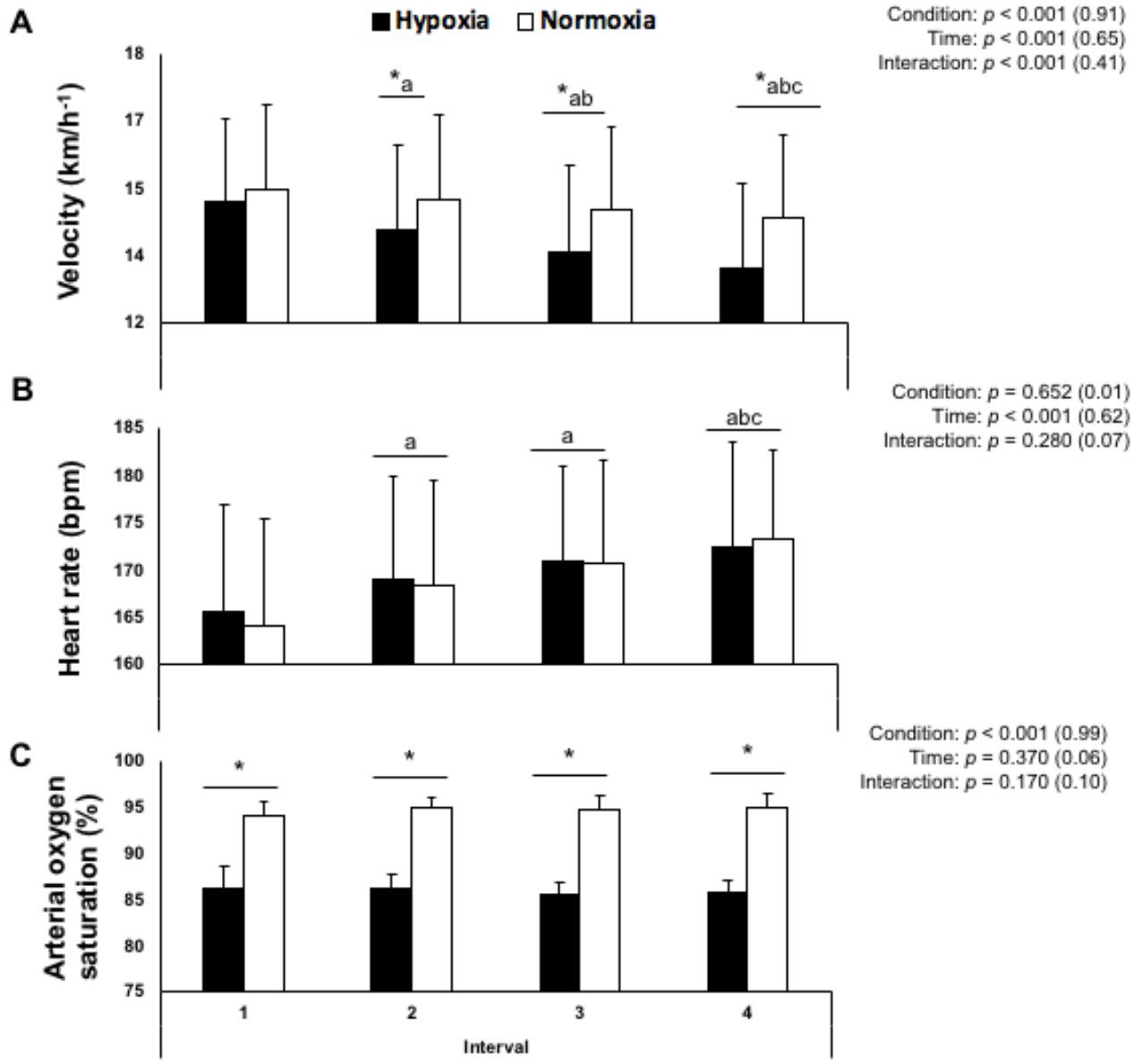

Figure 1 Changes in velocity (A), heart rate (B) and arterial oxygen saturation (C) during the high-intensity intermittent running protocol. Data are presented as mean ± SD. ANOVA main effects of time, condition and interaction are presented along with partial-eta squared for effect size into brackets. Black bars = hypoxic condition; white bars = normoxic condition. * denotes a statistically significant difference between conditions for a given interval ($p < 0.05$), a, b and c denotes a statistically significant difference vs. interval 1, 2 and 3, respectively ($p < 0.05$).

Changes in [La$^+$] and attention and executive function

The pre- to post-exercise increase in [La^+] was larger ($p = 0.001$) in HYP (1.7 ± 0.8 *vs.* 13.1 ± 3.8 mmol/l^{-1}) *vs.* NOR (2.1 ± 0.9 *vs.* 10.1 ± 3.9 mmol/l^{-1}). During the Stropp test, accuracy was

unaffected by condition and time (Figure 4A). Participants' reaction time was faster (+11%) post *vs.* pre **HIIT** ($p < 0.01$; Figure 4B), independently of condition.

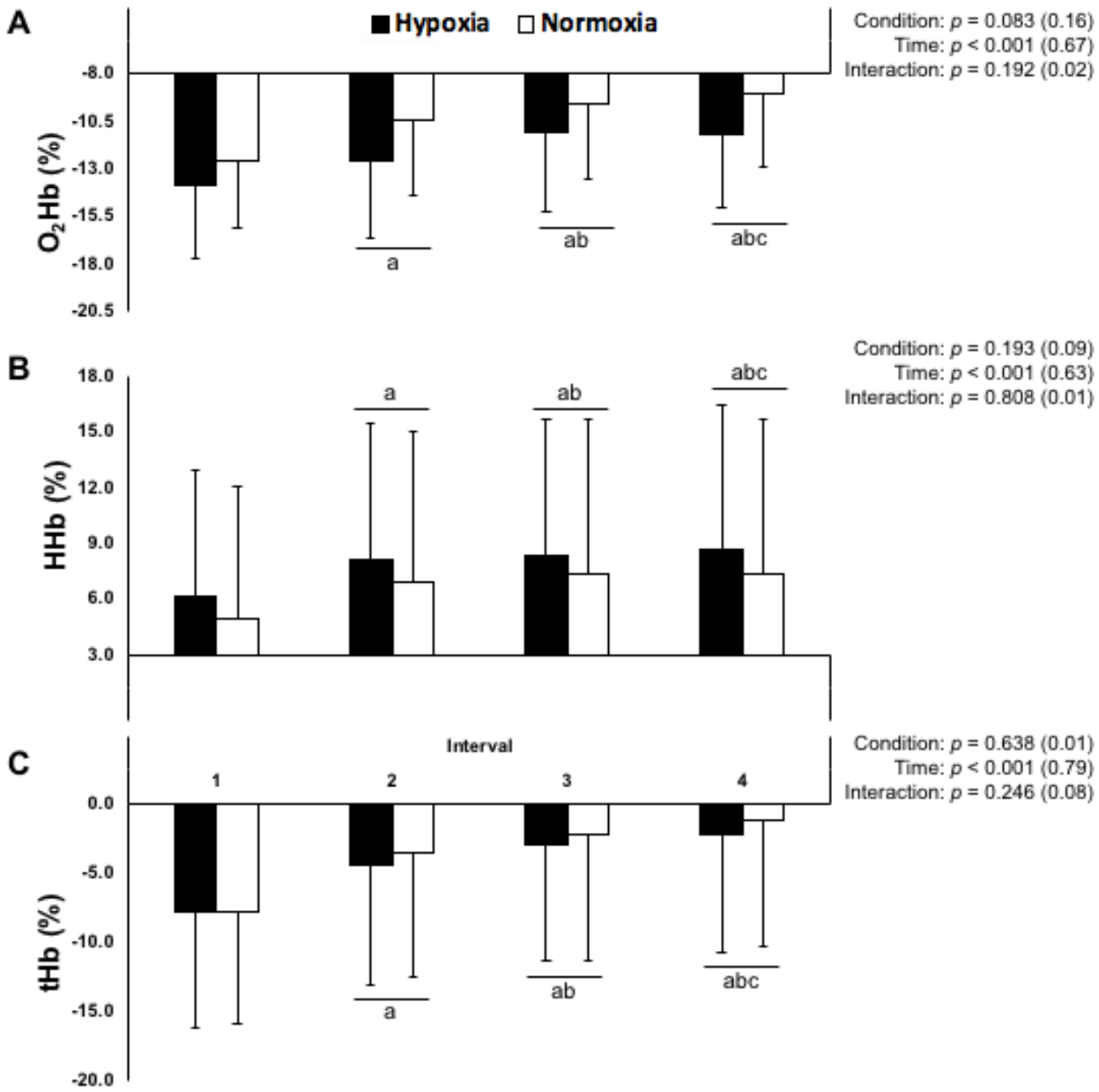

Figure 2 Changes in Oxygenated (A; O_2Hb), deoxygenated (B; HHb) and total hemoglobin (C; tHb) during the high-intensity intermittent running protocol. Data are calculated as a percentage difference from baseline (%) and presented as mean ± SD. ANOVA main effects of time, condition and interaction are presented along with partial-eta squared for effect size into brackets. Black bars = hypoxic condition; white bars = normoxic condition. a, b and c denotes a statistically significant difference vs. interval 1, 2 and 3, respectively ($p < 0.05$).

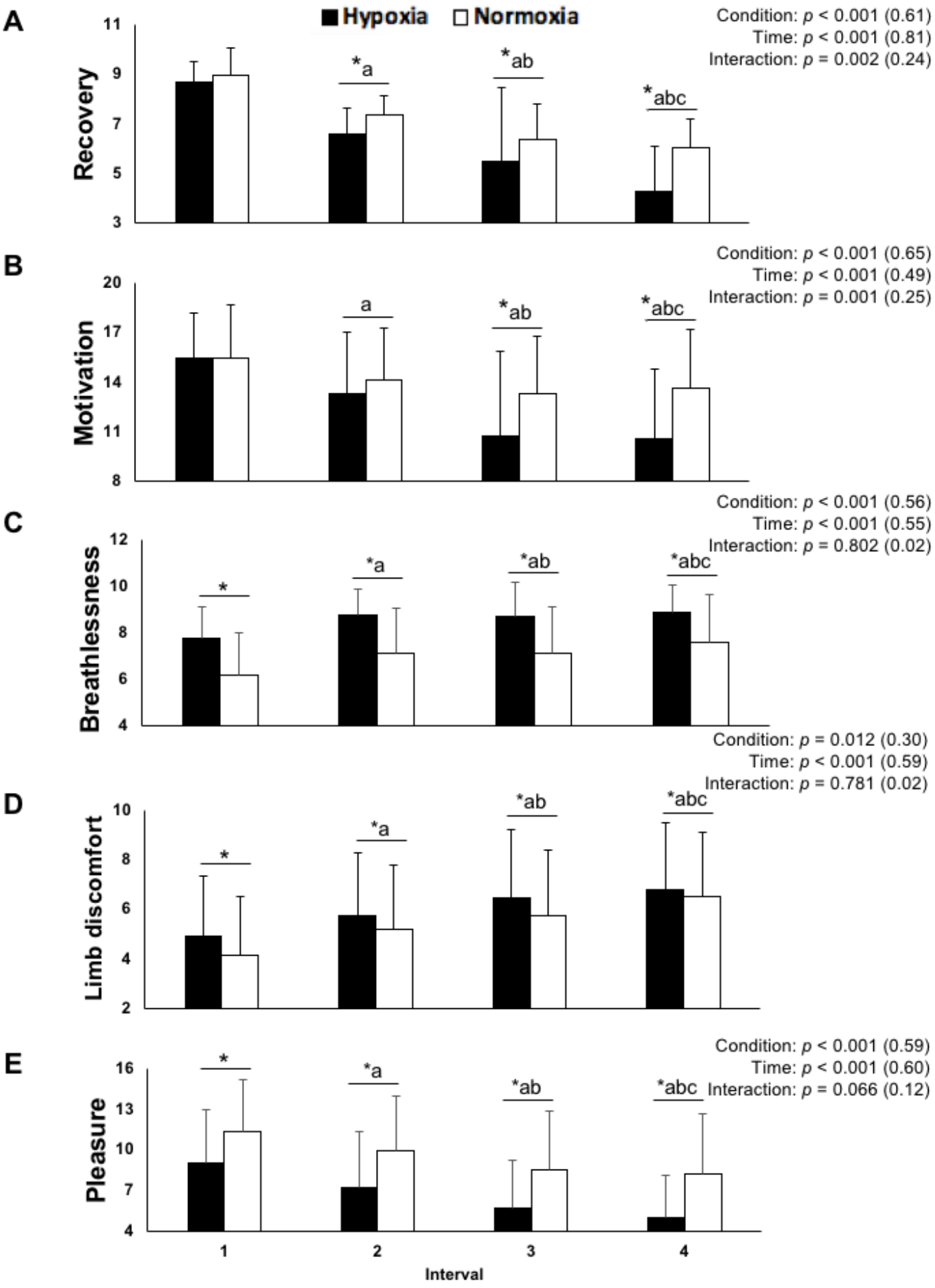
A
Hypoxia
Normoxia
Condition: p < 0.001 (0.61)
Time: p < 0.001 (0.81)
Interaction: p = 0.002 (0.24)
Recovery
11
9
7
5
3
*a
*ab
*abc
B
Condition: p < 0.001 (0.65)
Time: p < 0.001 (0.49)
Interaction: p = 0.001 (0.25)
Motivation
20
17
14
11
8
a
*ab
*abc
C
Condition: p < 0.001 (0.56)
Time: p < 0.001 (0.55)
Interaction: p = 0.802 (0.02)
Breathlessness
12
10
8
6
4
*
*a
*ab
*abc
D
Condition: p = 0.012 (0.30)
Time: p < 0.001 (0.59)
Interaction: p = 0.781 (0.02)
Limb discomfort
10
8
6
4
2
*
*a
*ab
*abc
E
Condition: p < 0.001 (0.59)
Time: p < 0.001 (0.60)
Interaction: p = 0.066 (0.12)
Pleasure
16
13
10
7
4
*
*a
*ab
*abc
1
2
3
4
Interval

