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4 **Comments from the editors and reviewers:**

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6 **Reviewer 0**

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8 **General** **comments**

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

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

16
17 **Specific** **comments**

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

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

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

28
29 Authors' response: We thank the reviewers for this comment and have subsequently added the
30 age of the runners who participated in this study. An explanation regarding the absence of a
31 VO₂MAX assessment is provided below.

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33
34 P2 L4 – Nineteen **trained** runners (**33.4 ± 9.1 years**) completed a...

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

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42
43 Authors' response: We acknowledge the reviewers comment that 'HIIT' is a more conventional
44 acronym that 'HIIR', and have replaced the latter with the former throughout the manuscript.

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

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63 Authors' response: We thank the reviewer for highlighting this comment and have
64 subsequently added in further information regarding the time efficiency of HIIT compared to
65 MICT.
66

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68 P4 L5-8 – Compared to moderate-intensity continuous running, **HIIT** leads to similar
69 improvements in cardiorespiratory fitness **that is achieved with a shorter effective exercise**
70 **duration** per session (2). Due to the reduced time-commitment and **exercise** training volume...
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75 Reviewer: Line 25: and it could be argued that these perceptually regulated bouts better mirror
76 how exercisers actually choose to modify intensity during acute exercise.
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79 Authors' response: We thank the author for suggesting this important point, and have
80 subsequently added this information to the manuscript.
81

82 P5 L25-26 – ... offer a viable solution, **and is perhaps more reflective of how exercisers**
83 **modify intensity during acute exercise.**
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88 Reviewer: Lines 32-34: I am not familiar with this study, but exercise at 75 %HRmax does not
89 meet the criteria of Weston et al. (2014) designating HIIT of > 85 %HRmax.
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91
92 Authors' response: We thank the reviewer for highlighting the required percentage of maximal
93 heart rate for exercise to be considered as a high-intensity. According to Weston et al. (2014),
94 this does not classify the exercise employed by Chacaroun et al. (2018) as high-intensity the
95 reviewer suggests. However, Chacaroun et al. (2018) compared continuous (30 mins) and
96 interval (1 min on, 1 min off) cycling in hypoxic (clamped SpO₂ = 75%) and normoxic
97 conditions at a similar absolute heart rate (75% of max). The authors make reference to a
98 position stand from the ACSM (1998), highlighting that 75% of maximal heart rate is
99 recommended for continuous exercise. Therefore, although this intensity may not be aligned
100 with the more recent work of Weston et al. (2014), the intensity employed and findings of
101 Chacaroun et al. (2018) support our rationale. As such, we have not made any changes to the
102 current manuscript.
103
104

105
106 ACSM. The recommended quantity and quality of exercise for developing and maintaining
107 cardiorespiratory and muscular fitness, and flexibility in healthy adults. MSSE.
108 1998;30(6):975-991.
109

110
111 Chacaroun, S., Gonzalez, I. V. E., Flore, P., Doutreleau, S. and Verges, S. Physiological
112 responses to hypoxic constant-load and high-intensity interval exercise sessions in healthy
113 subjects. Euro J App Phys. 2018:1-12.
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123 Weston, K. S., Wisløff, U., & Coombes, J. S. High-intensity interval training in patients with
124 lifestyle-induced cardiometabolic disease: a systematic review and meta-analysis. Br J Sports
125 Med. 2014;48(16):1227-1234.
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130
131 Reviewer: Line 40: remember that the Bartlett et al. study that you cite here was in men with
132 VO₂max well above 55 mL/kg/min, so these results poorly generalize to the typical adult.
133

134 Authors' response: We thank the reviewer for highlighting the work we cite by Bartlett et al.
135 (2011) includes a participant cohort with a relatively high VO₂MAX, which may not be
136 representative of adults within the general population. As such, we have since replaced this
137 reference with a study comparing HIIT and continuous exercise (Thum et al., 2017). These
138 authors conclude that HIIT is more enjoyable in active males and females with a more
139 representative VO₂MAX of the general population (41.4 ± 4.1 mL/kg/min) (Thum et al., 2017).
140
141

142 P26 L447-449 – [Thum, J., Parsons, G., Whittle, T., & Astorino, T. \(2017\). High-intensity
143 interval training elicits higher enjoyment than moderate intensity continuous exercise.
144 PloS one. 2017;12\(1\):e0166299.](#)
145
146

147 Bartlett, J. D., Close, G. L., MacLaren, D. P. M., Gregson, W., Drust, B., Morton, J. P. High
148 intensity-interval running is perceived to be more enjoyable than moderate intensity continuous
149 exercise: implications for exercise adherence. J Sports Sci. 2011; 29:547–553.
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154 Reviewer: Please fix the typos in lines 44-45; thank you. Also, this text does not lay a solid or
155 clear foundation for this text referring to cognitive function, breathlessness, reaction time, etc.
156 as currently written. This information just appears here with little transition text to relate this
157 particular topic to the current study—please rewrite this text here to better denote the
158 importance or relevance of cognitive function, breathlessness, motivation, etc.
159
160

161 Authors' response: We thank the reviewer for pointing out the spelling errors in the manuscript
162 and these have been corrected accordingly. Cognitive function is usually decreased when
163 assessed in hypoxic conditions, or shortly after exercise at a relative, fixed-intensity in hypoxia,
164 compared to normoxia (McMorris et al., 2017). Similarly, exercise-related sensations are at a
165 premium during maximal repeated sprints in hypoxia compared to normoxia (Brocherie et al.,
166 2017). Therefore, the importance of our work relates to attempting to incorporate a
167 perceptually-regulated exercise intensity to compensate for the negative influence hypoxia has
168 on fixed-intensity exercise versus normoxia, denoted via defects in cognitive function and
169 exercise-related sensations. We have re-written the section highlighted by the reviewer to better
170 explain the transition into exercise-related sensations and cognitive function.
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174 P5 L47-P6 L51 – ... to [maintain](#) exercise-related sensations [contributing](#) to RPE (16) in
175 hypoxia and normoxia. [Cycling continuously for 10 min at a fixed-intensity \(corresponding](#)
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182
183 **to 50% VO_{2Max}) in hypoxia versus normoxia negatively impacts cognitive function (17).**

184 Slower self-selected running velocities may assist **with mitigating** hypoxic-induced negative
185 cognitive function compared to normoxia (18).
186

187
188 Brocherie, F., Millet, G. P., & Girard, O. (2017). Psychophysiological responses to repeated-
189 sprint training in normobaric hypoxia and normoxia. *International Journal of Sports Physiology*
190 *and Performance*, 12(1), 115-123.
191

192
193 McMorris, T., Hale, B. J., Barwood, M., Costello, J., & Corbett, J. (2017). Effect of acute
194 hypoxia on cognition: A systematic review and meta-regression analysis. *Neuroscience &*
195 *Biobehavioral Reviews*, 74, 225-232.
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199
200 Reviewer: Please list a rationale for this study aim—why does this really matter or to whom
201 do these data apply? Is this for training purposes or something else?
202

203 Authors' response: We thank the reviewer for suggesting to list a short rationale after the aim
204 of the study. We have subsequently added this into the manuscript which can also be found
205 below.
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208 P6 L59-61 – **Decreasing external load with matched internal load during perceptually-**
209 **regulated HIIT in hypoxia compared to normoxia may benefit athletes during heavy**
210 **training blocks prior to competition.**
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215 Reviewer: Is it wise to have only 3 women in the study? Please comment.
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217 Authors' response: In response to the reviewers comment, our aim was not to investigate the
218 effect of gender in response to perceptually-regulated interval running in hypoxia and
219 normoxia. Rather our intention was to investigate the effect of perceptually-regulated interval
220 running in hypoxia and normoxia on adjustments in running velocity and associated exercise-
221 related sensations of trained runners. During our recruitment period, three eligible females
222 volunteered for the study who matched the inclusion criteria (P6 L67-69). We have calculated
223 groups means \pm SD and re-analysed the primary outcomes of our study (velocity, heart rate,
224 SpO₂ and exercise-related sensations) only with the 16 male participants (excluding the three
225 females). As shown at the bottom of this response document, this analysis indicates that
226 including only three females does not lead to different groups means \pm SD, probability values
227 and effect sizes compared to a dataset of 16 males. Consequently, including the 3 female
228 participants in our final sample of 19 participants does not change the overall message of the
229 study. Therefore, we believe that keeping the three females within the current participant total
230 (n = 19) is warranted since our power calculation indicated 21 participants are required to yield
231 sufficient power in the statistical tests carried out (P6 L73-P7 L76). This would not be achieved
232 if the data from the three females were removed (n = 16).
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246 Reviewer: Is there a reason why a VO₂max test was not undertaken?
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248 Authors' response: We thank the reviewer for raising this comment. Although identifying and
249 presenting VO₂MAX values of the participants in our study would have been informative, we
250 didn't feel it was necessary. This is because we used a modified, and validated, method (Martin
251 et al., 1992) to determine the individual velocity required for each individual to run at an RPE
252 of 16, which is presented (P17 L268-269) and the main purpose of our work. As such, of the
253 ceiling value (VO₂MAX) did not need to be identified in the current study.
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256 Martin, P. E., Rothstein, D. E., Larish, D. D. Effects of age and physical activity status on the
257 speed-aerobic demand relationship of walking. J Appl Phys 1992;73:200–206.
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261

262 Reviewer: Were participants informed about the study aim e.g. to test changes in your measures
263 in hypoxia vs. normoxia?
264

265 Authors' response: We appreciate the reviewer raising this important comment. Prior to
266 enrolling onto the study, participants were informed that they will perform two HIIT protocols,
267 randomly in hypoxic and normoxic conditions. We explained the measures that we would be
268 performing, but did not directly outline that we would be looking at the comparison between
269 hypoxic and normoxic conditions to the participants. Naturally, this may have impacted their
270 perceptions or lead to social desirability bias in response to perceptual scales and assessment
271 of attention and executive function. Further, as outlined in the manuscript (P9 L132-135),
272 participants were blinded to the environmental condition during the HIIT protocol as we
273 removed the hypoxic generator from their view, and simulated 100 m (machine switched on)
274 during normoxia. We have subsequently added in some further information regarding this
275 comment to the manuscript as outlined below.
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280 P7 L86-88 – **To minimise the impact of social desirability bias, participants were made**
281 **aware of the purpose of the study but were naïve to experimental hypotheses.**
282

283 Adams, S. A., Matthews, C. E., Ebbeling, C. B., Moore, C. G., Cunningham, J. E., Fulton, J.,
284 & Hebert, J. R. The effect of social desirability and social approval on self-reports of physical
285 activity. Am J Epidemiol, 2005;161(4):389-398.
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291 Reviewer: I think the Results would be better structured by describing the fidelity of HIIT first,
292 by denoting the HR and velocity data. This confirms that these bouts actually represent HIIT
293 based on 85 %HRmax. Then, follow this with your other outcomes.
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304 Authors' response: We acknowledge and agree with the reviewer that the results structure
305 would be better when beginning the first section with velocity and heart rate data. The heading
306 of this section has been renamed, and only includes velocity and heart rate data.
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308 P12 L190 – *Changes in velocity and HR*
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314 Reviewer: I also think that the Results text needs better subheadings to clarify its organization
315 e.g. change in HR and running velocity in response to..; change in muscle deoxygenation in
316 response to, etc.
317

318 Authors' response: We appreciate the reviewer suggesting better subheadings within the results
319 section. These have subsequently been renamed as below.
320

321 P12 L196 – *Changes in SpO₂ and muscle oxygenation*
322

323 P12 L201 – *Changes in exercise-related sensations*
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325 P13 L222 – *Changes in [La⁺] and attention and executive function*
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330 Reviewer: Line 186 needs a clearer subheading e.g. change in recovery and .. in response to..
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332 Authors' response: Please see response above regarding this comment.
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337 Reviewer: Line 244, Discussion; so what is the importance of these findings to the athlete,
338 coach, clinician, etc.? Please cite this here.
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341 Authors' response: We acknowledge the reviewers comment that the importance of our
342 findings should be stated here for those in an applied setting. We have subsequently added this
343 information in to the manuscript, which can also be found below.
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346 P17 L261-266 – *A matched internal workload for a decreased external workload during*
347 *perceptually-regulated HIIT in hypoxia versus normoxia may assist athletes to reach*
348 *intended session goals with minimal over-induced physiological stress. However,*
349 *perceptually-regulated HIIT exacerbates exercise-related sensations and blood lactate*
350 *concentrations in hypoxia compared to normoxia. This may then have negative carry-*
351 *over effects on training responsiveness in the following days.*
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363 Reviewer: Line 269; so what is the importance or application of this particular finding?
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365 Authors' response: We understand the reviewers comment that this take home message can be
366 further developed for importance and application. We have subsequently added this
367 information in to the manuscript, which can also be found below.
368
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370 P18 L291-294 – **This finding may be of benefit to athletes who are unable or advised by**
371 **their coach not to be training at a full intensity. Completing perceptually-regulated HIIT**
372 **in hypoxia that requires slower running velocities compared to normoxia may in turn**
373 **minimise mechanical constraints and eventually injury risk.**
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378 Reviewer: Line 302: what do you mean by ‘metabolic by product?’ this is blood lactate so just
379 represent this as is to be most clear. And why does this excess accumulation of BL_a matter to
380 the scientist or athlete/practitioner?
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382

383 Authors' response: We thank the reviewer for suggesting more clarity regarding the take home
384 message of this paragraph in the discussion, and have replaced ‘*metabolic by-product*’ with
385 ‘[La⁺]’. We have also added in a sentence regarding the implications of this finding in an
386 applied setting.
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389 P19 L327 – ... to increased [La⁺] at slower...