Figure 3 Changes in perceived recovery (A), motivation (B), breathlessness (C), limb discomfort (D) and pleasure (E) during the high-intensity intermittent running protocol. Data are presented as mean ± SD. ANOVA main effects of time, condition and interaction are presented along with partial-eta squared for effect size into brackets. Black bars = hypoxic condition; white bars = normoxic condition. * denotes a statistically significant difference between conditions for a given interval ($p < 0.05$), a, b and c denotes a statistically significant difference vs. interval 1, 2 and 3, respectively ($p < 0.05$).

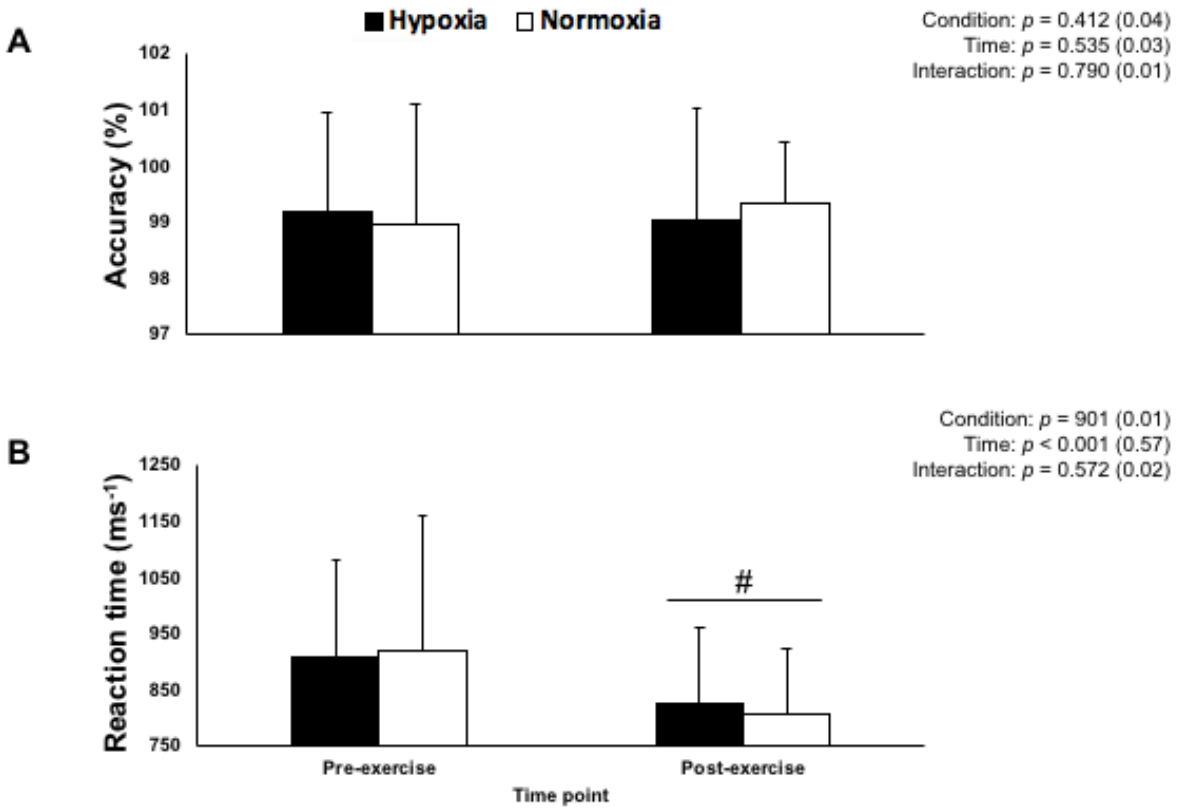

Figure 4 Changes in accuracy (A) and reaction time (B) pre and post high-intensity intermittent running protocol. Data are averaged over 3 mins and presented as mean ± SD. ANOVA main effects of time, condition and interaction are presented along with partial-eta squared for effect size into brackets. Black bars = hypoxic condition; white bars = normoxic condition. # denotes a statistically significant difference vs. pre-exercise ($p < 0.01$).

Discussion

Using a perceptually-regulated (RPE = 16) exercise model, we observed: 1) participants ran progressively slower during HIIT with larger decreases in HYP *versus* NOR, 2) HR and muscle oxygenation trends (during intervals) and cognitive responses (pre *vs*. post HIIT) were similar between conditions, 3) greater breathlessness and limb discomfort, and lower recovery,

motivation and pleasure scores were stated during recovery between HYP *vs.* NOR, and 4) blood lactate concentration was larger after HYP *vs.* NOR. Overall, using a manipulation of oxygen availability, reduced external workload (i.e., running velocity) during perceptually-regulated interval running is associated with a similar internal load (i.e., physiological responses). Although no cognitive function differences were found between conditions, this is achieved with less favourable exercise-related sensations. **A matched internal workload for a decreased external workload during perceptually-regulated HIIT in hypoxia *versus* normoxia may assist athletes to reach intended session goals with minimal over-induced physiological stress. However, perceptually-regulated HIIT exacerbates exercise-related sensations and blood lactate concentrations in hypoxia compared to normoxia. This may then have negative carry-over effects on training responsiveness in the following days.**

Exercise intervals

The velocity deemed equal to RPE 16 (PRV) was as expected for **trained** runners (~15 km/h^{-1}) (28). Interestingly, running velocity did not differ between conditions during the first **HIIT** interval, despite lower SpO_2 in hypoxia *versus* normoxia. Smith & Billaut (29) found maintained SpO_2 during repeated-sprinting in normoxia (20 × 5-s all out, 25-s recovery) until after the fifth sprint in national-level soccer players, whereby peak power significantly decreased compared to sprint one. Overall, it seems that initial decreases in SpO_2 (within interval one) do not necessarily impact on **HIIT** compared to sprint intervals.

We found that participants selected a progressively slower running velocity during **HIIT** in both conditions. In highly-trained middle to long-distance runners, a 6% reduction in vVO_{2MAX} when running in hypoxia *versus* normoxia is acceptable to match the acute physiological stress induced (5). It can be suggested that self-selected velocity adjustments found in the current study to maintain RPE 16 are matched with modifications in hypoxic *versus* normoxic traning

sessions employed by coaches and sport scientists for athletes (30). Decreased external workloads have been reported by Pramsohler et al. (31) during continuous cycling (seven 30-min sessions over 3-wk), whereby participants cycled at -28% lower power output in hypoxia (FiO_2 = 15.3%) *versus* normoxia for a similar HR. Differences in these findings and ours may be due to the inclusion of geriatric patients completing pre-set (in normoxia) fixed-intensity cycling compared to **trained** runners self-regulating **HIIT** in the current study. However, Fernández-Menéndez et al. (10) reported preferred walking velocity (RPE of 10) in hypoxia (FiO_2 = 15.3%) was 7% slower than normoxia in obese adults over 3 weeks. Using a self-paced model, irrespective of RPE target, population demographics and training block duration, lower external workloads are selected in hypoxia compared to normoxia. Overall, decreases in self-paced running velocity occured to a greater extent in hypoxia than normoxia to maintain RPE 16, suggesting of a lower external workload. **This finding may be of benefit to athletes who are unable or advised by their coach not to be training at a full intensity. Completing perceptually-regulated HIIT in hypoxia that requires slower running velocities compared to normoxia may in turn minimise mechanical constraints and eventually injury risk.**

Our data show HR increased progressively during **HIIT**, irrespective of condition. This matches our hypothesis that HR will be comparable between hypoxia and normoxia, even though running velocity was lower in hypoxia. Other studies employing moderate continuous-intensity exercise have also found matched HR responses between hypoxic and normoxic training interventions (~4 weeks) when cycling at a -21.0% power output in healthy males (32) and walking/running at a -17.5% velocity in obese adults (33) in hypoxia *verus* normoxia. Although exercise intensities in these studies were fixed, we believe similar increases in HR between conditions occur due to the environmental stressor (hypoxia) augmenting autonomic cardiac regulation (34). Overall, it seems self-paced exercise in hypoxia provides an added

environmental stressor that is able to mimick HR responses in normoxia for a lower external load.

Lower [O_2Hb] and [tHb], and greater [HHb] of the *vastus lateralis* were recorded across **HIIT**, irrespective of condition. Decreases in [O_2Hb] and increases in [HHb] were expected during **HIIT** as oxygen delivery is outweighed by utilisation, whilst decreases in [tHb] reflect a lower localised blood flow (35). Active musculature oxygenation is negatively impacted during fixed-intensity exercise in hypoxia compared to normoxia due to a lower FiO_2 (7). In support of this, Chacaroun et al. (11) reported lower [O_2Hb] and greater [HHb] with maintained [tHb] of the *vastus lateralis* during fixed, relative high-intensity cycling in hypoxia (85% maximal power output in normoxia; FiO_2 = 13.5%) *versus* normoxia. Where we employed a self-paced exercise model, similar [O_2Hb] and [HHb] responses are achieved between conditions. This is likely explained through the decreased workload (i.e., slower running velocity) in hypoxia compared to normoxia, subsequently lowering oxygen utilisation. Discrepants findings in [tHb] may be due to different exercise modalities (cycling *versus* running) modifying blood flow regulation (36). Similar to HR responses (central) previously discussed, it can be suggested here that local (tissue oxygenation) physiological stress is matched between conditions during **HIIT** in hypoxia at a slower velocity compared with normoxia.

Elevations in [La^+] following **HIIT** were higher in HYP than NOR. Values in the current study (10–13 mmol/l^{-1}) are somewhat higher than those (5–6 mmol/l^{-1}) reported elsewhere following a single **HIIT** session (6 × 4-min intervals at a RPE ~17, 4-min recoveries) (19). This maybe due to a 1:0.75 work:rest ratio implemented during our protocol compared to 1:1 employed by Seiler & Sjursen (19). [La^+] normalization during shorter recovery periods may not occur to the extent following longer recovery periods due to excess pyruvate accumulation (37). This suggests that **HIIT** in hypoxia *per se* leads to increased **[La^+]** at slower running velocities compared to normoxia for similar physiological stress amounts. **Practitioners should be**

aware that perceptually-regulated HIIT in hypoxia is a viable method for matching indices of physiological stress to normoxia. However, the blood lactate concentration increases after exercise were larger in hypoxia compared to normoxia. This may have negative implications on the muscle fatigue recovery process.

During recovery

Perceptual responses to **HIIT** were negatively impacted (i.e., lower recovery, and motivation) when assessed before intervals, with further exacerbations in hypoxia. Participants were instructed to maintain a RPE of 16 throughout **HIIT** by adjusting their velocity where necessary. It might be surprising at first that perceptual responses were worse in hypoxia compared to normoxia. However, perceived recovery and motivation are important affects associated with exercise intensity regulation (38). Our results indicate that hypoxia negatively impacts these affects during **HIIT** compared with normoxia. This may be explained through lower perceived capabilities of hypoxic **HIIT** completion over normoxia (39), lowering perceived recovery and motivation. **Further, it could be postulated that cerebral deoxygenation was greater during HIIT in hypoxia *versus* normoxia, as demonstrated by Subudhi et al. during incremental cycling (40, 41). Accordingly, cerebral deoxygenation during HIIT may contribute to an integrative decision regarding negative perceptions, in which hypoxia hastens this effect (41). Given that the perceptually-regulated exercise model is governed centrally, this may provide a potential explanation as to why exercise-related sensations were more elevated in the hypoxic trial.** Overall, our data poses a disconnection between RPE and exercise-related sensations (i.e., recovery and motivation). Further research should look to optimise **HIIT** in hypoxia for positive perceptual responses.

Perceptual responses after intervals were negatively impacted (i.e., higher breathlessness and limb discomfort, lower pleasure), and to a further extent in hypoxia than normoxia. Buchheit

et al. (5) reported that 3-min absolute-intenxity running intervals (84% vVO_{2MAX}) in hypoxia (FiO_2 = 15.4%) led to larger perceived limb discomfort compared to a lower absolute intensity in normoxia (90% vVO_{2MAX}). We expected exercise-related sensations to be similar between conditions as parcipants could adjust their velocity where necessary. However, this was not the case. Similar responses have been shown elsewhere (42), with greater perceived overall discomfort, breathlessness and limb discomfort following progressive, sub-maximal, self-paced cycling intervals (RPE = 3; modified CR10 Borg scale) in hypoxia (FiO_2 = 13.0%) compared to normoxia at a similar power output. Perceived breathlessness, limb discomfort and pleasure are exercise-related sensations contributing to overall RPE during exercise (16). However, there is a detachment between these when immediately assessed after **HIIT** intervals. We suggest that self-paced **HIIT** in hypoxia leads to unfavourable exercise-related sensations before and after running intervals, compared to normoxia.

Pre- and post-exercise

During the Stroop test, alertness increased (i.e., faster reaction time) whilst accuracy was maintained following **HIIT**, irrespective of condition. It is well known that **HIIT** in normoxia generally increases cognitive performance *versus* rest (i.e., faster reaction time, better accuracy) (43). However, during fixed-intensity exercise in hypoxia, cognitive performance (i.e., attention and executive function) is worsened compared to normoxia (17,18). We report that even though exercise-related sensations were worsened during **HIIT**, cognitive performance (assessed post-**HIIT**) was not negatively affected. Ochi et al. (18) reported decreased Stroop performance 15 mins after 10 mins of moderate-continuous intensity exercise (50% peak oxygen uptake) in hypoxia (FiO_2 = 13.5%) *versus* normoxia. Our results likely differ to the aforementioned study due to cognitive testing performed in normoxia and following different exercise modalities. Our data show that alertness is increased following **HIIT**, and not negatively impacted by hypoxia.

Limitations and perspectives

During self-paced exercise at a perceptually-regulated intensity in hypoxia, HR and muscle oxygenation responses are similar to normoxia for a lower running velocity. However, we used a single "hypoxic dose" (i.e., hypoxic severity and duration), target RPE and exercise duration during **HIIT**. Further investigations should refine self-selected protocols in hypoxia, such as the "hypoxic dose", target RPE and exercise duration to minimise the negative side effects of worsened exercise-related sensations found under the present circumstances. **In addition, whether there are gender differences in response to hypoxic exposure during perceptually-regulated HIIT should be investigated, given that our final sample size (n = 19) included only three females.**

Conclusion

When carrying out **HIIT** at a perceptually-regulated intensity (RPE equal to 16), larger running velocity decreases are needed in hypoxia than normoxia. This is accompanied by similar physiological stress (i.e., HR and muscle oxygenation) during **HIIT**, and cognitive function adjustments after. In hypoxia, exercise-related sensations and blood lactate concentrations were higher-than-normal with larger peripheral oxygen desaturation. Overall, perceptually-regulated running velocity in hypoxia compared to normoxia may be an effective alternative, at the expense of less favourable exercise-related sensations. **Our results suggest that athletes under the influence of hypoxia require lower external workloads to reach a perceptually-regulated target during HIIT than normoxia. If employed in a practical setting, coaches should consider the potential of negatively implicated exercise-related sensations and blood lactate concentrations which may have further negative carry-over effects on training responsiveness in the following days.**

Acknowledgements

The authors would like to thank the Sport and Exercise Science Research Centre of London South Bank University for a travel bursary and Dr. Sebastien Racinais of ASPETAR for accommodating Liam Hobbins. This work was supported by Qatar National Research Fund (grant number: NPRP 4–760–3–217).

Conflict of interest

The authors have no conflicts of interest or financial ties to disclose and no current or past relationship with companies or manufacturers who could benefit from the results of the present study.

References

1. Zois, J., Bishop, D. and Aughey, R., High-intensity warm-ups: effects during subsequent intermittent exercise. Int J Sports Phys Perf. 2015;10(4):498-503.
2. Gibala, M. J., Gillen, J. B. and Percival., M. E. Physiological and health-related adaptations to low-volume interval training: influences of nutrition and sex. Sports Med. 2014;44.2: 127-137.
3. Buchheit, M. and Laursen, P. B. High-intensity interval training, solutions to the programming puzzle. Sports Med. 2013;43(10):927-954.
4. Gillen, J. B. and Gibala, M. J. Is high-intensity interval training a time-efficient exercise strategy to improve health and fitness? App Phys Nutr Met. 2013;39(3):409-412.
5. Buchheit, M., Kuitunen, S., Voss, S. C., Williams, B.K., Mendez-Villanueva, A. and Bourdon, P.C. Physiological strain associated with high-intensity hypoxic intervals in highly trained young runners. J Strength Cond Res. 2012;26(1):94-105.
6. Laurent, C. M., Vervaecke, L. S., Kutz, M. R. and Green, J. M., Sex-specific responses to self-paced, high-intensity interval training with variable recovery periods. J Strength Cond Res. 2014;28(4):920-927.
7. Heinonen, I. H., Boushel, R. and Kalliokoski, K. K. The circulatory and metabolic responses to hypoxia in humans–with special reference to adipose tissue physiology and obesity. Front Endo. 2016;7:116.
8. Parfitt, G., Blisset, A., Rose, E. A. and Eston, R. Physiological and perceptual responses to affect-regulated exercise in healthy young women. Psychophysiology. 2012;49(1):104-110.
9. Hardy, C. J. and Rejeski, W. J. Not what, but how one feels: The measurement of affect during exercise. J Sport Exerc Psych. 1989;11(3):304-317.

10. Fernández Menéndez, A., Saudan, G., Sperisen, L., Hans, D., Saubade, M., Millet, G.P. and Malatesta, D. Effects of Short-Term Normobaric Hypoxic Walking Training on Energetics and Mechanics of Gait in Adults with Obesity. Obesity. 2018;26(5):819-827.

11. Chacaroun, S., Gonzalez, I. V. E., Flore, P., Doutreleau, S. and Verges, S. Physiological responses to hypoxic constant-load and high-intensity interval exercise sessions in healthy subjects. Euro J App Phys. 2018;1-12.

12. **Brocherie, F., Millet, G. P., & Girard, O. Psychophysiological responses to repeated-sprint training in normobaric hypoxia and normoxia. International J of Sports Phys Perform. 2017;12(1):115-123.**

13. **Thum, J., Parsons, G., Whittle, T., & Astorino, T. (2017). High-intensity interval training elicits higher enjoyment than moderate intensity continuous exercise. PloS one. 2017;12(1):e0166299.**

14. Lind, E., Joehns-Matre, R. R., and Ekkekakis, P. What intensity of physical activity do previously sedentary middle-aged women select? Evidence of a coherent pattern from physiological, perceptual and affective markers. Prev Med. 2005;40:407–419.

15. Friedmann, B., Bauer, T., Menold, E. and Bärtsch, P. Exercise with the intensity of the individual anaerobic threshold in acute hypoxia. Med Scie Sports Exerc. 2004;36(10):1737-1742.

16. Abbiss, C. R., Peiffer, J. J., Meeusen, R. and Skorski, S. Role of ratings of perceived exertion during self-paced exercise: what are we actually measuring? Sports Med. 2015;45(9):1235-1243.

17. Ochi, G., Yamada, Y., Hyodo, K., Suwabe, K., Fukuie, T., Byun, K., Dan, I. and Soya, H. Neural basis for reduced executive performance with hypoxic exercise. Neuroimage. 2018;171:75-83.

18. McMorris, T., Hale, B. J., Barwood, M., Costello, J. and Corbett, J. Effect of acute hypoxia on cognition: A systematic review and meta-regression analysis. Neuro Biobehavioral Revs. 2017;74:225-232.

19. Seiler, S. and Sjursen, J. E. Effect of work duration on physiological and rating scale of perceived exertion responses during self-paced interval training. Scand J Med Sci Sports. 2004;14(5):318-325.

20. Jeffries, O., Patterson, S. D., & Waldron, M. The effect of severe and moderate hypoxia on exercise at a fixed level of perceived exertion. Euro J App Phys. 2019;1-12.

21. Martin, P. E., Rothstein, D. E., Larish, D. D. Effects of age and physical activity status on the speed-aerobic demand relationship of walking. J Appl Phys 1992;73:200–206.

22. Borg, G. A. V. Perceived exertion as an indicator of somatic stress. Scand J Rehab Med. 1970;2:92-98.

23. Laurent, C.M., Green, J. M., Bishop, P. A., Sjökvist, J., Schumacker, R. E., Richardson, M. T. and Curtner-Smith, M. A practical approach to monitoring recovery: development of a perceived recovery status scale. J Strength Cond Res. 2011;25(3):620-628.

24. Crewther, B. T., Carruthers, J., Kilduff, L. P., Sanctuary, C. E. and Cook, C. J. Temporal associations between individual changes in hormones, training motivation and physical performance in elite and non-elite trained men. Bio Sport. 2016;33(3):215.

25. Ward, S. A. and Whipp, B. J. Effects of peripheral and central chemoreflex activation on the isopnoeic rating of breathing in exercising humans. J Phys. 1989;411(1):27-43.

26. Stroop, J. R. Studies of interference in serial verbal reactions. J Exp Psychol. 1935;18:643-662.

27. Cohen, J. Statistical power analysis for the behavioral sciences, 2nd ed. 1988. New Jersey: Lawrence Erlbaum Associates.
28. da Silva, D. F., Simões, H. G. and Machado, F. A., vVO2max versus Vpeak, what is the best predictor of running performances in middle-aged recreationally-trained runners?. Science & Sports. 2015;30(4):e85-e92.
29. Smith, K. J. and Billaut F. Influence of cerebral and muscle oxygenation on repeated-sprint ability. Eur J Appl Physiol. 2010;109(5):989-99
30. Dufour, S. P., Ponsot, E., Zoll, J., Doutreleau, S., Lonsdorfer-Wolf, E., Geny, B., Lampert, E., Fluck, M., Hoppeler, H., Billat, V. and Mettauer, B. Exercise training in normobaric hypoxia in endurance runners. I. Improvement in aerobic performance capacity. J App Phys. 2006;100(4):1238-1248.
31. Pramsohler, S., Burtscher, M., Faulhaber, M., Gatterer, H., Rausch, L., Eliasson, A. and Netzer, N. C. Endurance Training in Normobaric Hypoxia Imposes Less Physical Stress for Geriatric Rehabilitation. Front Phys, 2017;8:514.
32. Haufe, S., Wiesner, S., Engeli, S. et al. Influences of normobaric hypoxia training on metabolic risk markers in human subjects. Med Sci Sports Exerc. 2008;40(11):1939–1944.
33. Wiesner, S., Haufe, S., Engeli S, et al. Influences of normobaric hypoxia training on physical fitness and metabolic risk markers in overweight to obese subjects. Obesity (Silver Spring). 2010;18(1):116–120.
34. Krejčí, J., Botek, M. and McKune, A.J., 2018. Dynamics of the heart rate variability and oxygen saturation response to acute normobaric hypoxia within the first 10 min of exposure. Clin Phys Funct Imag. 2018;38(1):56-62.