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391 P19 L328-P20 L332 – **Practitioners should be aware that perceptually-regulated HIIT in**
392 **hypoxia is a viable method for matching indices of physiological stress to normoxia.**
393 **However, the blood lactate concentration increases after exercise were larger in hypoxia**
394 **compared to normoxia. This may have negative implications on the muscle fatigue**
395 **recovery process.**
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401 Reviewer: Lines 307-15: are there any data showing that hypoxia reduces O₂ delivery to the
402 brain which then may alter perceptions of exercise which are regulated by various brain
403 centers? Please comment on this.
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406 Authors' response: We thank the reviewer for raising this interesting point. Accordingly, we
407 have added some information from the work of Subudhi et al. (2007 & 2009) relating to the
408 negative implication hypoxia has on oxygen delivery to the brain, potentially altering
409 perceptions of exercise. We also believe that this point should be of consideration for further
410 research investigations, attempting to capture further measurements in response to HIIT in
411 hypoxia at a perceptually-regulated intensity compared to normoxia.
412
413

414 P20 L342-348 – **Further, it could be postulated that cerebral deoxygenation was greater**
415 **during HIIT in hypoxia versus normoxia, as demonstrated by Subudhi et al. during**
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423 **incremental cycling (40, 41). Accordingly, cerebral deoxygenation during HIIT may**
424 **contribute to an integrative decision regarding negative perceptions, in which hypoxia**
425 **hastens this effect (41). Given that the perceptually-regulated exercise model is governed**
426 **centrally, this may provide a potential explanation as to why exercise-related sensations**
427 **were more elevated in the hypoxic trial.**
428
429

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431 P28 L522-524 – **Subudhi, A. W., Dimmen, A. C., & Roach, R. C. Effects of acute hypoxia**
432 **on cerebral and muscle oxygenation during incremental exercise. J App Phys.**
433 **2007;103(1):177-183.**
434

435
436 P28 L525-527 – **Subudhi, A. W., Miramon, B. R., Granger, M. E., & Roach, R. C. Frontal**
437 **and motor cortex oxygenation during maximal exercise in normoxia and hypoxia. J App**
438 **Phys. 2009;106(4):1153-1158.**
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441

442 Reviewer: This text seems to be way too much of a ‘stretch’ from your particular study and
443 should be removed, as it is not relevant; thank you. *Athletes and clinical patients awaiting or*
444 *shortly proceeding surgery may exercise in hypoxia to increase the internal workload similar*
445 *to that achieved in normoxia for a lower external workload. This could decrease joint pain of*
446 *the lower extremities during ambulation.*
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449 Authors’ response: We understand the reviewers concern regarding some of the statements
450 presented in the limitations and perspectives section. We have since removed the points raised
451 by the reviewer.
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483 **Reviewer 2**
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486 Reviewer: This study was primarily aimed at investigating potential differences in running
487 velocities between perceptually-regulated high-intensity intervals in hypoxia and normoxia. It
488 has been demonstrated that running velocity progressively decreased from interval 1 to 4, more
489 pronounced in hypoxic conditions. Negative exercise-related sensations increased over time,
490 again more pronounced in hypoxia.
491

492
493 The authors deal with an interesting topic especially from a training-practical point of view
494 however, findings are not really unexpected and novelty of this study should be more
495 highlighted. Methods are well and reproducibly described and results are nicely presented.
496 Nevertheless, the authors may respond to the following comments:
497

498
499 Authors' response: We thank the reviewer for their careful consideration of our work. We have
500 responded to the comments individually raised below.
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504 Reviewer: In the introduction section, you may refer to studies demonstrating differences
505 between RPE and cardiorespiratory responses in hypoxia/altitude compared to normoxia.
506

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508 Authors' response: We thank the reviewer for raising our attention to this point and have added
509 in this information to the introduction section as outlined below.
510

511
512 P5 L36-38 – **Although HR was similar between conditions, RPE has been reported to be**
513 **higher in hypoxia compared to normoxia during fixed-intensity interval runs (5) and**
514 **repeated-sprint cycling (12).**
515

516
517 P26 L443-445 – **Brocherie, F., Millet, G. P., & Girard, O. Psychophysiological responses**
518 **to repeated-sprint training in normobaric hypoxia and normoxia. International J of**
519 **Sports Phys Perform. 2017;12(1):115-123.**
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526 Reviewer: Nineteen experienced runners have been recruited. As you might expect, I am not
527 happy with the inclusion of only 3 females. Such a sex distribution may reduce the
528 conclusiveness of the findings and does not allow to analyse potential sex differences.
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530
531 Authors' response: We understand the reviewers' concern regarding the small population of
532 females within our participant cohort. We would like to highlight that within the literature, it
533 is inconclusive as to whether gender distributions impact on acute responses to hypoxia – with
534 some confirming (Lombardi et al., 2013; Mortola & Saiki, 1996) and others rejecting (Loeppky
535 et al., 2001; Sandoval & Matt, 2002) this hypothesis.
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545 In response to the reviewers comment, our aim was not to investigate the effect of gender in
546 response to perceptually-regulated interval running in hypoxia and normoxia. Our aim was to
547 investigate the effect of perceptually-regulated interval running in hypoxia and normoxia on
548 trained runners. During our recruitment period, three eligible females volunteered for the
549 study who matched the inclusion criteria (P6 L67-69). We have calculated groups means \pm
550 SD and re-analysed the main findings of our study (velocity, heart rate, SpO₂ and exercise-
551 related sensations) without the presence of the three females (located at the bottom of this
552 response document) which does not change the overall message of the study. Therefore, we
553 believe that keeping the three females within the current participant total (n = 19) is
554 warranted since our power calculation indicated 21 participants are required to yield
555 sufficient power in the statistical tests carried out (P6 L73-P7 L76), which would not be
556 achieved if the data from the three females were removed (n = 16).
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560 We do believe that the reviewer raises an important comment, and have since highlighted this
561 in the limitations and perspectives section of the paper for future investigations.
562

563 P22 L384-387 – **In addition, whether there are gender differences in response to hypoxic**
564 **exposure during perceptually-regulated HIIT should be investigated, given that our final**
565 **sample size (n = 19) included only three females.**
566

567
568 Loeppky, J. A., Scotto, P., Charlton, G. C., Gates, L., Icenogle, M., & Roach, R. C. (2001).
569 Ventilation is greater in women than men, but the increase during acute altitude hypoxia is the
570 same. *Respiration physiology*, 125(3), 225-237.
571

572
573 Lombardi, C., Meriggi, P., Agostoni, P., Faini, A., Bilo, G., Revera, M., ... & Gregorini, F.
574 (2013). High-altitude hypoxia and periodic breathing during sleep: gender-related differences.
575 *Journal of sleep research*, 22(3), 322-330.
576

577
578 Mortola, J. P., & Saiki, C. (1996). Ventilatory response to hypoxia in rats: gender differences.
579 *Respiration physiology*, 106(1), 21-34.
580

581 Sandoval, D. A., & Matt, K. S. (2002). Gender differences in the endocrine and metabolic
582 responses to hypoxic exercise. *Journal of Applied Physiology*, 92(2), 504-512.
583
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587 Reviewer: Did you perform some type of power calculation? (at least a-posteriori).
588

589 Authors' response: We thank the reviewer for raising this comment. We did indeed carry out a
590 power analysis to determine the number of participants required for sufficient power in our
591 results. Information regarding this has been added to the manuscript, as found below.
592
593

594 P6 L72-P7 L78 – **A-priori sample size was calculated using G*Power (Version 3.1.9.3).**
595 **This was determined using published power output data by Jeffries et al. (19), whereby**
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603 **healthy individuals cycled at a perceptually-regulated intensity (RPE = 16) in hypoxic**
604 **(FiO₂ = 15.0%) and normoxic conditions. Twenty-one participants were deemed**
605 **sufficient to yield a power of 0.8 at an α probability of 0.05. Two individuals dropped out**
606 **due to injuries sustained during their time enrolled onto the study, not associated with**
607 **the HIIT protocols we employed.**
608
609

610 P26 L467-469 – **Jeffries, O., Patterson, S. D., & Waldron, M. The effect of severe and**
611 **moderate hypoxia on exercise at a fixed level of perceived exertion. Euro J App Phys.**
612 **2019;1-12.**
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620 Reviewer: What means experienced runners? Can you report race times, VO₂max, etc.?
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622 Authors' response: We appreciate the reviewers comment regarding our use of the term
623 'experienced runners'. As we did not collect information regarding race times and race history
624 nor did we assess VO₂MAX, we have replaced this term with 'trained runners' throughout the
625 manuscript. Further, the runners we recruited included those with middle and long distance
626 backgrounds. As such, it would be difficult to estimate or predict one particular race distance
627 (i.e., 10 km) for all participants if they had not competed in this distance previously. We believe
628 the term 'trained' better reflects the demographic of individuals recruited for the study, whom
629 may have a knowledge of different race times and race history, but we have no quantifiable
630 data to present.
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637 Reviewer: Please, provide a table depicting more characteristics of study participants, beside
638 anthropometric data, e.g. also performance parameters, regular physical sports/exercise
639 activity, medical history, coffee and/or alcohol drinking, smoking, medications, etc.
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641

642 Authors' response: We appreciate the reviewer suggesting to add further characteristics of the
643 participants who completed the study protocol. Prior to enrolling onto the study, we screened
644 volunteers (using a health questionnaire) for their medical history. As described in the methods
645 section (P6 L66-69), we only included individuals who were free of clinical signs of disease,
646 orthopedic, neurological, cardiovascular or respiratory problems. Further, runners were
647 recruited who trained for ≥ 6 h/wk. Therefore, we are unable to provide any further information
648 regarding the characteristics of participants as this was not collected, but re-assure the reviewer
649 that they were of a healthy status.
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663 Reviewer: The limitation section should be extended and the statements that “athletes and
664 clinical patients awaiting or shortly proceeding surgery may exercise in hypoxia to increase
665 the internal workload similar to that achieved in normoxia for a lower external workload” and
666 “this could decrease joint pain of the lower extremities during ambulation” are in my opinion
667 not justified based on the presented findings and should rather be deleted.
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671 Authors’ response: We understand the reviewers concern regarding some of the statements
672 presented in the limitations and perspectives section. We have since removed the points raised
673 by the reviewer, and added in sentences regarding the need to investigate gender differences in
674 response to perceptually-regulated HIIT in hypoxia.
675

676 P22 L384-387 – **In addition, whether there are gender differences in response to hypoxic**
677 **exposure during perceptually-regulated HIIT should be investigated, given that our final**
678 **sample size (n = 19) included only three females.**
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686 Reviewer: The conclusion might a bit more focus on the training-practical importance of the
687 findings.
688

689 Authors’ response: We thank the reviewer for raising this important point, and have
690 subsequently added a sentence within the conclusion section of our manuscript highlighting
691 the practical considerations of our findings.
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694 P22 L396-401 – **Our results suggest that athletes under the influence of hypoxia require**
695 **lower external workloads to reach a perceptually-regulated target during HIIT than**
696 **normoxia. If employed in a practical setting, coaches should consider the potential of**
697 **negatively implicated exercise-related sensations and blood lactate concentrations which**
698 **may have further negative carry-over effects on training responsiveness in the following**
699 **days.**
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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 \pm SD, *p* values and effects sizes are presented for velocity, heart rate, SpO₂ and exercise-related sensations.