35. Van Beekvelt, M. C., Colier, W. N., Wevers, R. A., Van Engelen, B. G. Performance of near-infrared spectroscopy in measuring local O_2 consumption and blood flow in skeletal muscle. J Appl Physiol. 2001;90:511–519.

36. Joyner, M. J. and Casey, D. P. Regulation of increased blood flow (hyperemia) to muscles during exercise: a hierarchy of competing physiological needs. Phys Revs. 2015;95(2):549-601.

37. Howlett, R. A., Heigenhauser, G. J., Hultman, E., Hollidge-Horvat, M. G. and Spriet, L. L. Effects of dichloroacetate infusion on human skeletal muscle metabolism at the onset of exercise. Am J Phys Endo Met. 1999;277(1):E18-E25.

38. Renfree, A., Martin, L., Micklewright, D., and Gibson, A. S. C. Application of decision-making theory to the regulation of muscular work rate during self-paced competitive endurance activity. Sports Med. 2014;44:147–158.

39. Stork, M. J., Gibala, M. J. and Martin, K. G. Psychological and Behavioral Responses to Interval and Continuous Exercise. Med Scie Sports Exerc. 2018;50(10):2110-2121.

40. Subudhi, A. W., Dimmen, A. C., & Roach, R. C. Effects of acute hypoxia on cerebral and muscle oxygenation during incremental exercise. J App Phys. 2007;103(1):177-183.

41. Subudhi, A. W., Miramon, B. R., Granger, M. E., & Roach, R. C. Frontal and motor cortex oxygenation during maximal exercise in normoxia and hypoxia. J App Phys. 2009;106(4):1153-1158.

42. Christian, R. J., Bishop, D., Girard, O., & Billaut, F. The role of sense of effort on self-selected cycling power output. Front in Phys. 2014;5:115.

43. Lambourne, K. and Tomporowski, P. The effect of exercise-induced arousal on cognitive task performance: a meta-regression analysis. Brain Res. 2010;1341:12-24.

Psycho-physiological responses to perceptually-regulated interval runs in hypoxia and normoxia

- Our primary aim was to investigate whether perceptually-regulated high-intensity intervals in hypoxia are associated with slower running velocities *versus* normoxia, whilst physiological responses and exercise-related sensations do not differ.

- Our findings show that participants adjusted to a progressively slower running velocity over the course of the protocol, and more so in hypoxic compared to normoxic conditions.

- Whilst SpO_2 was intuitively lower in hypoxia *versus* normoxia, heart rate and muscle oxygenation haemodynamics values changed over time but were matched between environmental conditions.

- Further, exercise-related sensations (*i.e.,* perceived recovery, motivation, breathlessness, limb discomfort and pleasure) were negatively impacted over time, and more so in hypoxic compared with normoxic conditions.

- Overall, slower interval running velocities in hypoxia achieve similar heart rate and muscle oxygenation responses to those observed in normoxia when perceptually-regulated, yet at the expense of less favourable exercise-related sensations.

Title

Psycho-physiological responses to perceptually-regulated interval runs in hypoxia and normoxia

Author names and affiliations

Hobbins L[a], Gaoua N[a], Hunter S[a], Girard O[bc]

[a]Sport and Exercise Science Research Centre (SESRC), London South Bank University, London, United Kingdom

[b]Murdoch Applied Sports Science (MASS) Laboratory, Murdoch University, Perth, Australia

[c]Athlete Health and Performance Research Center, ASPETAR, Qatar Orthopedic and Sports Medicine Hospital, Doha, QATAR

Corresponding author

Mr. Liam Hobbins

hobbinsl@lsbu.ac.uk

Sport and Exercise Science Research Centre

London South Bank University

103 Borough Road

London

SE1 0AA

Abstract

We investigated whether perceptually-regulated high-intensity intervals in hypoxia are associated with slower running velocities *versus* normoxia, when physiological responses and exercise-related sensations remain the same. Nineteen trained runners (33.4 ± 9.1 years) completed a high-intensity interval running protocol (4 × 4-min intervals at a clamped perceived rating exertion of 16 on the 6–20 Borg scale, 3-min passive recoveries) in either hypoxic (HYP; FiO_2 15.0%) or normoxic (NOR; FiO_2 20.9%) conditions. Participants adjusted to a progressively slower running velocity from interval 1–4 (-7.0%), and more so in HYP *vs.* NOR for intervals 2, 3 and 4 (-4.6%, -6.4% and -7.9%, respectively; $p < 0.01$). Heart rate increased from interval 1–4 (+4.8%; $p < 0.01$), independent of condition. Arterial oxygen saturation was lower in HYP *vs.* NOR (86.0% *vs*. 94.8%; $p < 0.01$). Oxyhemoglobin (-23.7%) and total hemoglobin (-77.0%) decreased, whilst deoxyhemoglobin increased (+44.9%) from interval 1–4 ($p < 0.01$), independent of condition. Perceived recovery (-41.6%) and motivation (-21.8%) were progressively lower from interval 1–4, and more so in HYP *vs.* NOR for intervals 2, 3 and 4 (recovery: -8.8%, -24.2% and -29.3%; motivation: -5.3%, -20.3% and -22.4%, respectively; $p < 0.01$). Perceived breathlessness (+18.6%), limb discomfort (+44.0%) and pleasure (-32.2%) changed from interval 1–4, with significant differences (+21.8%, +11.3% and -31.3%, respectively) between HYP and NOR ($p < 0.01$). Slower interval running velocities in hypoxia achieve similar heart rate and muscle oxygenation responses to those observed in normoxia when perceptually-regulated, yet at the expense of less favourable exercise-related sensations.

Key words

High-intensity intermittent running; normobaric hypoxia; perceptually-regulated exercise; ratings of perceived exertion; near-infrared spectroscopy; effort perception.

Introduction

High-intensity interval training (HIIT) is a popular exercise format in athletic and clinical populations (1,2). HIIT includes repeated short-to-long (2–5 min) intense exercise bouts (80–90% of the velocity associated with maximal oxygen uptake or vVO_{2Max}) interspersed with shorter (1–3 min) recoveries (3). Compared to moderate-intensity continuous running, HIIT leads to similar improvements in cardiorespiratory fitness that is achieved with a shorter effective exercise duration per session (2). Due to the reduced time-commitment and exercise training volume, investigations surrounding the potential physiological and performance benefits of HIIT have surged (4).

HIIT in normobaric hypoxia (a lower inspired oxygen fraction or FiO_2) is receiving attention for its potential in further advancing athletic performance compared to HIIT in normoxia. Buchheit et al. (5) employed a HIIT protocol (3 × 5-min, 90-s recovery) carried out in hypoxia (vVO_{2Max} = 84%; FiO_2 = 15.4%) and normoxia (vVO_{2MAX} = 90%) at a fixed-intensity (determined in normoxia) in highly-trained runners. A reduced physiological stress (i.e., lower heart rate or HR) was observed during hypoxia compared to normoxia, likely due to a lower vVO_{2Max} in hypoxia *versus* normoxia. However, fixed exercise intensities, regardless of environmental conditions, do not permit adjustments (i.e., increases or decreases of workload) during exercise to match the intensity target (i.e., vVO_{2MAX}). In turn, over-induced physiological stress may be counter-productive (i.e., greater deoxygenated muscle heamoglobin, lower oxygenated haemoglobin) for intended session goals (6). Furthermore, matched absolute fixed exercise intensities (i.e., a similar percentage of vVO_{2MAX}) lead to greater physiological stress (i.e., compensatory increase in HR) in hypoxia compared to normoxia due to reduced FiO_2 (7). Perceptually-regulated exercise intensities, that allow velocity adjustments based upon exercise-related sensations in order to maintain a target effort

level, may offer a viable solution, and is perhaps more reflective of how exercisers modify intensity during acute exercise.

Perceptually-regulated exercise permits the individual exercising to self-regulate external workload (i.e., running velocity/cycling power production) based upon Borg's rating of perceived exertion (RPE) scale (8). The validity and usefulness of using RPE for perceptually-regulating exercise has been described (9). The reduced oxygen availability in hypoxia makes the expectation tenable that there would be a slower self-selected running velocity in hypoxia for a given RPE, while velocity in normoxia would be more preserved, as evidenced previously (10). Chacaroun et al. (11) demonstrated for a lower power output (-15%), *vastus lateralis* muscle deoxyhemoglobin was higher and oxyhemoglobin lower in hypoxia (FiO_2 = 13.5%) compared to normoxia during a single interval session (15 × 1-min at 75% of maximal HR, 1-min recoveries). Although HR was similar between conditions, RPE has been reported to be higher in hypoxia compared to normoxia during fixed-intensity interval runs (5) and repeated-sprint cycling (12). Employing self-paced exercise, in replace of fixed-intensity exercise, may assist in overcoming the over-excessive physiological stress observed when exercising in hypoxia *versus* normoxia, due to the likelihood of greater velocity preservations in the latter than the former.

In normoxia at pre-determined fixed intensities, HIIT is perceived as more enjoyable compared to moderate-intensity continuous running (13). However, during HIIT at fixed-intensities, exercise-related sensations decrease when the exercise intensity rises above threshold preference (14). Further, HIIT in hypoxia at fixed-intensities typically surpasses the preferred threshold in normoxia (15). Implementing a self-paced exercise model may permit modifications required (i.e., slower running velocities) to maintain exercise-related sensations contributing to RPE (16) in hypoxia and normoxia. Cyling continuously for 10 min at a fixed-intensity (corresponding to 50% VO_{2Max}) in hypoxia *versus* normoxia negatively impacts

cognitive function (17). Slower self-selected running velocities may assist with mitigating hypoxic-induced negative cognitive function compared to normoxia (18). These potential findings may benefit athletes exercising intensely in hypoxia, shortly followed by skills requiring attention and accuracy.

Therefore, the aim of this study was to investigate the effect of HIIT at a clamped RPE of 16 (typically used by athletes during HIIT) (19) in hypoxia and normoxia on adjustments in running velocity and associated exercise-related sensations of trained runners. We hypothesized that running velocity would be progressively slower in hypoxia compared to normoxia across intervals, whilst physiological and cognitive responses, and exercise-related sensations would not differ between conditions. Decreasing external load with matched internal load during perceptually-regulated HIIT in hypoxia compared to normoxia may benefit athletes during heavy training blocks prior to competition.

Methods

Participants

Nineteen trained runners (3 females, 16 males; age: 33.4 ± 9.1 years; height: 176 ± 88 cm; weight: 76.3 ± 10.9 kg) provided written informed consent to participate. Participants had no musculoskeletal injuries and met the following eligibility criteria: a training volume ≥6 h/wk, free of clinical signs of disease, orthopedic, neurological, cardiovascular or respiratory problems, and no hypoxic exposure >2000 m for >48 h 6 months before the study. The study was carried out in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Anti-Doping Lab Qatar institutional review board (Agreement SCH-ADL-170). A-priori sample size was calculated using G*Power (Version 3.1.9.3). This was

determined using published power output data by Jeffries et al. (20), whereby healthy individuals cycled at a perceptually-regulated intensity (RPE = 16) in hypoxic (FiO_2 = 15.0%) and normoxic conditions. Twenty-one participants were deemed sufficient to yield a power of 0.8 at an α probability of 0.05. Two individuals dropped out due to injuries sustained during their time enrolled onto the study, not associated with the HIIT protocols we employed.

Experimental design

Participants reported to the laboratory on three occasions, each separated by ≥48 h. The first session included study familiarisation. The second and third visits included completing a HIIT protocol in either hypoxia or normoxia in a randomized, conterbalanced order. Physiological, perceptual and cognitive responses were assessed continuously, immediately before and after each interval, and before and after the HIIT protocol, respectively. Participants were instructed to refrain from any intense exercise 48 h prior to each visit and consume their last meal at least 2 h prior to the HIIT sessions. To minimise the impact of social desirability bias, participants were made aware of the purpose of the study but were naïve to experimental hypotheses. Laboratory conditions were similar throughout all sessions (mean temperature ~22˚C, relative humidity ~50%) and time of day was standardized for each participant.