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

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1 **Title**

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

4
5 **Author names and affiliations**

6 Hobbins L^a, Gaoua N^a, Hunter S^a, Girard O^{b,c}

7
8 ^aSport and Exercise Science Research Centre (SESRC), London South Bank University,
9 London, United Kingdom

10 ^bMurdoch Applied Sports Science (MASS) Laboratory, Murdoch University, Perth, Australia
11 ^c**Athlete Health and Performance Research Center, ASPETAR, Qatar Orthopedic and**
12 **Sports Medicine Hospital, Doha, QATAR**

13
14 **Corresponding author**

15 Mr. Liam Hobbins

16 hobbinsl@lsbu.ac.uk

17 Sport and Exercise Science Research Centre

18 London South Bank University

19 103 Borough Road

20 London

21 SE1 0AA

60
61
62 **1 Abstract**
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64
65 2 We investigated whether perceptually-regulated high-intensity intervals in hypoxia are
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67 3 associated with slower running velocities *versus* normoxia, when physiological responses and
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69 4 exercise-related sensations remain the same. Nineteen **trained** runners (**33.4 ± 9.1 years**)
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71 5 completed a high-intensity interval running protocol (4 × 4-min intervals at a clamped
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73 6 perceived rating exertion of 16 on the 6–20 Borg scale, 3-min passive recoveries) in either
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75 7 hypoxic (HYP; FiO₂ 15.0%) or normoxic (NOR; FiO₂ 20.9%) conditions. Participants adjusted
76
77 8 to a progressively slower running velocity from interval 1–4 (-7.0%), and more so in HYP *vs.*
78
79 9 NOR for intervals 2, 3 and 4 (-4.6%, -6.4% and -7.9%, respectively; *p* < 0.01). Heart rate
80
81 10 increased from interval 1–4 (+4.8%; *p* < 0.01), independent of condition. Arterial oxygen
82
83 11 saturation was lower in HYP *vs.* NOR (86.0% *vs.* 94.8%; *p* < 0.01). Oxyhemoglobin (-23.7%)
84
85 12 and total hemoglobin (-77.0%) decreased, whilst deoxyhemoglobin increased (+44.9%) from
86
87 13 interval 1–4 (*p* < 0.01), independent of condition. Perceived recovery (-41.6%) and motivation
88
89 14 (-21.8%) were progressively lower from interval 1–4, and more so in HYP *vs.* NOR for
90
91 15 intervals 2, 3 and 4 (recovery: -8.8%, -24.2% and -29.3%; motivation: -5.3%, -20.3% and -
92
93 16 22.4%, respectively; *p* < 0.01). Perceived breathlessness (+18.6%), limb discomfort (+44.0%)
94
95 17 and pleasure (-32.2%) changed from interval 1–4, with significant differences (+21.8%,
96
97 18 +11.3% and -31.3%, respectively) between HYP and NOR (*p* < 0.01). Slower interval running
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99 19 velocities in hypoxia achieve similar heart rate and muscle oxygenation responses to those
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101 20 observed in normoxia when perceptually-regulated, yet at the expense of less favourable
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103 21 exercise-related sensations.
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23 **Key words**

24 High-intensity intermittent running; normobaric hypoxia; perceptually-regulated exercise;

25 ratings of perceived exertion; near-infrared spectroscopy; effort perception.

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180 **1 Introduction**
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183 2 High-intensity interval **training (HIIT)** is a popular exercise format in athletic and clinical
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185 3 populations (1,2). **HIIT** includes repeated short-to-long (2–5 min) intense exercise bouts (80–
186
187 4 90% of the velocity associated with maximal oxygen uptake or $v\dot{V}O_{2Max}$) interspersed with
188
189 5 shorter (1–3 min) recoveries (3). Compared to moderate-intensity continuous running, **HIIT**
190
191 6 leads to similar improvements in cardiorespiratory fitness **that is achieved with a shorter**
192
193 7 **effective exercise duration** per session (2). Due to the reduced time-commitment and **exercise**
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195 8 training volume, investigations surrounding the potential physiological and performance
196
197 9 benefits of **HIIT** have surged (4).
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201 10 **HIIT** in normobaric hypoxia (a lower inspired oxygen fraction or FiO_2) is receiving attention
202
203 11 for its potential in further advancing athletic performance compared to **HIIT** in normoxia.
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205 12 Buchheit et al. (5) employed a **HIIT** protocol (3 × 5-min, 90-s recovery) carried out in hypoxia
206
207 13 ($v\dot{V}O_{2Max} = 84\%$; $FiO_2 = 15.4\%$) and normoxia ($v\dot{V}O_{2MAX} = 90\%$) at a fixed-intensity
208
209 14 (determined in normoxia) in highly-trained runners. A reduced physiological stress (i.e., lower
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211 15 heart rate or HR) was observed during hypoxia compared to normoxia, likely due to a lower
212
213 16 $v\dot{V}O_{2Max}$ in hypoxia *versus* normoxia. However, fixed exercise intensities, regardless of
214
215 17 environmental conditions, do not permit adjustments (i.e., increases or decreases of workload)
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217 18 during exercise to match the intensity target (i.e., $v\dot{V}O_{2MAX}$). In turn, over-induced
218
219 19 physiological stress may be counter-productive (i.e., greater deoxygenated muscle
220
221 20 heamoglobin, lower oxygenated haemoglobin) for intended session goals (6). Furthermore,
222
223 21 matched absolute fixed exercise intensities (i.e., a similar percentage of $v\dot{V}O_{2MAX}$) lead to
224
225 22 greater physiological stress (i.e., compensatory increase in HR) in hypoxia compared to
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227 23 normoxia due to reduced FiO_2 (7). Perceptually-regulated exercise intensities, that allow
228
229 24 velocity adjustments based upon exercise-related sensations in order to maintain a target effort
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239 level, may offer a viable solution, and is perhaps more reflective of how exercisers modify
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241 intensity during acute exercise.
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244 27 Perceptually-regulated exercise permits the individual exercising to self-regulate external
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246 28 workload (i.e., running velocity/cycling power production) based upon Borg's rating of
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248 29 perceived exertion (RPE) scale (8). The validity and usefulness of using RPE for perceptually-
249
250 30 regulating exercise has been described (9). The reduced oxygen availability in hypoxia makes
251
252 31 the expectation tenable that there would be a slower self-selected running velocity in hypoxia
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254 32 for a given RPE, while velocity in normoxia would be more preserved, as evidenced previously
255
256 33 (10). Chacaroun et al. (11) demonstrated for a lower power output (-15%), *vastus lateralis*
257
258 34 muscle deoxyhemoglobin was higher and oxyhemoglobin lower in hypoxia ($FiO_2 = 13.5\%$)
259
260 35 compared to normoxia during a single interval session ($15 \times 1\text{-min}$ at 75% of maximal HR, 1-
261
262 36 min recoveries). Although HR was similar between conditions, RPE has been reported to
263
264 37 be higher in hypoxia compared to normoxia during fixed-intensity interval runs (5) and
265
266 38 repeated-sprint cycling (12). Employing self-paced exercise, in replace of fixed-intensity
267
268 39 exercise, may assist in overcoming the over-excessive physiological stress observed when
269
270 40 exercising in hypoxia *versus* normoxia, due to the likelihood of greater velocity preservations
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272 41 in the latter than the former.

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274
275 42 In normoxia at pre-determined fixed intensities, HIIT is perceived as more enjoyable compared
276
277 43 to moderate-intensity continuous running (13). However, during HIIT at fixed-intensities,
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279 44 exercise-related sensations decrease when the exercise intensity rises above threshold
280
281 45 preference (14). Further, HIIT in hypoxia at fixed-intensities typically surpasses the preferred
282
283 46 threshold in normoxia (15). Implementing a self-paced exercise model may permit
284
285 47 modifications required (i.e., slower running velocities) to maintain exercise-related sensations
286
287 48 contributing to RPE (16) in hypoxia and normoxia. Cycling continuously for 10 min at a
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289 49 fixed-intensity (corresponding to 50% VO_{2Max}) in hypoxia *versus* normoxia negatively
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298 50 impacts cognitive function (17). Slower self-selected running velocities may assist with
299
300 51 mitigating hypoxic-induced negative cognitive function compared to normoxia (18). These
301
302 52 potential findings may benefit athletes exercising intensely in hypoxia, shortly followed by
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304 53 skills requiring attention and accuracy.
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307
308 54 Therefore, the aim of this study was to investigate the effect of HIIT at a clamped RPE of 16
309
310 55 (typically used by athletes during HIIT) (19) in hypoxia and normoxia on adjustments in
311
312 56 running velocity and associated exercise-related sensations of trained runners. We
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314 57 hypothesized that running velocity would be progressively slower in hypoxia compared to
315
316 58 normoxia across intervals, whilst physiological and cognitive responses, and exercise-related
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318 59 sensations would not differ between conditions. Decreasing external load with matched
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320 60 internal load during perceptually-regulated HIIT in hypoxia compared to normoxia may
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322 61 benefit athletes during heavy training blocks prior to competition.
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328 63 **Methods**

329 64 *Participants*

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334 65 Nineteen trained runners (3 females, 16 males; age: 33.4 ± 9.1 years; height: 176 ± 88 cm;
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336 66 weight: 76.3 ± 10.9 kg) provided written informed consent to participate. Participants had no
337
338 67 musculoskeletal injuries and met the following eligibility criteria: a training volume ≥ 6 h/wk,
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340 68 free of clinical signs of disease, orthopedic, neurological, cardiovascular or respiratory
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342 69 problems, and no hypoxic exposure >2000 m for >48 h 6 months before the study. The study
343
344 70 was carried out in accordance with the Declaration of Helsinki and was approved by the Ethics
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346 71 Committee of the Anti-Doping Lab Qatar institutional review board (Agreement SCH-ADL-
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348 72 170). A-priori sample size was calculated using G*Power (Version 3.1.9.3). This was
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357 73 determined using published power output data by Jeffries et al. (20), whereby healthy
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359 74 individuals cycled at a perceptually-regulated intensity (RPE = 16) in hypoxic (FiO₂ =
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361 75 15.0%) and normoxic conditions. Twenty-one participants were deemed sufficient to
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363 76 yield a power of 0.8 at an α probability of 0.05. Two individuals dropped out due to
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365 77 injuries sustained during their time enrolled onto the study, not associated with the HIIT
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367 78 protocols we employed.
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371 *Experimental design*

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374 80 Participants reported to the laboratory on three occasions, each separated by ≥ 48 h. The first
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376 81 session included study familiarisation. The second and third visits included completing a **HIIT**
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378 82 protocol in either hypoxia or normoxia in a randomized, counterbalanced order. Physiological,
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380 83 perceptual and cognitive responses were assessed continuously, immediately before and after
381
382 84 each interval, and before and after the **HIIT** protocol, respectively. Participants were instructed
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384 85 to refrain from any intense exercise 48 h prior to each visit and consume their last meal at least
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386 86 2 h prior to the **HIIT** sessions. To minimise the impact of social desirability bias,
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388 87 participants were made aware of the purpose of the study but were naïve to experimental
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390 88 hypotheses. Laboratory conditions were similar throughout all sessions (mean temperature
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392 89 $\sim 22^\circ\text{C}$, relative humidity $\sim 50\%$) and time of day was standardized for each participant.
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396 *Familiarization session*