Familiarization session

At the preliminary visit to the laboratory, participants were familiarised with the perceptual scales and cognitive test. Preferred running velocity (PRV) was determined for each participant in normoxia using a modified version of identifying preferred walking speed (21). After a 5-min warm up at 10 km/h^{-1}, participants completed four ramped treadmill runs (increasing and decreasing velocities) on an instrumented treadmill (ADAL3D-WR, Medical Development–HEF Tecmachine, France). After every 20 s per ramp, participants rated their RPE of the current velocity (controlled by the investigator and out of sight of the participant) in accordance

with Borg's (20) 6 ("*no exertion at all*") – 20 ("*maximal exertion*") numeric scale. Ramp one started at 10 km/h^{-1}, increasing by 0.8 km/h^{-1} every 20 s until the velocity was considered as RPE ≥18; ramp two started at +1.5 km/h^{-1} the previous end velocity, decreasing by 0.8 km/h^{-1} until the velocity was considerd as RPE ≤12; ramp three started at the velocity considered as an RPE of 14 in ramp two, increasing by 0.5 km/h^{-1} until the velocity was considerd as RPE ≥18; and ramp four started at +1.0 km/h^{-1} the previous end velocity, decreasing by 0.5 km/h^{-1} until the velocity was considered as RPE ≤12. Ramps two, three and four began once the participants declared their perceived recovery level as a 7 out of 10 following the previous ramp (23). HR was recorded every 20-s through each ramp. PRV corresponded to the velocity participants considered as a RPE of 16 (between "*hard*" and "*very hard*") or closest to a HR of 160 bpm. After 10 min of rest, participants completed one 4-min interval composing the HIIT protocol (see below) for habituation.

Experimental trials

Participants completed two experimental trials in normoxia (NOR; FiO_2 = 20.9%) and hypoxia (HYP; FiO_2 = 15.0%, equivalent to ~2700 m above sea level). After a standardised warm up (5-min at 10 km/h^{-1}), a facemask connected to a portable hypoxic generator (See *Hypoxic simulation* section) was attached. Participants rested for 1-min (quiet standing) before a 1-min run at their PRV (RPE = 16). Participants then rested for 3 min before completing the HIIT protocol. The HIIT protocol was based upon aerobic interval-training (2). Participants completed four, 4-min intervals, interspersed with 3-min recoveries (quiet standing). The first 30 s of each 4-min interval began at participants' PRV; participants were then free to decide if or how treadmill velocity needed to be adjusted (manually by one experimenter) to ensure maintenance of a RPE of 16 every 30 s. Participants hand-signalled in response to the current velocity (finger up to increase, finger down to decrease, and circle using index finger and thumb

to maintain); and signalled again to inform how much of an increase/decrease in velocity is required [1, 2 or 3 fingers up (faster) or down (slower) for 0.5, 1.0 or 1.5 km/h^{-1} changes, respectively]. Signals were trialled during familiarisation. Mild verbal encouragement to keep running at an RPE of 16 was used throughout HIIT. Total hypoxic exposure corresponded to exactly 28 min.

Hypoxic simulation

Participants were fitted with a facemask fastened with a Velcro headset connected via plastic tubing to a hypoxic generator (Altitrainer, SMTec SA, Nyon, Switzerland) to simulate hypoxia. The gas mixing system enriches inspired air by adding a fixed quantity of nitrogen via a 30-L mixing chamber, with the dilution being constantly controlled by a PO_2 probe (precision = T0.82 torr, safety FiO_2 = 9.7%). The hypoxic generator was hidden from participant viewing to ensure condition blinding. When breathing 'normal air' during normoxia, the hypoxic generator was on (for background noise) and set at a simulated altitude of 100 m to increase the strength of blinding.

Measures

Exercise intervals

HR was monitored telemetrically with a Polar transmitter-receiver (Polar S810, Kempele, Finland) and recorded 20 s before and every 30 s during each interval. Arterial oxygen saturation (SpO_2) was assessed via finger pulse oximetery (Palmsat 2500, NONIN Medical Inc., Plymouth, MI, USA) at the same time intervals. HR and SpO_2 were obtained before (i.e., after a 2-min seated period) and at the end of the warm-up procedure (i.e., prior to HIIT). Both the HR watch (RS400, Polar) and oximeter receiver were attached on the handrails of the treadmill outside of the participants' view.

Muscle oxygenation trends of the right *vastus lateralis* muscle were recorded using near-infrared spectroscopy (NIRS; Portalite, Artinis, Netherlands) in real-time. A wireless bi-polar optode sensor was attached (~10 cm above the proximal patella border) and secured to skin via adhesive tape. Sampling frequency was set at 10 Hz (11) following a 'zero set' of all signals. Bandages were fastened around the lower limb and optode to prevent external light distorting readings. Oxy- (Δ; [O_2Hb]), deoxy- (Δ; [HHb]) and total haemoglobin (μmol; [tHb]) were exported (1 Hz). For analysis, each interval was averaged and normalized to a 10 s sample prior to interval one (reference value) for each respective condition and presented as percentage change.

During recovery

Perceived recovery and motivation to exercise were assessed 30 s before each interval. Perceived recovery was assessed by answering '*how recovered do you feel currently?*' via a numeric scale, ranging from 0 ("*very poorly recovered*") to 10 ("*very well recovered*") (23). Recovery was assessed before interval one to determine perceptions following the warm up. Perceived motivation to exercise was assessed via a 20-cm visual analog scale (24). Participants were asked '*how motivated do you feel to exercise right now?*' and answered by adjusting the level on the scale between 0 ("*extremely low*"; white colored) and 20 ("*extremely high*"; black colored). Immediately after each interval, ratings of perceived breathlessness, limb discomfort and pleasure were assessed. Perceived breathlessness was assessed by answering '*how does your breathing feel currently?*' via a numeric scale, ranging from 0 ("*nothing at all*") to 10 ("*very, very severe*") (25). Using the same scale, perceived limb discomfort was assessed by answering '*how do your legs feel currently?*'. A 20-cm visual analog scale (same as motivation above) was used to assess '*how pleasant was that run?*' ranging from 0 ("*extremely unpleasant*") and 20 ("*extremely pleasant*").

Pre- and post-exercise

A capillary blood sample taken from the fingertip was analyzed for blood lactate concentration ([La^+]) with the Lactate Pro (LT-1710, Arkray, Japan) portable analyzer before the warm-up and 2 min after HIIT. An offline Stroop colour-word test (26) assessed attention and executive function. Using one hand and as quickly as possible, participants selected the colored key on the keyboard representing the color of the text appearing on the screen (red, yellow, green or blue). The cognitive test lasted for 3 min, and took place in a silent environment before the warm up and 3 min after HIIT. Reaction time (ms; time taken to select a color) and accuracy (%; correct color selected) were averaged over each test for analysis.

Statistical analysis

Data distribution was assessed via a Shapiro-Wilk test. A parametric within-subject two-way analysis of variance was used to investigate the main effect of condition (NOR *vs*. HYP), time (interval 1, 2, 3 *vs*. 4 or pre *vs.* post) and the condition × time interaction for normally distributed data. Partial eta-squared (η^2) was calculated as a measure of effect size. Values of 0.01, 0.06 and above 0.14 were considered as small, medium and large, respectively (27). A related samples Friedman's non-parametric test was used for data not normally distributed. Bonferroni post-hoc pairwise comparisons were used to identify locations of significant effects. Statistical testing was carried out in SPSS (v21; CED, Cambridge, United Kingdom). Data was considered significant if $p \leq 0.05$. All data are presented as group means ± SD.

Results

Changes in velocity and HR

Compared to interval 1, participants adjusted to a progressively slower running velocity during intervals 2, 3 and 4 (-2.8%, -5.2% and -7.0%, respectively; $p < 0.01$), and more so in HYP *vs.* NOR for intervals 2, 3 and 4 (-4.6%, -6.4% and -7.9%, respectively; $p < 0.01$; Figure 1A). Compared to interval 1, HR increased during intervals 2, 3 and 4 (+2.3%, +3.6% and 4.8%, respectively; $p < 0.01$; Figure 1B), independently of condition ($p = 0.65$).

Changes in SpO_2 and muscle oxygenation

SpO_2 was globally lower in HYP *vs.* NOR (-9.3% average across intervals; $p < 0.01$; Figure 1C), independently of time ($p = 0.37$). From interval 1 to 4, [O_2Hb] and [tHb] decreased (-23.7% and -77.0%, respectively) whilst [HHb] increased (+44.9%; $p < 0.01$; Figures 2A–C), independently of condition ($p > 0.08$).

Changes in exercise-related sensations

Perceived recovery decreased progressively from interval 1 to 4 (-41.6%; $p < 0.01$), and more so in HYP *vs.* NOR before intervals 2, 3 and 4 (-8.8%, -24.2% and -29.3%, respectively; $p = 0.02$; Figure 3A). Perceived motivation decreased progressively from interval 1 to 4 (-21.8%; $p < 0.01$), and more so in HYP *vs.* NOR before intervals 3 and 4 (-20.3% and -22.4%, respectively; $p < 0.01$; Figure 3B). Compared to interval 1, perceived breathlessness increased following intervals 2, 3 and 4 (+14.0%, +13.6% and +18.6%, respectively; $p < 0.01$; Figure 3C), independently of condition. Breathlessness was rated globally higher in HYP *vs.* NOR (+21.8%; $p < 0.05$), irrespective of time. Compared to interval 1, perceived limb discomfort increased following intervals 2, 3 and 4 (+23.3%, +35.3% and +44.0%, respectively; $p < 0.01$; Figure 3D), independently of condition. Limb discomfort was rated globally higher in HYP *vs.* NOR (+11.3%; $p = 0.01$), irrespective of time. The time-dependent decreases in perceived pleasure across intervals (-14.7%, -25.4% and -32.3%, intervals 2, 3 and 4 *vs.* 1, respectively; $p < 0.01$; Figure 3E) tended to be larger in HYP *vs.* NOR (-31.3%, $p = 0.06$).