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399 91 At the preliminary visit to the laboratory, participants were familiarised with the perceptual
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401 92 scales and cognitive test. Preferred running velocity (PRV) was determined for each participant
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403 93 in normoxia using a modified version of identifying preferred walking speed (21). After a 5-
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405 94 min warm up at 10 km/h^{-1} , participants completed four ramped treadmill runs (increasing and
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407 95 decreasing velocities) on an instrumented treadmill (ADAL3D-WR, Medical Development–
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409 96 HEF Tecmachine, France). After every 20 s per ramp, participants rated their RPE of the
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416 97 current velocity (controlled by the investigator and out of sight of the participant) in accordance
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418 98 with Borg's (20) 6 ("no exertion at all") – 20 ("maximal exertion") numeric scale. Ramp one
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420 99 started at 10 km/h⁻¹, increasing by 0.8 km/h⁻¹ every 20 s until the velocity was considered as
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422
423 100 RPE ≥18; ramp two started at +1.5 km/h⁻¹ the previous end velocity, decreasing by 0.8 km/h⁻¹
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425 101 until the velocity was considered as RPE ≤12; ramp three started at the velocity considered as
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427 102 an RPE of 14 in ramp two, increasing by 0.5 km/h⁻¹ until the velocity was considered as RPE
428
429 103 ≥18; and ramp four started at +1.0 km/h⁻¹ the previous end velocity, decreasing by 0.5 km/h⁻¹
430
431 104 until the velocity was considered as RPE ≤12. Ramps two, three and four began once the
432
433 105 participants declared their perceived recovery level as a 7 out of 10 following the previous
434
435 106 ramp (23). HR was recorded every 20-s through each ramp. PRV corresponded to the velocity
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437 107 participants considered as a RPE of 16 (between "hard" and "very hard") or closest to a HR of
438
439 108 160 bpm. After 10 min of rest, participants completed one 4-min interval composing the **HIIT**
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441 109 protocol (see below) for habituation.
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445 110 *Experimental trials*

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447
448 111 Participants completed two experimental trials in normoxia (NOR; FiO₂ = 20.9%) and hypoxia
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450 112 (HYP; FiO₂ = 15.0%, equivalent to ~2700 m above sea level). After a standardised warm up
451
452 113 (5-min at 10 km/h⁻¹), a facemask connected to a portable hypoxic generator (See *Hypoxic*
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454 114 *simulation* section) was attached. Participants rested for 1-min (quiet standing) before a 1-min
455
456 115 run at their PRV (RPE = 16). Participants then rested for 3 min before completing the **HIIT**
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458 116 protocol. The **HIIT** protocol was based upon aerobic interval-training (2). Participants
459
460 117 completed four, 4-min intervals, interspersed with 3-min recoveries (quiet standing). The first
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462 118 30 s of each 4-min interval began at participants' PRV; participants were then free to decide if
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464 119 or how treadmill velocity needed to be adjusted (manually by one experimenter) to ensure
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466 120 maintenance of a RPE of 16 every 30 s. Participants hand-signalled in response to the current
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475 121 velocity (finger up to increase, finger down to decrease, and circle using index finger and thumb
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477 122 to maintain); and signalled again to inform how much of an increase/decrease in velocity is
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479 123 required [1, 2 or 3 fingers up (faster) or down (slower) for 0.5, 1.0 or 1.5 km/h⁻¹ changes,
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481
482 124 respectively]. Signals were trialled during familiarisation. Mild verbal encouragement to keep
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484 125 running at an RPE of 16 was used throughout **HIIT**. Total hypoxic exposure corresponded to
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486 126 exactly 28 min.

487 488 489 127 *Hypoxic simulation*

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492 128 Participants were fitted with a facemask fastened with a Velcro headset connected via plastic
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494 129 tubing to a hypoxic generator (Altitrainer, SMTec SA, Nyon, Switzerland) to simulate hypoxia.
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496 130 The gas mixing system enriches inspired air by adding a fixed quantity of nitrogen via a 30-L
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498 131 mixing chamber, with the dilution being constantly controlled by a PO₂ probe (precision =
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500 132 T0.82 torr, safety FiO₂ = 9.7%). The hypoxic generator was hidden from participant viewing
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502 133 to ensure condition blinding. When breathing ‘normal air’ during normoxia, the hypoxic
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504 134 generator was on (for background noise) and set at a simulated altitude of 100 m to increase
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506 135 the strength of blinding.

507 508 509 136 *Measures*

510 511 512 137 *Exercise intervals*

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515 138 HR was monitored telemetrically with a Polar transmitter-receiver (Polar S810, Kempele,
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517 139 Finland) and recorded 20 s before and every 30 s during each interval. Arterial oxygen
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519 140 saturation (SpO₂) was assessed via finger pulse oximetry (Palmsat 2500, NONIN Medical
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522 141 Inc., Plymouth, MI, USA) at the same time intervals. HR and SpO₂ were obtained before (i.e.,
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524 142 after a 2-min seated period) and at the end of the warm-up procedure (i.e., prior to **HIIT**). Both
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534 143 the HR watch (RS400, Polar) and oximeter receiver were attached on the handrails of the
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536 144 treadmill outside of the participants' view.
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539 145 Muscle oxygenation trends of the right *vastus lateralis* muscle were recorded using near-
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541 146 infrared spectroscopy (NIRS; Portalite, Artinis, Netherlands) in real-time. A wireless bi-polar
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543 147 optode sensor was attached (~10 cm above the proximal patella border) and secured to skin via
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545 148 adhesive tape. Sampling frequency was set at 10 Hz (11) following a 'zero set' of all signals.
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547 149 Bandages were fastened around the lower limb and optode to prevent external light distorting
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549 readings. Oxy- (Δ ; [O₂Hb]), deoxy- (Δ ; [HHb]) and total haemoglobin (μmol ; [tHb]) were
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551 150 exported (1 Hz). For analysis, each interval was averaged and normalized to a 10 s sample prior
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553 151 to interval one (reference value) for each respective condition and presented as percentage
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555 152 change.
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559 154 *During recovery*
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561
562 155 Perceived recovery and motivation to exercise were assessed 30 s before each interval.
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564 156 Perceived recovery was assessed by answering '*how recovered do you feel currently?*' via a
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566 157 numeric scale, ranging from 0 ("*very poorly recovered*") to 10 ("*very well recovered*") (23).
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569 158 Recovery was assessed before interval one to determine perceptions following the warm up.
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571 159 Perceived motivation to exercise was assessed via a 20-cm visual analog scale (24).
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573 160 Participants were asked '*how motivated do you feel to exercise right now?*' and answered by
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575 161 adjusting the level on the scale between 0 ("*extremely low*"; white colored) and 20 ("*extremely*
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577 162 *high*"; black colored). Immediately after each interval, ratings of perceived breathlessness, limb
578
579 163 discomfort and pleasure were assessed. Perceived breathlessness was assessed by answering
580
581 164 '*how does your breathing feel currently?*' via a numeric scale, ranging from 0 ("*nothing at*
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583 165 *all*") to 10 ("*very, very severe*") (25). Using the same scale, perceived limb discomfort was
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585 166 assessed by answering '*how do your legs feel currently?*'. A 20-cm visual analog scale (same
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592
593 167 as motivation above) was used to assess ‘*how pleasant was that run?*’ ranging from 0
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595 168 (“*extremely unpleasant*”) and 20 (“*extremely pleasant*”).
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598 169 *Pre- and post-exercise*
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600

601 170 A capillary blood sample taken from the fingertip was analyzed for blood lactate concentration
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603 171 ([La⁺]) with the Lactate Pro (LT-1710, Arkray, Japan) portable analyzer before the warm-up
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605 172 and 2 min after **HIIT**. An offline Stroop colour-word test (26) assessed attention and executive
606
607 173 function. Using one hand and as quickly as possible, participants selected the colored key on
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609 174 the keyboard representing the color of the text appearing on the screen (red, yellow, green or
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611 175 blue). The cognitive test lasted for 3 min, and took place in a silent environment before the
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613 176 warm up and 3 min after **HIIT**. Reaction time (ms; time taken to select a color) and accuracy
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615 177 (%; correct color selected) were averaged over each test for analysis.
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619 178 *Statistical analysis*
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622 179 Data distribution was assessed via a Shapiro-Wilk test. A parametric within-subject two-way
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624 180 analysis of variance was used to investigate the main effect of condition (NOR vs. HYP), time
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626 181 (interval 1, 2, 3 vs. 4 or pre vs. post) and the condition × time interaction for normally
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628 182 distributed data. Partial eta-squared (η^2) was calculated as a measure of effect size. Values of
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630 183 0.01, 0.06 and above 0.14 were considered as small, medium and large, respectively (27). A
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632 184 related samples Friedman’s non-parametric test was used for data not normally distributed.
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634 185 Bonferroni post-hoc pairwise comparisons were used to identify locations of significant effects.
635
636 186 Statistical testing was carried out in SPSS (v21; CED, Cambridge, United Kingdom). Data was
637
638 187 considered significant if $p \leq 0.05$. All data are presented as group means \pm SD.
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645 189 **Results**
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652 **190 Changes in velocity and HR**
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655 191 Compared to interval 1, participants adjusted to a progressively slower running velocity during
656
657 192 intervals 2, 3 and 4 (-2.8%, -5.2% and -7.0%, respectively; $p < 0.01$), and more so in HYP vs.
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659 193 NOR for intervals 2, 3 and 4 (-4.6%, -6.4% and -7.9%, respectively; $p < 0.01$; Figure 1A).
660
661 194 Compared to interval 1, HR increased during intervals 2, 3 and 4 (+2.3%, +3.6% and 4.8%,
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663
664 195 respectively; $p < 0.01$; Figure 1B), independently of condition ($p = 0.65$).
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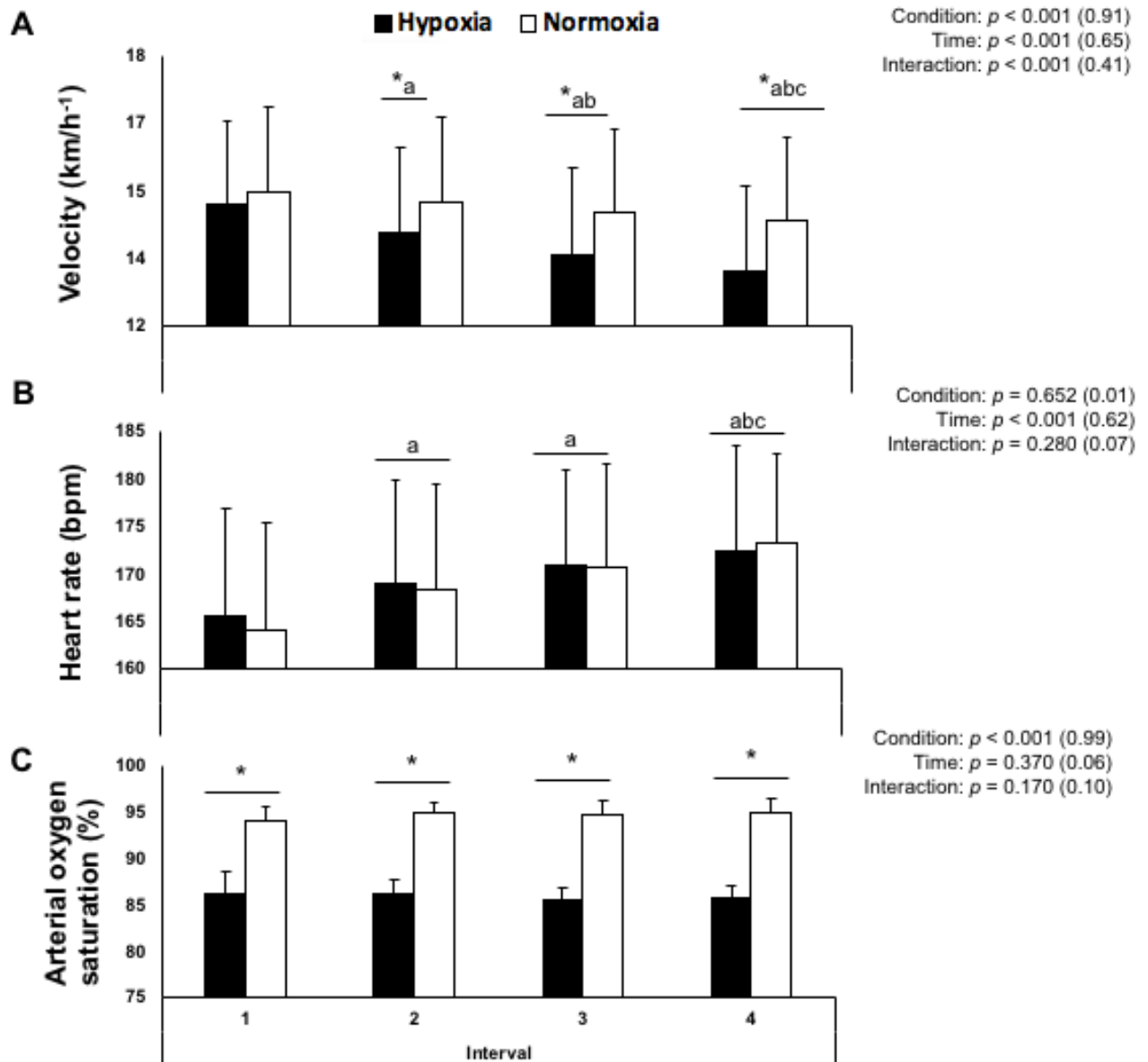
666
667 **196 Changes in SpO₂ and muscle oxygenation**
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669 197 SpO₂ was globally lower in HYP vs. NOR (-9.3% average across intervals; $p < 0.01$; Figure
670
671 198 1C), independently of time ($p = 0.37$). From interval 1 to 4, [O₂Hb] and [tHb] decreased (-
672
673 199 23.7% and -77.0%, respectively) whilst [HHb] increased (+44.9%; $p < 0.01$; Figures 2A–C),
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675
676 200 independently of condition ($p > 0.08$).
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678
679 **201 Changes in exercise-related sensations**
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681 202 Perceived recovery decreased progressively from interval 1 to 4 (-41.6%; $p < 0.01$), and more
682
683 203 so in HYP vs. NOR before intervals 2, 3 and 4 (-8.8%, -24.2% and -29.3%, respectively; $p =$
684
685 204 0.02; Figure 3A). Perceived motivation decreased progressively from interval 1 to 4 (-21.8%;
686
687 205 $p < 0.01$), and more so in HYP vs. NOR before intervals 3 and 4 (-20.3% and -22.4%,
688
689 206 respectively; $p < 0.01$; Figure 3B). Compared to interval 1, perceived breathlessness increased
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691 207 following intervals 2, 3 and 4 (+14.0%, +13.6% and +18.6%, respectively; $p < 0.01$; Figure
692
693 208 3C), independently of condition. Breathlessness was rated globally higher in HYP vs. NOR
694
695 209 (+21.8%; $p < 0.05$), irrespective of time. Compared to interval 1, perceived limb discomfort
696
697 210 increased following intervals 2, 3 and 4 (+23.3%, +35.3% and +44.0%, respectively; $p < 0.01$;
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699 211 Figure 3D), independently of condition. Limb discomfort was rated globally higher in HYP vs.
700
701 212 NOR (+11.3%; $p = 0.01$), irrespective of time. The time-dependent decreases in perceived
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213 pleasure across intervals (-14.7%, -25.4% and -32.3%, intervals 2, 3 and 4 vs. 1, respectively;
 214 $p < 0.01$; Figure 3E) tended to be larger in HYP vs. NOR (-31.3%, $p = 0.06$).