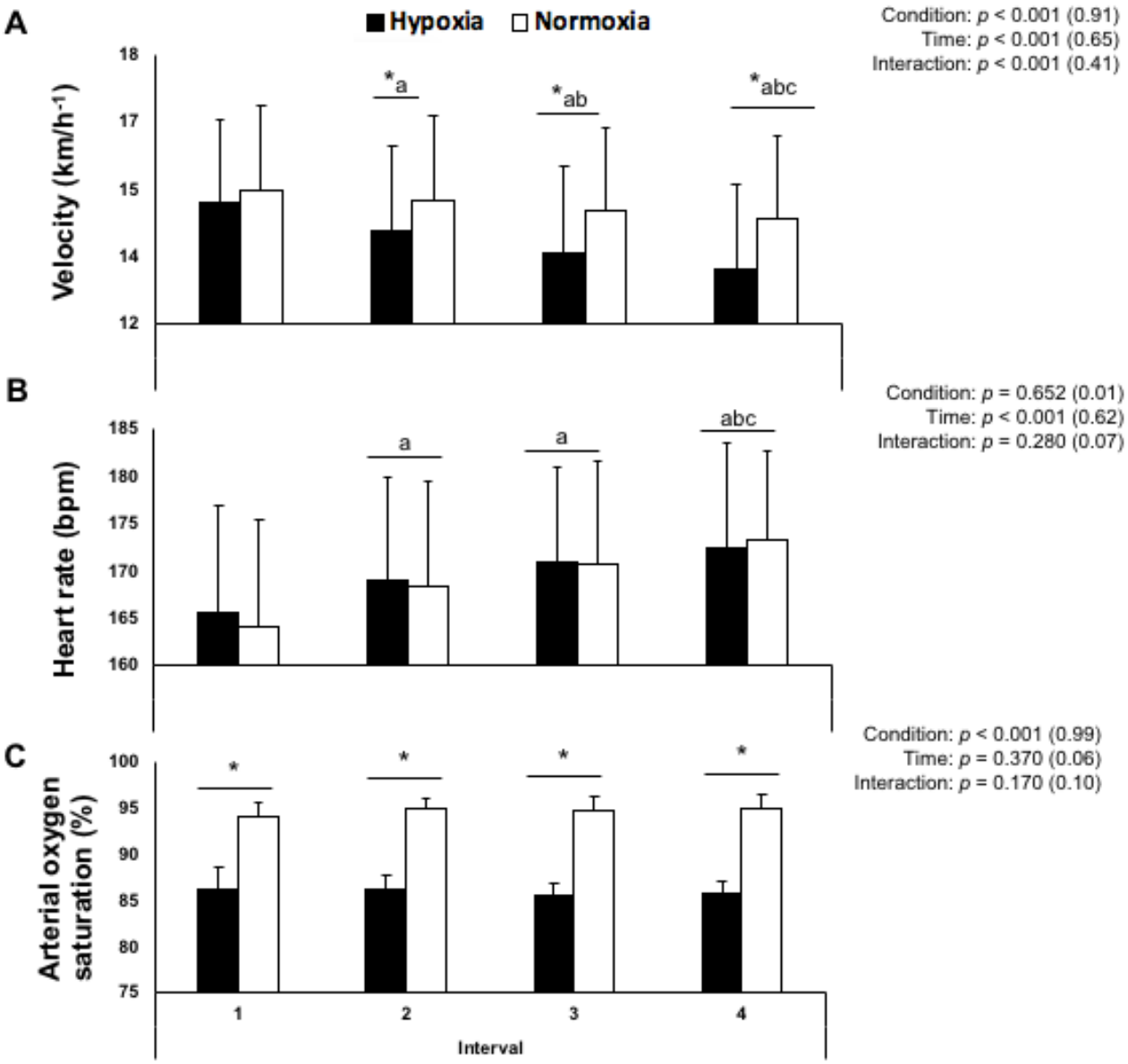

Figure 1 Changes in velocity (A), heart rate (B) and arterial oxygen saturation (C) during the high-intensity intermittent running protocol. Data are presented as mean ± SD. ANOVA main effects of time, condition and interaction are presented along with partial-eta squared for effect size into brackets. Black bars = hypoxic condition; white bars = normoxic condition. * denotes a statistically significant difference between conditions for a given interval ($p < 0.05$), a, b and c denotes a statistically significant difference vs. interval 1, 2 and 3, respectively ($p < 0.05$).

Changes in [La^+] and attention and executive function

The pre- to post-exercise increase in [La^+] was larger ($p = 0.001$) in HYP (1.7 ± 0.8 *vs*. 13.1 ± 3.8 mmol/l^{-1}) *vs.* NOR (2.1 ± 0.9 *vs*. 10.1 ± 3.9 mmol/l^{-1}). During the Stropp test, accuracy was unaffected by condition and time (Figure 4A). Participants' reaction time was faster (+11%) post *vs.* pre HIIT ($p < 0.01$; Figure 4B), independently of condition.

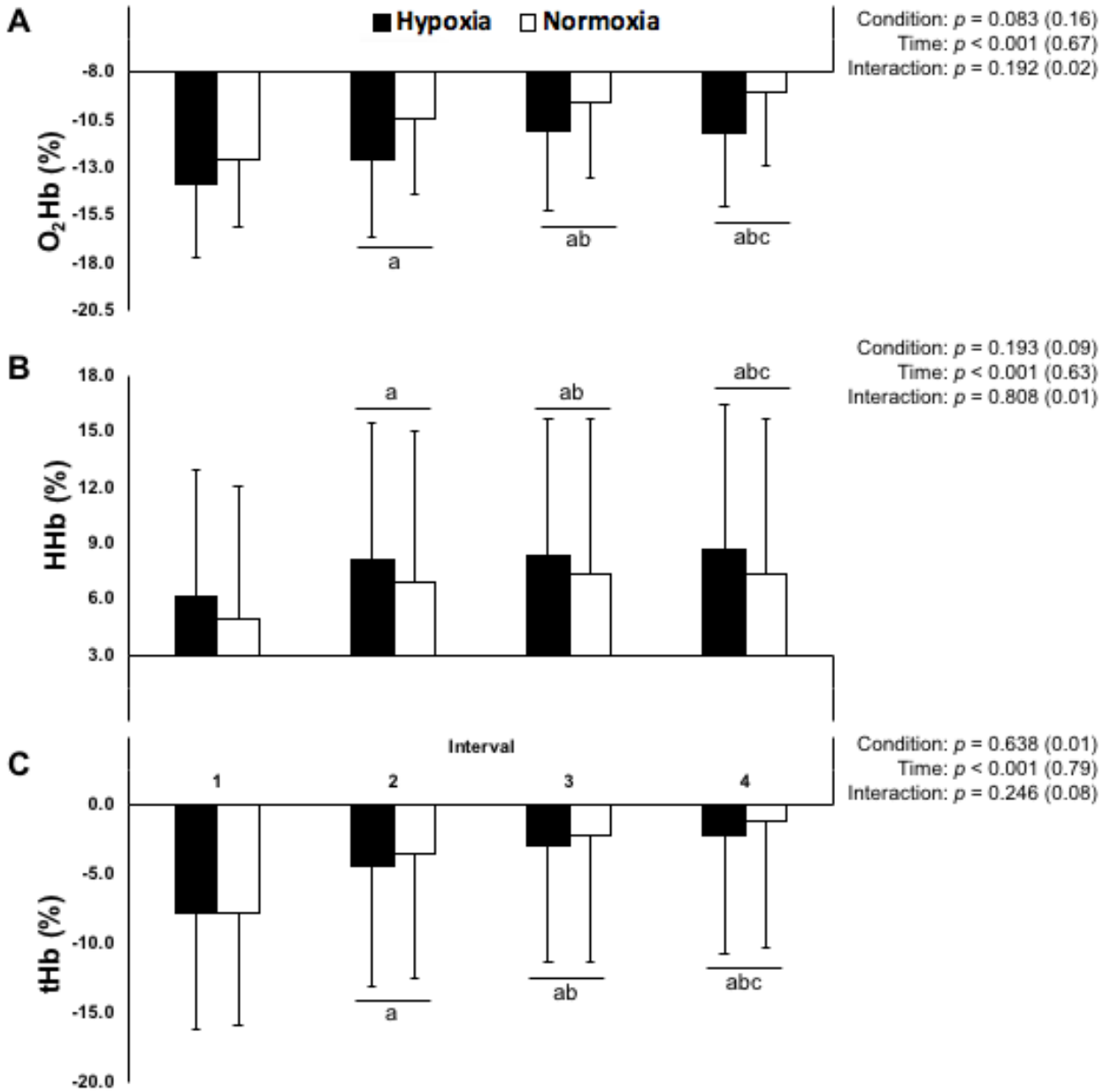

Figure 2 Changes in Oxygenated (A; O_2Hb), deoxygenated (B; HHb) and total hemoglobin (C; tHb) during the high-intensity intermittent running protocol. Data are calculated as a percentage difference from baseline (%) and presented as mean ± SD. ANOVA main effects of time, condition and interaction are presented along with partial-eta squared for effect size into brackets. Black bars = hypoxic condition; white bars = normoxic condition. a, b and c denotes a statistically significant difference vs. interval 1, 2 and 3, respectively ($p < 0.05$).

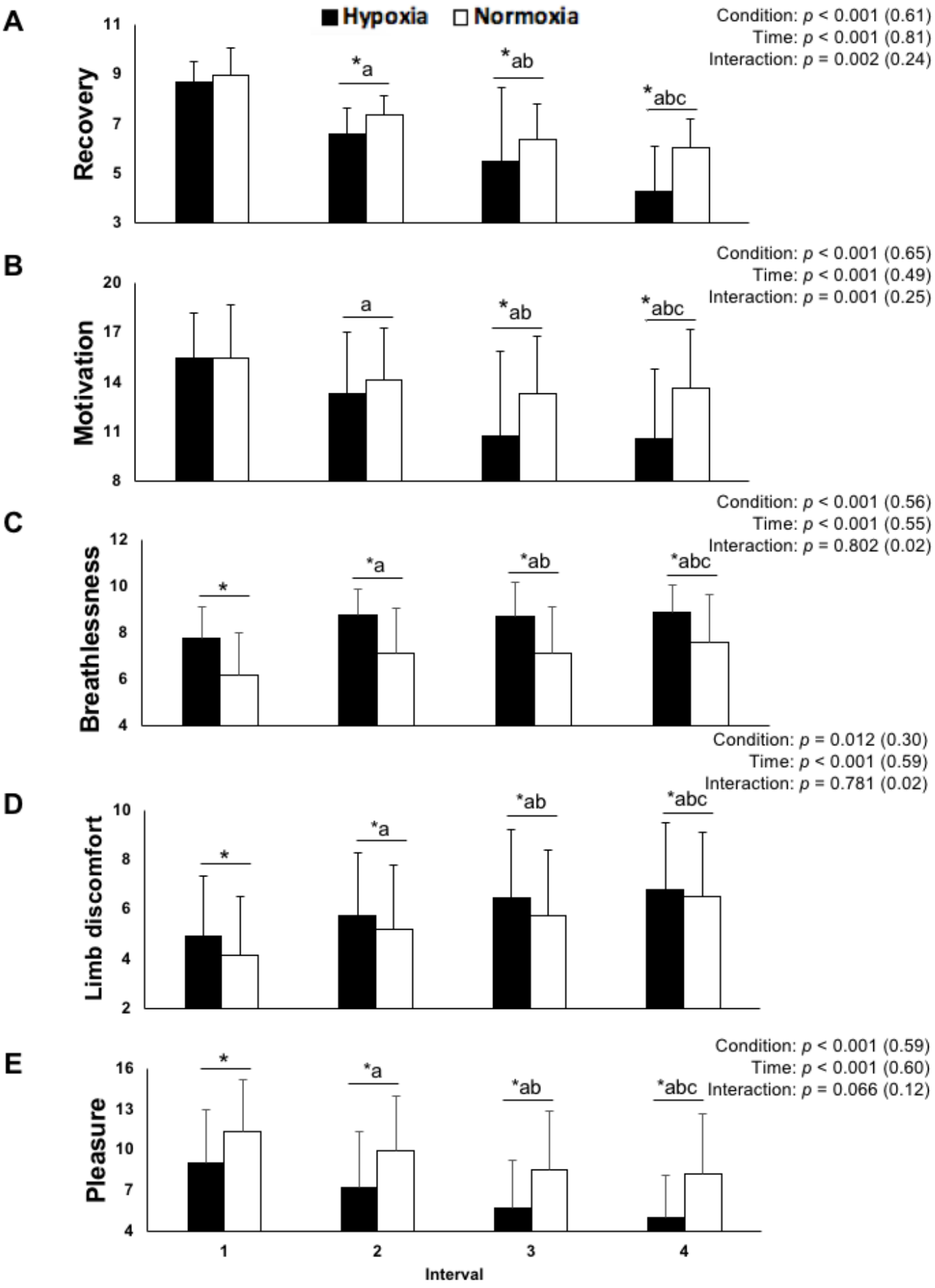
A
Hypoxia
Normoxia
Condition: p < 0.001 (0.61)
Time: p < 0.001 (0.81)
Interaction: p = 0.002 (0.24)
Recovery
11
9
7
5
3
*a
*ab
*abc
B
Condition: p < 0.001 (0.65)
Time: p < 0.001 (0.49)
Interaction: p = 0.001 (0.25)
Motivation
20
17
14
11
8
a
*ab
*abc
C
Condition: p < 0.001 (0.56)
Time: p < 0.001 (0.55)
Interaction: p = 0.802 (0.02)
Breathlessness
12
10
8
6
4
*
*a
*ab
*abc
D
Condition: p = 0.012 (0.30)
Time: p < 0.001 (0.59)
Interaction: p = 0.781 (0.02)
Limb discomfort
10
8
6
4
2
*
*a
*ab
*abc
E
Condition: p < 0.001 (0.59)
Time: p < 0.001 (0.60)
Interaction: p = 0.066 (0.12)
Pleasure
16
13
10
7
4
*
*a
*ab
*abc
1
2
3
4
Interval

Figure 3 Changes in perceived recovery (A), motivation (B), breathlessness (C), limb discomfort (D) and pleasure (E) during the high-intensity intermittent running protocol. Data are presented as mean ± SD. ANOVA main effects of time, condition and interaction are presented along with partial-eta squared for effect size into brackets. Black bars = hypoxic condition; white bars = normoxic condition. * denotes a statistically significant difference between conditions for a given interval ($p < 0.05$), a, b and c denotes a statistically significant difference vs. interval 1, 2 and 3, respectively ($p < 0.05$).

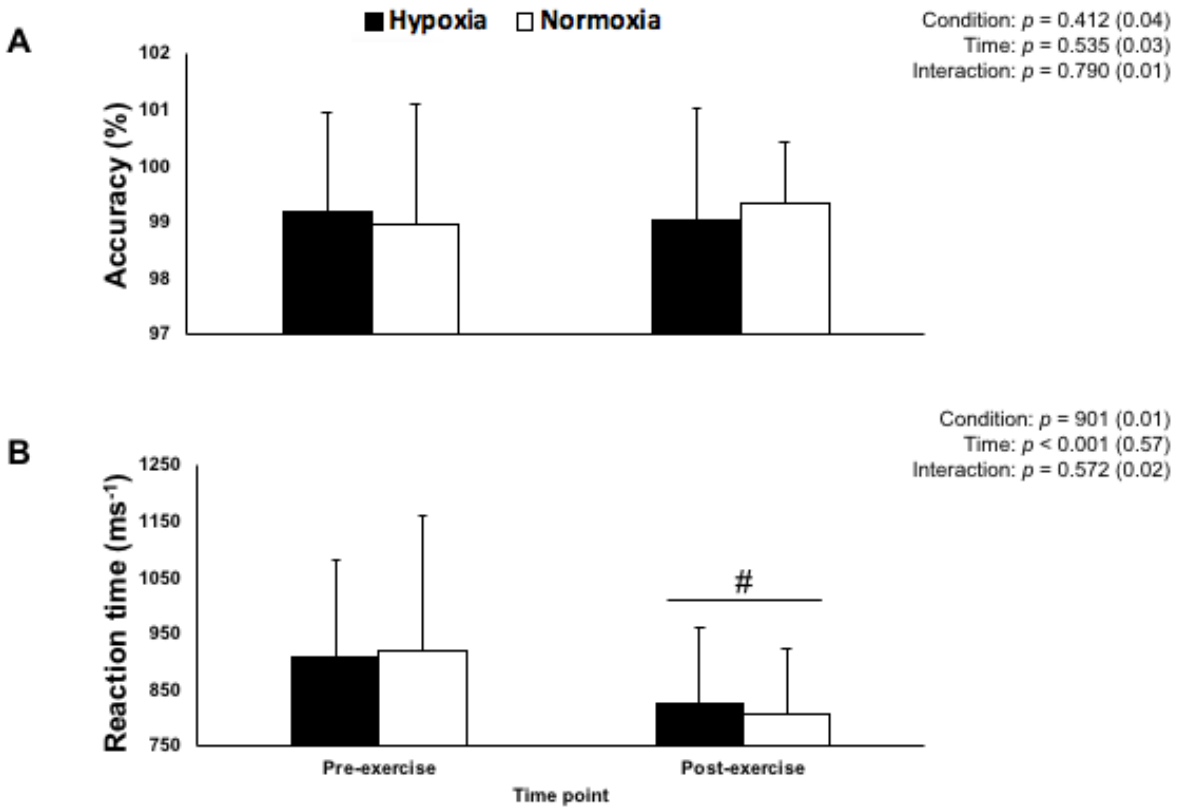

Figure 4 Changes in accuracy (A) and reaction time (B) pre and post high-intensity intermittent running protocol. Data are averaged over 3 mins and presented as mean ± SD. ANOVA main effects of time, condition and interaction are presented along with partial-eta squared for effect size into brackets. Black bars = hypoxic condition; white bars = normoxic condition. # denotes a statistically significant difference vs. pre-exercise ($p < 0.01$).

Discussion

Using a perceptually-regulated (RPE = 16) exercise model, we observed: 1) participants ran progressively slower during HIIT with larger decreases in HYP *versus* NOR, 2) HR and muscle oxygenation trends (during intervals) and cognitive responses (pre *vs*. post HIIT) were similar between conditions, 3) greater breathlessness and limb discomfort, and lower recovery,

motivation and pleasure scores were stated during recovery between HYP *vs.* NOR, and 4) blood lactate concentration was larger after HYP *vs.* NOR. Overall, using a manipulation of oxygen availability, reduced external workload (i.e., running velocity) during perceptually-regulated interval running is associated with a similar internal load (i.e., physiological responses). Although no cognitive function differences were found between conditions, this is achieved with less favourable exercise-related sensations. A matched internal workload for a decreased external workload during perceptually-regulated HIIT in hypoxia *versus* normoxia may assist athletes to reach intended session goals with minimal over-induced physiological stress. However, perceptually-regulated HIIT exacerbates exercise-related sensations and blood lactate concentrations in hypoxia compared to normoxia. This may then have negative carry-over effects on training responsiveness in the following days.

Exercise intervals

The velocity deemed equal to RPE 16 (PRV) was as expected for trained runners (~15 km/h^{-1}) (28). Interestingly, running velocity did not differ between conditions during the first HIIT interval, despite lower SpO_2 in hypoxia *versus* normoxia. Smith & Billaut (29) found maintained SpO_2 during repeated-sprinting in normoxia (20 × 5-s all out, 25-s recovery) until after the fifth sprint in national-level soccer players, whereby peak power significantly decreased compared to sprint one. Overall, it seems that initial decreases in SpO_2 (within interval one) do not necessarily impact on HIIT compared to sprint intervals.

We found that participants selected a progressively slower running velocity during HIIT in both conditions. In highly-trained middle to long-distance runners, a 6% reduction in vVO_{2MAX} when running in hypoxia *versus* normoxia is acceptable to match the acute physiological stress induced (5). It can be suggested that self-selected velocity adjustments found in the current study to maintain RPE 16 are matched with modifications in hypoxic *versus* normoxic traning

sessions employed by coaches and sport scientists for athletes (30). Decreased external workloads have been reported by Pramsohler et al. (31) during continuous cycling (seven 30-min sessions over 3-wk), whereby participants cycled at -28% lower power output in hypoxia (FiO_2 = 15.3%) *versus* normoxia for a similar HR. Differences in these findings and ours may be due to the inclusion of geriatric patients completing pre-set (in normoxia) fixed-intensity cycling compared to trained runners self-regulating HIIT in the current study. However, Fernández-Menéndez et al. (10) reported preferred walking velocity (RPE of 10) in hypoxia (FiO_2 = 15.3%) was 7% slower than normoxia in obese adults over 3 weeks. Using a self-paced model, irrespective of RPE target, population demographics and training block duration, lower external workloads are selected in hypoxia compared to normoxia. Overall, decreases in self-paced running velocity occured to a greater extent in hypoxia than normoxia to maintain RPE 16, suggesting of a lower external workload. This finding may be of benefit to athletes who are unable or advised by their coach not to be training at a full intensity. Completing perceptually-regulated HIIT in hypoxia that requires slower running velocities compared to normoxia may in turn minimise mechanical constraints and eventually injury risk.

Our data show HR increased progressively during HIIT, irrespective of condition. This matches our hypothesis that HR will be comparable between hypoxia and normoxia, even though running velocity was lower in hypoxia. Other studies employing moderate continuous-intensity exercise have also found matched HR responses between hypoxic and normoxic training interventions (~4 weeks) when cycling at a -21.0% power output in healthy males (32) and walking/running at a -17.5% velocity in obese adults (33) in hypoxia *verus* normoxia. Although exercise intensities in these studies were fixed, we believe similar increases in HR between conditions occur due to the environmental stressor (hypoxia) augmenting autonomic cardiac regulation (34). Overall, it seems self-paced exercise in hypoxia provides an added

environmental stressor that is able to mimick HR responses in normoxia for a lower external load.

Lower [O_2Hb] and [tHb], and greater [HHb] of the *vastus lateralis* were recorded across HIIT, irrespective of condition. Decreases in [O_2Hb] and increases in [HHb] were expected during HIIT as oxygen delivery is outweighed by utilisation, whilst decreases in [tHb] reflect a lower localised blood flow (35). Active musculature oxygenation is negatively impacted during fixed-intensity exercise in hypoxia compared to normoxia due to a lower FiO_2 (7). In support of this, Chacaroun et al. (11) reported lower [O_2Hb] and greater [HHb] with maintained [tHb] of the *vastus lateralis* during fixed, relative high-intensity cycling in hypoxia (85% maximal power output in normoxia; FiO_2 = 13.5%) *versus* normoxia. Where we employed a self-paced exercise model, similar [O_2Hb] and [HHb] responses are achieved between conditions. This is likely explained through the decreased workload (i.e., slower running velocity) in hypoxia compared to normoxia, subsequently lowering oxygen utilisation. Discrepants findings in [tHb] may be due to different exercise modalities (cycling *versus* running) modifying blood flow regulation (36). Similar to HR responses (central) previously discussed, it can be suggested here that local (tissue oxygenation) physiological stress is matched between conditions during HIIT in hypoxia at a slower velocity compared with normoxia.

Elevations in [La^+] following HIIT were higher in HYP than NOR. Values in the current study (10–13 mmol/l^{-1}) are somewhat higher than those (5–6 mmol/l^{-1}) reported elsewhere following a single HIIT session (6 × 4-min intervals at a RPE ~17, 4-min recoveries) (19). This maybe due to a 1:0.75 work:rest ratio implemented during our protocol compared to 1:1 employed by Seiler & Sjursen (19). [La^+] normalization during shorter recovery periods may not occur to the extent following longer recovery periods due to excess pyruvate accumulation (37). This suggests that HIIT in hypoxia *per se* leads to increased [La^+] at slower running velocities compared to normoxia for similar physiological stress amounts. Practitioners should be aware

that perceptually-regulated HIIT in hypoxia is a viable method for matching indices of physiological stress to normoxia. However, the blood lactate concentration increases after exercise were larger in hypoxia compared to normoxia. This may have negative implications on the muscle fatigue recovery process.

During recovery

Perceptual responses to HIIT were negatively impacted (i.e., lower recovery, and motivation) when assessed before intervals, with further exacerbations in hypoxia. Participants were instructed to maintain a RPE of 16 throughout HIIT by adjusting their velocity where necessary. It might be surprising at first that perceptual responses were worse in hypoxia compared to normoxia. However, perceived recovery and motivation are important affects associated with exercise intensity regulation (38). Our results indicate that hypoxia negatively impacts these affects during HIIT compared with normoxia. This may be explained through lower perceived capabilities of hypoxic HIIT completion over normoxia (39), lowering perceived recovery and motivation. Further, it could be postulated that cerebral deoxygenation was greater during HIIT in hypoxia *versus* normoxia, as demonstrated by Subudhi et al. during incremental cycling (40, 41). Accordingly, cerebral deoxygenation during HIIT may contribute to an integrative decision regarding negative perceptions, in which hypoxia hastens this effect (41). Given that the perceptually-regulated exercise model is governed centrally, this may provide a potential explanation as to why exercise-related sensations were more elevated in the hypoxic trial. Overall, our data poses a disconnection between RPE and exercise-related sensations (i.e., recovery and motivation). Further research should look to optimise HIIT in hypoxia for positive perceptual responses.

Perceptual responses after intervals were negatively impacted (i.e., higher breathlessness and limb discomfort, lower pleasure), and to a further extent in hypoxia than normoxia. Buchheit

et al. (5) reported that 3-min absolute-intenxity running intervals (84% vVO_{2MAX}) in hypoxia (FiO_2 = 15.4%) led to larger perceived limb discomfort compared to a lower absolute intensity in normoxia (90% vVO_{2MAX}). We expected exercise-related sensations to be similar between conditions as parcipants could adjust their velocity where necessary. However, this was not the case. Similar responses have been shown elsewhere (42), with greater perceived overall discomfort, breathlessness and limb discomfort following progressive, sub-maximal, self-paced cycling intervals (RPE = 3; modified CR10 Borg scale) in hypoxia (FiO_2 = 13.0%) compared to normoxia at a similar power output. Perceived breathlessness, limb discomfort and pleasure are exercise-related sensations contributing to overall RPE during exercise (16). However, there is a detachment between these when immediately assessed after HIIT intervals. We suggest that self-paced HIIT in hypoxia leads to unfavourable exercise-related sensations before and after running intervals, compared to normoxia.