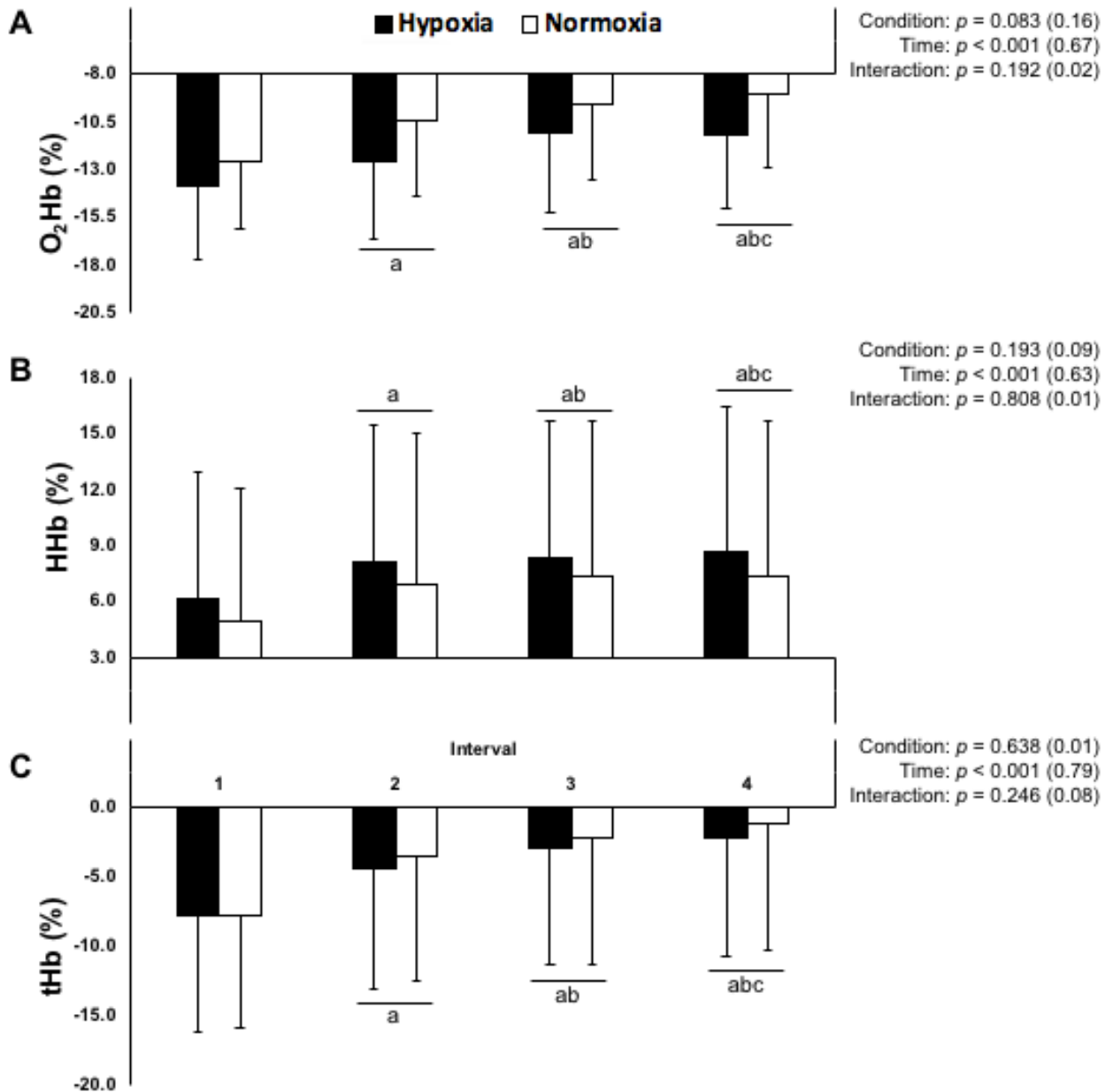
215 **Figure 1** Changes in velocity (A), heart rate (B) and arterial oxygen saturation (C) during the
 216 high-intensity intermittent running protocol. Data are presented as mean \pm SD. ANOVA main
 217 effects of time, condition and interaction are presented along with partial-eta squared for effect
 218 size into brackets. Black bars = hypoxic condition; white bars = normoxic condition. * denotes
 219 a statistically significant difference between conditions for a given interval ($p < 0.05$), a, b and
 220 c denotes a statistically significant difference vs. interval 1, 2 and 3, respectively ($p < 0.05$).
 221

222 **Changes in [La⁺] and attention and executive function**

223 The pre- to post-exercise increase in [La⁺] was larger ($p = 0.001$) in HYP (1.7 ± 0.8 vs. $13.1 \pm$
 224 3.8 mmol/l⁻¹) vs. NOR (2.1 ± 0.9 vs. 10.1 ± 3.9 mmol/l⁻¹). During the Stroop test, accuracy was

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

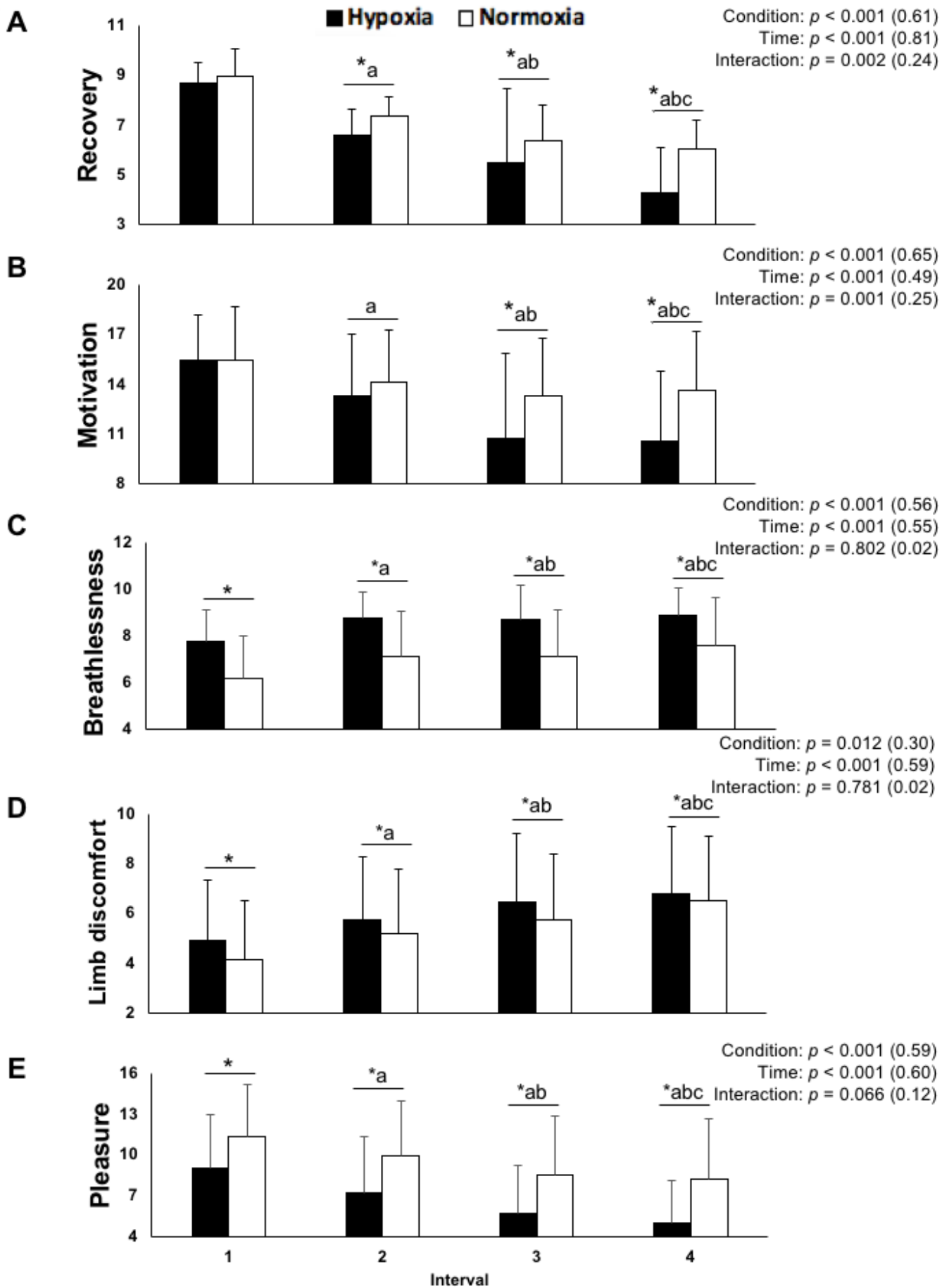
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228 **Figure 2** Changes in Oxygenated (A; O₂Hb), deoxygenated (B; HHb) and total hemoglobin
 229 (C; tHb) during the high-intensity intermittent running protocol. Data are calculated as a
 230 percentage difference from baseline (%) and presented as mean \pm SD. ANOVA main effects
 231 of time, condition and interaction are presented along with partial-eta squared for effect size
 232 into brackets. Black bars = hypoxic condition; white bars = normoxic condition. a, b and c
 233 denotes a statistically significant difference vs. interval 1, 2 and 3, respectively ($p < 0.05$).
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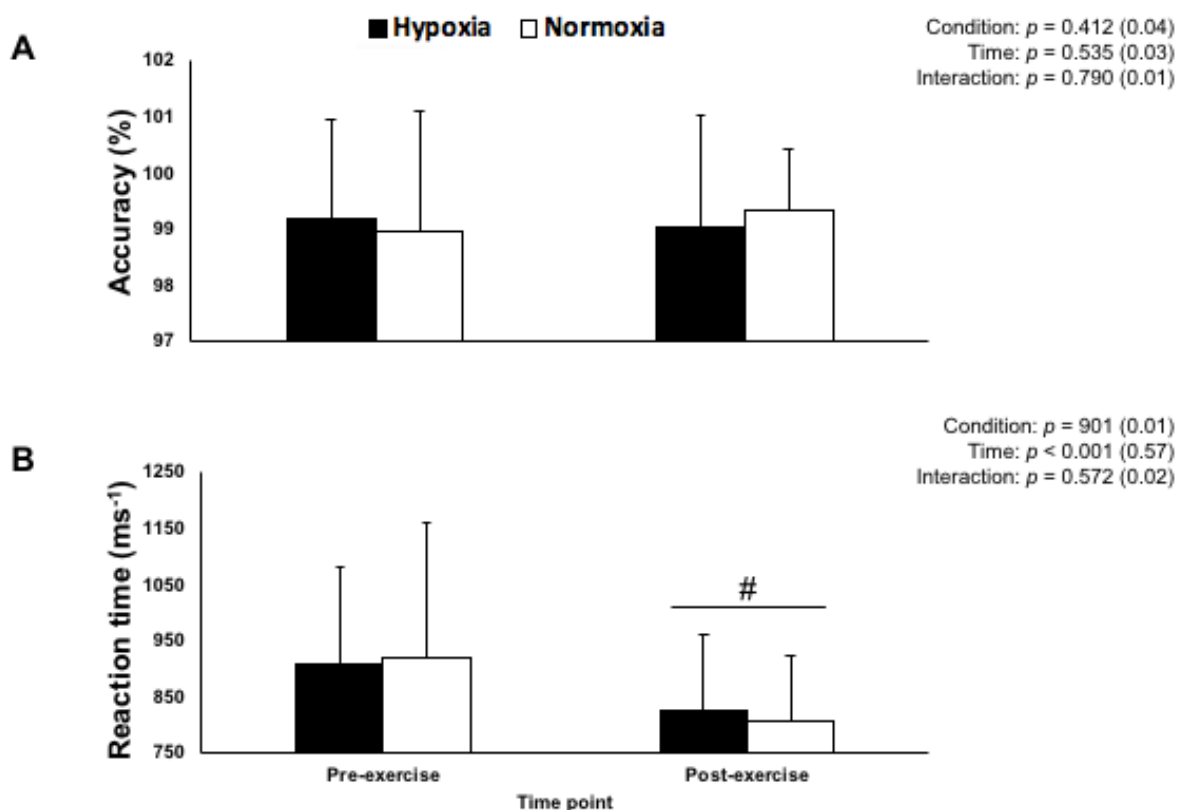
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237 **Figure 3** Changes in perceived recovery (A), motivation (B), breathlessness (C), limb
238 discomfort (D) and pleasure (E) during the high-intensity intermittent running protocol. Data
239 are presented as mean \pm SD. ANOVA main effects of time, condition and interaction are
240 presented along with partial-eta squared for effect size into brackets. Black bars = hypoxic
241 condition; white bars = normoxic condition. * denotes a statistically significant difference
242 between conditions for a given interval ($p < 0.05$), a, b and c denotes a statistically significant
243 difference vs. interval 1, 2 and 3, respectively ($p < 0.05$).