Pre- and post-exercise

During the Stroop test, alertness increased (i.e., faster reaction time) whilst accuracy was maintained following HIIT, irrespective of condition. It is well known that HIIT in normoxia generally increases cognitive performance *versus* rest (i.e., faster reaction time, better accuracy) (43). However, during fixed-intensity exercise in hypoxia, cognitive performance (i.e., attention and executive function) is worsened compared to normoxia (17,18). We report that even though exercise-related sensations were worsened during HIIT, cognitive performance (assessed post-HIIT) was not negatively affected. Ochi et al. (18) reported decreased Stroop performance 15 mins after 10 mins of moderate-continuous intensity exercise (50% peak oxygen uptake) in hypoxia (FiO_2 = 13.5%) *versus* normoxia. Our results likely differ to the aforementioned study due to cognitive testing performed in normoxia and following different exercise modalities. Our data show that alertness is increased following HIIT, and not negatively impacted by hypoxia.

Limitations and perspectives

During self-paced exercise at a perceptually-regulated intensity in hypoxia, HR and muscle oxygenation responses are similar to normoxia for a lower running velocity. However, we used a single "hypoxic dose" (i.e., hypoxic severity and duration), target RPE and exercise duration during HIIT. Further investigations should refine self-selected protocols in hypoxia, such as the "hypoxic dose", target RPE and exercise duration to minimise the negative side effects of worsened exercise-related sensations found under the present circumstances. In addition, whether there are gender differences in response to hypoxic exposure during perceptually-regulated HIIT should be investigated, given that our final sample size (n = 19) included only three females.

Conclusion

When carrying out HIIT at a perceptually-regulated intensity (RPE equal to 16), larger running velocity decreases are needed in hypoxia than normoxia. This is accompanied by similar physiological stress (i.e., HR and muscle oxygenation) during HIIT, and cognitive function adjustments after. In hypoxia, exercise-related sensations and blood lactate concentrations were higher-than-normal with larger peripheral oxygen desaturation. Overall, perceptually-regulated running velocity in hypoxia compared to normoxia may be an effective alternative, at the expense of less favourable exercise-related sensations. Our results suggest that athletes under the influence of hypoxia require lower external workloads to reach a perceptually-regulated target during HIIT than normoxia. If employed in a practical setting, coaches should consider the potential of negatively implicated exercise-related sensations and blood lactate concentrations which may have further negative carry-over effects on training responsiveness in the following days.

Acknowledgements

The authors would like to thank the Sport and Exercise Science Research Centre of London South Bank University for a travel bursary and Dr. Sebastien Racinais of ASPETAR for accommodating Liam Hobbins. This work was supported by Qatar National Research Fund (grant number: NPRP 4–760–3–217).

Conflict of interest

The authors have no conflicts of interest or financial ties to disclose and no current or past relationship with companies or manufacturers who could benefit from the results of the present study.

References

1. Zois, J., Bishop, D. and Aughey, R., High-intensity warm-ups: effects during subsequent intermittent exercise. Int J Sports Phys Perf. 2015;10(4):498-503.
2. Gibala, M. J., Gillen, J. B. and Percival., M. E. Physiological and health-related adaptations to low-volume interval training: influences of nutrition and sex. Sports Med. 2014;44.2: 127-137.
3. Buchheit, M. and Laursen, P. B. High-intensity interval training, solutions to the programming puzzle. Sports Med. 2013;43(10):927-954.
4. Gillen, J. B. and Gibala, M. J. Is high-intensity interval training a time-efficient exercise strategy to improve health and fitness? App Phys Nutr Met. 2013;39(3):409-412.
5. Buchheit, M., Kuitunen, S., Voss, S. C., Williams, B.K., Mendez-Villanueva, A. and Bourdon, P.C. Physiological strain associated with high-intensity hypoxic intervals in highly trained young runners. J Strength Cond Res. 2012;26(1):94-105.
6. Laurent, C. M., Vervaecke, L. S., Kutz, M. R. and Green, J. M., Sex-specific responses to self-paced, high-intensity interval training with variable recovery periods. J Strength Cond Res. 2014;28(4):920-927.
7. Heinonen, I. H., Boushel, R. and Kalliokoski, K. K. The circulatory and metabolic responses to hypoxia in humans–with special reference to adipose tissue physiology and obesity. Front Endo. 2016;7:116.
8. Parfitt, G., Blisset, A., Rose, E. A. and Eston, R. Physiological and perceptual responses to affect-regulated exercise in healthy young women. Psychophysiology. 2012;49(1):104-110.
9. Hardy, C. J. and Rejeski, W. J. Not what, but how one feels: The measurement of affect during exercise. J Sport Exerc Psych. 1989;11(3):304-317.

10. Fernández Menéndez, A., Saudan, G., Sperisen, L., Hans, D., Saubade, M., Millet, G.P. and Malatesta, D. Effects of Short-Term Normobaric Hypoxic Walking Training on Energetics and Mechanics of Gait in Adults with Obesity. Obesity. 2018;26(5):819-827.
11. Chacaroun, S., Gonzalez, I. V. E., Flore, P., Doutreleau, S. and Verges, S. Physiological responses to hypoxic constant-load and high-intensity interval exercise sessions in healthy subjects. Euro J App Phys. 2018;1-12.
12. Brocherie, F., Millet, G. P., & Girard, O. Psychophysiological responses to repeated-sprint training in normobaric hypoxia and normoxia. International J of Sports Phys Perform. 2017;12(1):115-123.
13. Thum, J., Parsons, G., Whittle, T., & Astorino, T. (2017). High-intensity interval training elicits higher enjoyment than moderate intensity continuous exercise. PloS one. 2017;12(1):e0166299.
14. Lind, E., Joehns-Matre, R. R., and Ekkekakis, P. What intensity of physical activity do previously sedentary middle-aged women select? Evidence of a coherent pattern from physiological, perceptual and affective markers. Prev Med. 2005;40:407–419.
15. Friedmann, B., Bauer, T., Menold, E. and Bärtsch, P. Exercise with the intensity of the individual anaerobic threshold in acute hypoxia. Med Scie Sports Exerc. 2004;36(10):1737-1742.
16. Abbiss, C. R., Peiffer, J. J., Meeusen, R. and Skorski, S. Role of ratings of perceived exertion during self-paced exercise: what are we actually measuring? Sports Med. 2015;45(9):1235-1243.
17. Ochi, G., Yamada, Y., Hyodo, K., Suwabe, K., Fukuie, T., Byun, K., Dan, I. and Soya, H. Neural basis for reduced executive performance with hypoxic exercise. Neuroimage. 2018;171:75-83.

18. McMorris, T., Hale, B. J., Barwood, M., Costello, J. and Corbett, J. Effect of acute hypoxia on cognition: A systematic review and meta-regression analysis. Neuro Biobehavioral Revs. 2017;74:225-232.
19. Seiler, S. and Sjursen, J. E. Effect of work duration on physiological and rating scale of perceived exertion responses during self-paced interval training. Scand J Med Sci Sports. 2004;14(5):318-325.
20. Jeffries, O., Patterson, S. D., & Waldron, M. The effect of severe and moderate hypoxia on exercise at a fixed level of perceived exertion. Euro J App Phys. 2019;1-12.
21. Martin, P. E., Rothstein, D. E., Larish, D. D. Effects of age and physical activity status on the speed-aerobic demand relationship of walking. J Appl Phys 1992;73:200–206.
22. Borg, G. A. V. Perceived exertion as an indicator of somatic stress. Scand J Rehab Med. 1970;2:92-98.
23. Laurent, C.M., Green, J. M., Bishop, P. A., Sjökvist, J., Schumacker, R. E., Richardson, M. T. and Curtner-Smith, M. A practical approach to monitoring recovery: development of a perceived recovery status scale. J Strength Cond Res. 2011;25(3):620-628.
24. Crewther, B. T., Carruthers, J., Kilduff, L. P., Sanctuary, C. E. and Cook, C. J. Temporal associations between individual changes in hormones, training motivation and physical performance in elite and non-elite trained men. Bio Sport. 2016;33(3):215.
25. Ward, S. A. and Whipp, B. J. Effects of peripheral and central chemoreflex activation on the isopnoeic rating of breathing in exercising humans. J Phys. 1989;411(1):27-43.
26. Stroop, J. R. Studies of interference in serial verbal reactions. J Exp Psychol. 1935;18:643-662.
27. Cohen, J. Statistical power analysis for the behavioral sciences, 2nd ed. 1988. New Jersey: Lawrence Erlbaum Associates.

28. da Silva, D. F., Simões, H. G. and Machado, F. A., vVO2max versus Vpeak, what is the best predictor of running performances in middle-aged recreationally-trained runners?. Science & Sports. 2015;30(4):e85-e92.

29. Smith, K. J. and Billaut F. Influence of cerebral and muscle oxygenation on repeated-sprint ability. Eur J Appl Physiol. 2010;109(5):989-99

30. Dufour, S. P., Ponsot, E., Zoll, J., Doutreleau, S., Lonsdorfer-Wolf, E., Geny, B., Lampert, E., Fluck, M., Hoppeler, H., Billat, V. and Mettauer, B. Exercise training in normobaric hypoxia in endurance runners. I. Improvement in aerobic performance capacity. J App Phys. 2006;100(4):1238-1248.

31. Pramsohler, S., Burtscher, M., Faulhaber, M., Gatterer, H., Rausch, L., Eliasson, A. and Netzer, N. C. Endurance Training in Normobaric Hypoxia Imposes Less Physical Stress for Geriatric Rehabilitation. Front Phys, 2017;8:514.

32. Haufe, S., Wiesner, S., Engeli, S. et al. Influences of normobaric hypoxia training on metabolic risk markers in human subjects. Med Sci Sports Exerc. 2008;40(11):1939–1944.

33. Wiesner, S., Haufe, S., Engeli S, et al. Influences of normobaric hypoxia training on physical fitness and metabolic risk markers in overweight to obese subjects. Obesity (Silver Spring). 2010;18(1):116–120.

34. Krejčí, J., Botek, M. and McKune, A.J., 2018. Dynamics of the heart rate variability and oxygen saturation response to acute normobaric hypoxia within the first 10 min of exposure. Clin Phys Funct Imag. 2018;38(1):56-62.

35. Van Beekvelt, M. C., Colier, W. N., Wevers, R. A., Van Engelen, B. G. Performance of near-infrared spectroscopy in measuring local O_2 consumption and blood flow in skeletal muscle. J Appl Physiol. 2001;90:511–519.

36. Joyner, M. J. and Casey, D. P. Regulation of increased blood flow (hyperemia) to muscles during exercise: a hierarchy of competing physiological needs. Phys Revs. 2015;95(2):549-601.

37. Howlett, R. A., Heigenhauser, G. J., Hultman, E., Hollidge-Horvat, M. G. and Spriet, L. L. Effects of dichloroacetate infusion on human skeletal muscle metabolism at the onset of exercise. Am J Phys Endo Met. 1999;277(1):E18-E25.

38. Renfree, A., Martin, L., Micklewright, D., and Gibson, A. S. C. Application of decision-making theory to the regulation of muscular work rate during self-paced competitive endurance activity. Sports Med. 2014;44:147–158.

39. Stork, M. J., Gibala, M. J. and Martin, K. G. Psychological and Behavioral Responses to Interval and Continuous Exercise. Med Scie Sports Exerc. 2018;50(10):2110-2121.

40. Subudhi, A. W., Dimmen, A. C., & Roach, R. C. Effects of acute hypoxia on cerebral and muscle oxygenation during incremental exercise. J App Phys. 2007;103(1):177-183.

41. Subudhi, A. W., Miramon, B. R., Granger, M. E., & Roach, R. C. Frontal and motor cortex oxygenation during maximal exercise in normoxia and hypoxia. J App Phys. 2009;106(4):1153-1158.

42. Christian, R. J., Bishop, D., Girard, O., & Billaut, F. The role of sense of effort on self-selected cycling power output. Front in Phys. 2014;5:115.

43. Lambourne, K. and Tomporowski, P. The effect of exercise-induced arousal on cognitive task performance: a meta-regression analysis. Brain Res. 2010;1341:12-24.