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

251 Discussion

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

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947 256 motivation and pleasure scores were stated during recovery between HYP vs. NOR, and 4)
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949 257 blood lactate concentration was larger after HYP vs. NOR. Overall, using a manipulation of
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951 258 oxygen availability, reduced external workload (i.e., running velocity) during perceptually-
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953 259 regulated interval running is associated with a similar internal load (i.e., physiological
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955 260 responses). Although no cognitive function differences were found between conditions, this is
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957 261 achieved with less favourable exercise-related sensations. **A matched internal workload for**
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959 262 **a decreased external workload during perceptually-regulated HIIT in hypoxia versus**
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961 263 **normoxia may assist athletes to reach intended session goals with minimal over-induced**
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963 264 **physiological stress. However, perceptually-regulated HIIT exacerbates exercise-related**
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965 265 **sensations and blood lactate concentrations in hypoxia compared to normoxia. This may**
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967 266 **then have negative carry-over effects on training responsiveness in the following days.**
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972 267 *Exercise intervals*

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974 268 The velocity deemed equal to RPE 16 (PRV) was as expected for **trained** runners (~15 km/h
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976 269 ¹⁾ (28). Interestingly, running velocity did not differ between conditions during the first **HIIT**
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978 270 interval, despite lower SpO₂ in hypoxia *versus* normoxia. Smith & Billaut (29) found
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980 271 maintained SpO₂ during repeated-sprinting in normoxia (20 × 5-s all out, 25-s recovery) until
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982 272 after the fifth sprint in national-level soccer players, whereby peak power significantly
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984 273 decreased compared to sprint one. Overall, it seems that initial decreases in SpO₂ (within
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986 274 interval one) do not necessarily impact on **HIIT** compared to sprint intervals.
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990 275 We found that participants selected a progressively slower running velocity during **HIIT** in
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992 276 both conditions. In highly-trained middle to long-distance runners, a 6% reduction in vVO_{2MAX}
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994 277 when running in hypoxia *versus* normoxia is acceptable to match the acute physiological stress
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996 278 induced (5). It can be suggested that self-selected velocity adjustments found in the current
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998 279 study to maintain RPE 16 are matched with modifications in hypoxic *versus* normoxic training
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1006 280 sessions employed by coaches and sport scientists for athletes (30). Decreased external
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1008 281 workloads have been reported by Pramsöhler et al. (31) during continuous cycling (seven 30-
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1010 282 min sessions over 3-wk), whereby participants cycled at -28% lower power output in hypoxia
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1012 283 ($\text{FiO}_2 = 15.3\%$) *versus* normoxia for a similar HR. Differences in these findings and ours may
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1014 284 be due to the inclusion of geriatric patients completing pre-set (in normoxia) fixed-intensity
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1016 285 cycling compared to **trained** runners self-regulating **HIIT** in the current study. However,
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1018 286 Fernández-Menéndez et al. (10) reported preferred walking velocity (RPE of 10) in hypoxia
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1020 287 ($\text{FiO}_2 = 15.3\%$) was 7% slower than normoxia in obese adults over 3 weeks. Using a self-paced
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1022 288 model, irrespective of RPE target, population demographics and training block duration, lower
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1024 289 external workloads are selected in hypoxia compared to normoxia. Overall, decreases in self-
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1026 290 paced running velocity occurred to a greater extent in hypoxia than normoxia to maintain RPE
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1028 291 16, suggesting of a lower external workload. **This finding may be of benefit to athletes who**
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1030 292 **are unable or advised by their coach not to be training at a full intensity. Completing**
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1032 293 **perceptually-regulated HIIT in hypoxia that requires slower running velocities compared**
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1034 294 **to normoxia may in turn minimise mechanical constraints and eventually injury risk.**
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1039 295 Our data show HR increased progressively during **HIIT**, irrespective of condition. This
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1041 296 matches our hypothesis that HR will be comparable between hypoxia and normoxia, even
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1043 297 though running velocity was lower in hypoxia. Other studies employing moderate continuous-
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1045 298 intensity exercise have also found matched HR responses between hypoxic and normoxic
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1047 299 training interventions (~4 weeks) when cycling at a -21.0% power output in healthy males (32)
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1049 300 and walking/running at a -17.5% velocity in obese adults (33) in hypoxia *versus* normoxia.
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1051 301 Although exercise intensities in these studies were fixed, we believe similar increases in HR
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1053 302 between conditions occur due to the environmental stressor (hypoxia) augmenting autonomic
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1055 303 cardiac regulation (34). Overall, it seems self-paced exercise in hypoxia provides an added
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1065 304 environmental stressor that is able to mimick HR responses in normoxia for a lower external
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1067 305 load.
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1070 306 Lower [O₂Hb] and [tHb], and greater [HHb] of the *vastus lateralis* were recorded across **HIIT**,
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1072 307 irrespective of condition. Decreases in [O₂Hb] and increases in [HHb] were expected during
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1074 308 **HIIT** as oxygen delivery is outweighed by utilisation, whilst decreases in [tHb] reflect a lower
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1076 309 localised blood flow (35). Active musculature oxygenation is negatively impacted during
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1078 310 fixed-intensity exercise in hypoxia compared to normoxia due to a lower FiO₂ (7). In support
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1080 311 of this, Chacaroun et al. (11) reported lower [O₂Hb] and greater [HHb] with maintained [tHb]
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1082 312 of the *vastus lateralis* during fixed, relative high-intensity cycling in hypoxia (85% maximal
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1084 313 power output in normoxia; FiO₂ = 13.5%) *versus* normoxia. Where we employed a self-paced
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1086 314 exercise model, similar [O₂Hb] and [HHb] responses are achieved between conditions. This is
1087
1088 315 likely explained through the decreased workload (i.e., slower running velocity) in hypoxia
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1090 316 compared to normoxia, subsequently lowering oxygen utilisation. Discrepant findings in [tHb]
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1092 317 may be due to different exercise modalities (cycling *versus* running) modifying blood flow
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1094 318 regulation (36). Similar to HR responses (central) previously discussed, it can be suggested
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1096 319 here that local (tissue oxygenation) physiological stress is matched between conditions during
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1098 320 **HIIT** in hypoxia at a slower velocity compared with normoxia.
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1102 321 Elevations in [La⁺] following **HIIT** were higher in HYP than NOR. Values in the current study
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1104 322 (10–13 mmol/l⁻¹) are somewhat higher than those (5–6 mmol/l⁻¹) reported elsewhere following
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1106 323 a single **HIIT** session (6 × 4-min intervals at a RPE ~17, 4-min recoveries) (19). This maybe
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1108 324 due to a 1:0.75 work:rest ratio implemented during our protocol compared to 1:1 employed by
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1110 325 Seiler & Sjursen (19). [La⁺] normalization during shorter recovery periods may not occur to
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1112 326 the extent following longer recovery periods due to excess pyruvate accumulation (37). This
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1114 327 suggests that **HIIT** in hypoxia *per se* leads to increased **[La⁺]** at slower running velocities
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1116 328 compared to normoxia for similar physiological stress amounts. **Practitioners should be**

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

333 *During recovery*

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

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

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1183 353 et al. (5) reported that 3-min absolute-intensity running intervals (84% $v\dot{V}O_{2MAX}$) in hypoxia
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1185 354 ($FiO_2 = 15.4\%$) led to larger perceived limb discomfort compared to a lower absolute intensity
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1187 355 in normoxia (90% $v\dot{V}O_{2MAX}$). We expected exercise-related sensations to be similar between
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1189 356 conditions as participants could adjust their velocity where necessary. However, this was not the
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1191 357 case. Similar responses have been shown elsewhere (42), with greater perceived overall
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1193 358 discomfort, breathlessness and limb discomfort following progressive, sub-maximal, self-
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1195 359 paced cycling intervals (RPE = 3; modified CR10 Borg scale) in hypoxia ($FiO_2 = 13.0\%$)
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1197 360 compared to normoxia at a similar power output. Perceived breathlessness, limb discomfort
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1199 361 and pleasure are exercise-related sensations contributing to overall RPE during exercise (16).
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1201 362 However, there is a detachment between these when immediately assessed after **HIT** intervals.
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1203 363 We suggest that self-paced **HIT** in hypoxia leads to unfavourable exercise-related sensations
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1205 364 before and after running intervals, compared to normoxia.

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1210 365 *Pre- and post-exercise*

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1212 366 During the Stroop test, alertness increased (i.e., faster reaction time) whilst accuracy was
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1214 367 maintained following **HIT**, irrespective of condition. It is well known that **HIT** in normoxia
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1216 368 generally increases cognitive performance *versus* rest (i.e., faster reaction time, better
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1218 369 accuracy) (43). However, during fixed-intensity exercise in hypoxia, cognitive performance
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1220 370 (i.e., attention and executive function) is worsened compared to normoxia (17,18). We report
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1222 371 that even though exercise-related sensations were worsened during **HIT**, cognitive
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1224 372 performance (assessed post-**HIT**) was not negatively affected. Ochi et al. (18) reported
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1226 373 decreased Stroop performance 15 mins after 10 mins of moderate-continuous intensity exercise
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1228 374 (50% peak oxygen uptake) in hypoxia ($FiO_2 = 13.5\%$) *versus* normoxia. Our results likely
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1230 375 differ to the aforementioned study due to cognitive testing performed in normoxia and
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1232 376 following different exercise modalities. Our data show that alertness is increased following
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1234 377 **HIT**, and not negatively impacted by hypoxia.

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1242 378 *Limitations and perspectives*
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1245 379 During self-paced exercise at a perceptually-regulated intensity in hypoxia, HR and muscle
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1247 380 oxygenation responses are similar to normoxia for a lower running velocity. However, we used
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1249 381 a single “hypoxic dose” (i.e., hypoxic severity and duration), target RPE and exercise duration
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1251 382 during **HIIT**. Further investigations should refine self-selected protocols in hypoxia, such as
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1253 383 the “hypoxic dose”, target RPE and exercise duration to minimise the negative side effects of
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1255 384 worsened exercise-related sensations found under the present circumstances. **In addition,**
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1257 385 **whether there are gender differences in response to hypoxic exposure during**
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1259 386 **perceptually-regulated HIIT should be investigated, given that our final sample size (n =**
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1261 387 **19) included only three females.**
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1268 389 **Conclusion**
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1271 390 When carrying out **HIIT** at a perceptually-regulated intensity (RPE equal to 16), larger running
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1273 391 velocity decreases are needed in hypoxia than normoxia. This is accompanied by similar
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1275 392 physiological stress (i.e., HR and muscle oxygenation) during **HIIT**, and cognitive function
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1277 393 adjustments after. In hypoxia, exercise-related sensations and blood lactate concentrations were
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1279 394 higher-than-normal with larger peripheral oxygen desaturation. Overall, perceptually-regulated
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1281 395 running velocity in hypoxia compared to normoxia may be an effective alternative, at the
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1283 396 expense of less favourable exercise-related sensations. **Our results suggest that athletes**
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1285 397 **under the influence of hypoxia require lower external workloads to reach a perceptually-**
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1287 398 **regulated target during HIIT than normoxia. If employed in a practical setting, coaches**
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1289 399 **should consider the potential of negatively implicated exercise-related sensations and**
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1291 400 **blood lactate concentrations which may have further negative carry-over effects on**
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1293 401 **training responsiveness in the following days.**
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407

408 Conflict of interest

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

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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 SpO₂ 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.

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1 **Title**

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

5 **Author names and affiliations**

6 Hobbins L^a, Gaoua N^a, Hunter S^a, Girard O^{bc}

8 ^aSport and Exercise Science Research Centre (SESRC), London South Bank University,
9 London, United Kingdom

10 ^bMurdoch Applied Sports Science (MASS) Laboratory, Murdoch University, Perth, Australia

11 ^cAthlete Health and Performance Research Center, ASPETAR, Qatar Orthopedic and Sports
12 Medicine Hospital, Doha, QATAR

14 **Corresponding author**

15 Mr. Liam Hobbins

16 hobbinsl@lsbu.ac.uk

17 Sport and Exercise Science Research Centre

18 London South Bank University

19 103 Borough Road

20 London

21 SE1 0AA

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62 **1 Abstract**
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64

65 2 We investigated whether perceptually-regulated high-intensity intervals in hypoxia are
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67 3 associated with slower running velocities *versus* normoxia, when physiological responses and
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69 4 exercise-related sensations remain the same. Nineteen trained runners (33.4 ± 9.1 years)
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71 5 completed a high-intensity interval running protocol (4×4 -min intervals at a clamped
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73 6 perceived rating exertion of 16 on the 6–20 Borg scale, 3-min passive recoveries) in either
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75 7 hypoxic (HYP; FiO_2 15.0%) or normoxic (NOR; FiO_2 20.9%) conditions. Participants adjusted
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77 8 to a progressively slower running velocity from interval 1–4 (-7.0%), and more so in HYP *vs.*
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79 9 NOR for intervals 2, 3 and 4 (-4.6%, -6.4% and -7.9%, respectively; $p < 0.01$). Heart rate
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81 10 increased from interval 1–4 (+4.8%; $p < 0.01$), independent of condition. Arterial oxygen
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83 11 saturation was lower in HYP *vs.* NOR (86.0% *vs.* 94.8%; $p < 0.01$). Oxyhemoglobin (-23.7%)
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85 12 and total hemoglobin (-77.0%) decreased, whilst deoxyhemoglobin increased (+44.9%) from
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87 13 interval 1–4 ($p < 0.01$), independent of condition. Perceived recovery (-41.6%) and motivation
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89 14 (-21.8%) were progressively lower from interval 1–4, and more so in HYP *vs.* NOR for
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91 15 intervals 2, 3 and 4 (recovery: -8.8%, -24.2% and -29.3%; motivation: -5.3%, -20.3% and -
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93 16 22.4%, respectively; $p < 0.01$). Perceived breathlessness (+18.6%), limb discomfort (+44.0%)
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95 17 and pleasure (-32.2%) changed from interval 1–4, with significant differences (+21.8%,
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97 18 +11.3% and -31.3%, respectively) between HYP and NOR ($p < 0.01$). Slower interval running
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99 19 velocities in hypoxia achieve similar heart rate and muscle oxygenation responses to those
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101 20 observed in normoxia when perceptually-regulated, yet at the expense of less favourable
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103 21 exercise-related sensations.
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23 **Key words**

24 High-intensity intermittent running; normobaric hypoxia; perceptually-regulated exercise;

25 ratings of perceived exertion; near-infrared spectroscopy; effort perception.

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180 **1 Introduction**
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183 2 High-intensity interval training (HIIT) is a popular exercise format in athletic and clinical
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185 3 populations (1,2). HIIT includes repeated short-to-long (2–5 min) intense exercise bouts (80–
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187 4 90% of the velocity associated with maximal oxygen uptake or $v\text{VO}_{2\text{Max}}$) interspersed with
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189 5 shorter (1–3 min) recoveries (3). Compared to moderate-intensity continuous running, HIIT
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191 6 leads to similar improvements in cardiorespiratory fitness that is achieved with a shorter
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193 7 effective exercise duration per session (2). Due to the reduced time-commitment and exercise
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195 8 training volume, investigations surrounding the potential physiological and performance
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197 9 benefits of HIIT have surged (4).

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201 10 HIIT in normobaric hypoxia (a lower inspired oxygen fraction or FiO_2) is receiving attention
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203 11 for its potential in further advancing athletic performance compared to HIIT in normoxia.
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205 12 Buchheit et al. (5) employed a HIIT protocol (3 × 5-min, 90-s recovery) carried out in hypoxia
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207 13 ($v\text{VO}_{2\text{Max}} = 84\%$; $\text{FiO}_2 = 15.4\%$) and normoxia ($v\text{VO}_{2\text{MAX}} = 90\%$) at a fixed-intensity
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209 14 (determined in normoxia) in highly-trained runners. A reduced physiological stress (i.e., lower
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211 15 heart rate or HR) was observed during hypoxia compared to normoxia, likely due to a lower
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213 16 $v\text{VO}_{2\text{Max}}$ in hypoxia *versus* normoxia. However, fixed exercise intensities, regardless of
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215 17 environmental conditions, do not permit adjustments (i.e., increases or decreases of workload)
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217 18 during exercise to match the intensity target (i.e., $v\text{VO}_{2\text{MAX}}$). In turn, over-induced
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219 19 physiological stress may be counter-productive (i.e., greater deoxygenated muscle
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221 20 heamoglobin, lower oxygenated haemoglobin) for intended session goals (6). Furthermore,
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223 21 matched absolute fixed exercise intensities (i.e., a similar percentage of $v\text{VO}_{2\text{MAX}}$) lead to
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225 22 greater physiological stress (i.e., compensatory increase in HR) in hypoxia compared to
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227 23 normoxia due to reduced FiO_2 (7). Perceptually-regulated exercise intensities, that allow
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229 24 velocity adjustments based upon exercise-related sensations in order to maintain a target effort
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239 25 level, may offer a viable solution, and is perhaps more reflective of how exercisers modify
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241 26 intensity during acute exercise.
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244 27 Perceptually-regulated exercise permits the individual exercising to self-regulate external
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246 28 workload (i.e., running velocity/cycling power production) based upon Borg's rating of
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248 29 perceived exertion (RPE) scale (8). The validity and usefulness of using RPE for perceptually-
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250 30 regulating exercise has been described (9). The reduced oxygen availability in hypoxia makes
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252 31 the expectation tenable that there would be a slower self-selected running velocity in hypoxia
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254 32 for a given RPE, while velocity in normoxia would be more preserved, as evidenced previously
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256 33 (10). Chacaroun et al. (11) demonstrated for a lower power output (-15%), *vastus lateralis*
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258 34 muscle deoxyhemoglobin was higher and oxyhemoglobin lower in hypoxia ($FiO_2 = 13.5\%$)
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260 35 compared to normoxia during a single interval session (15×1 -min at 75% of maximal HR, 1-
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262 36 min recoveries). Although HR was similar between conditions, RPE has been reported to be
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264 37 higher in hypoxia compared to normoxia during fixed-intensity interval runs (5) and repeated-
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266 38 sprint cycling (12). Employing self-paced exercise, in replace of fixed-intensity exercise, may
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268 39 assist in overcoming the over-excessive physiological stress observed when exercising in
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270 40 hypoxia *versus* normoxia, due to the likelihood of greater velocity preservations in the latter
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272 41 than the former.
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276 42 In normoxia at pre-determined fixed intensities, HIIT is perceived as more enjoyable compared
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278 43 to moderate-intensity continuous running (13). However, during HIIT at fixed-intensities,
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280 44 exercise-related sensations decrease when the exercise intensity rises above threshold
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282 45 preference (14). Further, HIIT in hypoxia at fixed-intensities typically surpasses the preferred
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284 46 threshold in normoxia (15). Implementing a self-paced exercise model may permit
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286 47 modifications required (i.e., slower running velocities) to maintain exercise-related sensations
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288 48 contributing to RPE (16) in hypoxia and normoxia. Cycling continuously for 10 min at a fixed-
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290 49 intensity (corresponding to 50% VO_{2Max}) in hypoxia *versus* normoxia negatively impacts
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298 50 cognitive function (17). Slower self-selected running velocities may assist with mitigating
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300 51 hypoxic-induced negative cognitive function compared to normoxia (18). These potential
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302 52 findings may benefit athletes exercising intensely in hypoxia, shortly followed by skills
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304 53 requiring attention and accuracy.
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307 54 Therefore, the aim of this study was to investigate the effect of HIIT at a clamped RPE of 16
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309 55 (typically used by athletes during HIIT) (19) in hypoxia and normoxia on adjustments in
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311 56 running velocity and associated exercise-related sensations of trained runners. We
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313 57 hypothesized that running velocity would be progressively slower in hypoxia compared to
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315 58 normoxia across intervals, whilst physiological and cognitive responses, and exercise-related
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317 59 sensations would not differ between conditions. Decreasing external load with matched internal
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319 60 load during perceptually-regulated HIIT in hypoxia compared to normoxia may benefit athletes
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321 61 during heavy training blocks prior to competition.
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328 63 **Methods**

331 64 *Participants*

334 65 Nineteen trained runners (3 females, 16 males; age: 33.4 ± 9.1 years; height: 176 ± 88 cm;
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336 66 weight: 76.3 ± 10.9 kg) provided written informed consent to participate. Participants had no
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338 67 musculoskeletal injuries and met the following eligibility criteria: a training volume ≥ 6 h/wk,
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340 68 free of clinical signs of disease, orthopedic, neurological, cardiovascular or respiratory
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342 69 problems, and no hypoxic exposure >2000 m for >48 h 6 months before the study. The study
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344 70 was carried out in accordance with the Declaration of Helsinki and was approved by the Ethics
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346 71 Committee of the Anti-Doping Lab Qatar institutional review board (Agreement SCH-ADL-
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348 72 170). A-priori sample size was calculated using G*Power (Version 3.1.9.3). This was
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357 73 determined using published power output data by Jeffries et al. (20), whereby healthy
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359 74 individuals cycled at a perceptually-regulated intensity (RPE = 16) in hypoxic ($\text{FiO}_2 = 15.0\%$)
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361 75 and normoxic conditions. Twenty-one participants were deemed sufficient to yield a power of
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363 76 0.8 at an α probability of 0.05. Two individuals dropped out due to injuries sustained during
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365 77 their time enrolled onto the study, not associated with the HIIT protocols we employed.
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368 78 *Experimental design*

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371 79 Participants reported to the laboratory on three occasions, each separated by ≥ 48 h. The first
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373 80 session included study familiarisation. The second and third visits included completing a HIIT
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375 81 protocol in either hypoxia or normoxia in a randomized, counterbalanced order. Physiological,
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377 82 perceptual and cognitive responses were assessed continuously, immediately before and after
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379 83 each interval, and before and after the HIIT protocol, respectively. Participants were instructed
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381 84 to refrain from any intense exercise 48 h prior to each visit and consume their last meal at least
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383 85 2 h prior to the HIIT sessions. To minimise the impact of social desirability bias, participants
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385 86 were made aware of the purpose of the study but were naïve to experimental hypotheses.
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387 87 Laboratory conditions were similar throughout all sessions (mean temperature $\sim 22^\circ\text{C}$, relative
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389 88 humidity $\sim 50\%$) and time of day was standardized for each participant.
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393 89 *Familiarization session*

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396 90 At the preliminary visit to the laboratory, participants were familiarised with the perceptual
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398 91 scales and cognitive test. Preferred running velocity (PRV) was determined for each participant
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400 92 in normoxia using a modified version of identifying preferred walking speed (21). After a 5-
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402 93 min warm up at 10 km/h^{-1} , participants completed four ramped treadmill runs (increasing and
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404 94 decreasing velocities) on an instrumented treadmill (ADAL3D-WR, Medical Development-
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406 95 HEF Tecmachine, France). After every 20 s per ramp, participants rated their RPE of the
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408 96 current velocity (controlled by the investigator and out of sight of the participant) in accordance
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416 97 with Borg's (20) 6 ("no exertion at all") – 20 ("maximal exertion") numeric scale. Ramp one
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418 98 started at 10 km/h⁻¹, increasing by 0.8 km/h⁻¹ every 20 s until the velocity was considered as
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420 99 RPE ≥18; ramp two started at +1.5 km/h⁻¹ the previous end velocity, decreasing by 0.8 km/h⁻¹
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423 100 until the velocity was considered as RPE ≤12; ramp three started at the velocity considered as
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425 101 an RPE of 14 in ramp two, increasing by 0.5 km/h⁻¹ until the velocity was considered as RPE
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427 102 ≥18; and ramp four started at +1.0 km/h⁻¹ the previous end velocity, decreasing by 0.5 km/h⁻¹
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429 103 until the velocity was considered as RPE ≤12. Ramps two, three and four began once the
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431 104 participants declared their perceived recovery level as a 7 out of 10 following the previous
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433 105 ramp (23). HR was recorded every 20-s through each ramp. PRV corresponded to the velocity
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435 106 participants considered as a RPE of 16 (between "hard" and "very hard") or closest to a HR of
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437 107 160 bpm. After 10 min of rest, participants completed one 4-min interval composing the HIIT
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439 108 protocol (see below) for habituation.
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443 109 *Experimental trials*

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446 110 Participants completed two experimental trials in normoxia (NOR; FiO₂ = 20.9%) and hypoxia
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448 111 (HYP; FiO₂ = 15.0%, equivalent to ~2700 m above sea level). After a standardised warm up
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450 112 (5-min at 10 km/h⁻¹), a facemask connected to a portable hypoxic generator (See *Hypoxic*
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452 113 *simulation* section) was attached. Participants rested for 1-min (quiet standing) before a 1-min
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454 114 run at their PRV (RPE = 16). Participants then rested for 3 min before completing the HIIT
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456 115 protocol. The HIIT protocol was based upon aerobic interval-training (2). Participants
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458 116 completed four, 4-min intervals, interspersed with 3-min recoveries (quiet standing). The first
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460 117 30 s of each 4-min interval began at participants' PRV; participants were then free to decide if
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462 118 or how treadmill velocity needed to be adjusted (manually by one experimenter) to ensure
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464 119 maintenance of a RPE of 16 every 30 s. Participants hand-signalled in response to the current
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466 120 velocity (finger up to increase, finger down to decrease, and circle using index finger and thumb
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475 121 to maintain); and signalled again to inform how much of an increase/decrease in velocity is
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477 122 required [1, 2 or 3 fingers up (faster) or down (slower) for 0.5, 1.0 or 1.5 km/h⁻¹ changes,
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479 123 respectively]. Signals were trialled during familiarisation. Mild verbal encouragement to keep
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481 124 running at an RPE of 16 was used throughout HIIT. Total hypoxic exposure corresponded to
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483 125 exactly 28 min.

486 126 *Hypoxic simulation*

489 127 Participants were fitted with a facemask fastened with a Velcro headset connected via plastic
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491 128 tubing to a hypoxic generator (Altitrainer, SMTec SA, Nyon, Switzerland) to simulate hypoxia.
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493 129 The gas mixing system enriches inspired air by adding a fixed quantity of nitrogen via a 30-L
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495 130 mixing chamber, with the dilution being constantly controlled by a PO₂ probe (precision =
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497 131 T0.82 torr, safety FiO₂ = 9.7%). The hypoxic generator was hidden from participant viewing
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499 132 to ensure condition blinding. When breathing ‘normal air’ during normoxia, the hypoxic
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501 133 generator was on (for background noise) and set at a simulated altitude of 100 m to increase
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503 134 the strength of blinding.

507 135 *Measures*

510 136 *Exercise intervals*

513 137 HR was monitored telemetrically with a Polar transmitter-receiver (Polar S810, Kempele,
514
515 138 Finland) and recorded 20 s before and every 30 s during each interval. Arterial oxygen
516
517 139 saturation (SpO₂) was assessed via finger pulse oximetry (Palmsat 2500, NONIN Medical
518
519 140 Inc., Plymouth, MI, USA) at the same time intervals. HR and SpO₂ were obtained before (i.e.,
520
521 141 after a 2-min seated period) and at the end of the warm-up procedure (i.e., prior to HIIT). Both
522
523 142 the HR watch (RS400, Polar) and oximeter receiver were attached on the handrails of the
524
525 143 treadmill outside of the participants’ view.

532
533
534 144 Muscle oxygenation trends of the right *vastus lateralis* muscle were recorded using near-
535
536 145 infrared spectroscopy (NIRS; Portalite, Artinis, Netherlands) in real-time. A wireless bi-polar
537
538 146 optode sensor was attached (~10 cm above the proximal patella border) and secured to skin via
539
540 147 adhesive tape. Sampling frequency was set at 10 Hz (11) following a ‘zero set’ of all signals.
541
542 148 Bandages were fastened around the lower limb and optode to prevent external light distorting
543
544 149 readings. Oxy- (Δ ; [O₂Hb]), deoxy- (Δ ; [HHb]) and total haemoglobin (μmol ; [tHb]) were
545
546 150 exported (1 Hz). For analysis, each interval was averaged and normalized to a 10 s sample prior
547
548 151 to interval one (reference value) for each respective condition and presented as percentage
549
550 152 change.

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552
553
554 153 *During recovery*
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556
557 154 Perceived recovery and motivation to exercise were assessed 30 s before each interval.
558
559 155 Perceived recovery was assessed by answering ‘*how recovered do you feel currently?*’ via a
560
561 156 numeric scale, ranging from 0 (“*very poorly recovered*”) to 10 (“*very well recovered*”) (23).
562
563 157 Recovery was assessed before interval one to determine perceptions following the warm up.
564
565 158 Perceived motivation to exercise was assessed via a 20-cm visual analog scale (24).
566
567 159 Participants were asked ‘*how motivated do you feel to exercise right now?*’ and answered by
568
569 160 adjusting the level on the scale between 0 (“*extremely low*”; white colored) and 20 (“*extremely*
570
571 161 *high*”; black colored). Immediately after each interval, ratings of perceived breathlessness, limb
572
573 162 discomfort and pleasure were assessed. Perceived breathlessness was assessed by answering
574
575 163 ‘*how does your breathing feel currently?*’ via a numeric scale, ranging from 0 (“*nothing at*
576
577 164 *all*”) to 10 (“*very, very severe*”) (25). Using the same scale, perceived limb discomfort was
578
579 165 assessed by answering ‘*how do your legs feel currently?*’. A 20-cm visual analog scale (same
580
581 166 as motivation above) was used to assess ‘*how pleasant was that run?*’ ranging from 0
582
583 167 (“*extremely unpleasant*”) and 20 (“*extremely pleasant*”).
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593 168 *Pre- and post-exercise*
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596 169 A capillary blood sample taken from the fingertip was analyzed for blood lactate concentration
597
598 170 ($[La^+]$) with the Lactate Pro (LT-1710, Arkray, Japan) portable analyzer before the warm-up
599
600 171 and 2 min after HIIT. An offline Stroop colour-word test (26) assessed attention and executive
601
602 172 function. Using one hand and as quickly as possible, participants selected the colored key on
603
604 173 the keyboard representing the color of the text appearing on the screen (red, yellow, green or
605
606 174 blue). The cognitive test lasted for 3 min, and took place in a silent environment before the
607
608 175 warm up and 3 min after HIIT. Reaction time (ms; time taken to select a color) and accuracy
609
610 176 (%; correct color selected) were averaged over each test for analysis.
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614 177 *Statistical analysis*
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617 178 Data distribution was assessed via a Shapiro-Wilk test. A parametric within-subject two-way
618
619 179 analysis of variance was used to investigate the main effect of condition (NOR vs. HYP), time
620
621 180 (interval 1, 2, 3 vs. 4 or pre vs. post) and the condition \times time interaction for normally
622
623 181 distributed data. Partial eta-squared (η^2) was calculated as a measure of effect size. Values of
624
625 182 0.01, 0.06 and above 0.14 were considered as small, medium and large, respectively (27). A
626
627 183 related samples Friedman's non-parametric test was used for data not normally distributed.
628
629 184 Bonferroni post-hoc pairwise comparisons were used to identify locations of significant effects.
630
631 185 Statistical testing was carried out in SPSS (v21; CED, Cambridge, United Kingdom). Data was
632
633 186 considered significant if $p \leq 0.05$. All data are presented as group means \pm SD.
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640 188 **Results**
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643 189 *Changes in velocity and HR*
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652 190 Compared to interval 1, participants adjusted to a progressively slower running velocity during
653
654 191 intervals 2, 3 and 4 (-2.8%, -5.2% and -7.0%, respectively; $p < 0.01$), and more so in HYP vs.
655
656 192 NOR for intervals 2, 3 and 4 (-4.6%, -6.4% and -7.9%, respectively; $p < 0.01$; Figure 1A).
657
658 193 Compared to interval 1, HR increased during intervals 2, 3 and 4 (+2.3%, +3.6% and 4.8%,
659
660 194 respectively; $p < 0.01$; Figure 1B), independently of condition ($p = 0.65$).

663
664 195 *Changes in SpO₂ and muscle oxygenation*

665
666 196 SpO₂ was globally lower in HYP vs. NOR (-9.3% average across intervals; $p < 0.01$; Figure
667
668 197 1C), independently of time ($p = 0.37$). From interval 1 to 4, [O₂Hb] and [tHb] decreased (-
669
670 198 23.7% and -77.0%, respectively) whilst [HHb] increased (+44.9%; $p < 0.01$; Figures 2A–C),
671
672 199 independently of condition ($p > 0.08$).

673
674 200 *Changes in exercise-related sensations*

675
676 201 Perceived recovery decreased progressively from interval 1 to 4 (-41.6%; $p < 0.01$), and more
677
678 202 so in HYP vs. NOR before intervals 2, 3 and 4 (-8.8%, -24.2% and -29.3%, respectively; $p =$
679
680 203 0.02; Figure 3A). Perceived motivation decreased progressively from interval 1 to 4 (-21.8%;
681
682 204 $p < 0.01$), and more so in HYP vs. NOR before intervals 3 and 4 (-20.3% and -22.4%,
683
684 205 respectively; $p < 0.01$; Figure 3B). Compared to interval 1, perceived breathlessness increased
685
686 206 following intervals 2, 3 and 4 (+14.0%, +13.6% and +18.6%, respectively; $p < 0.01$; Figure
687
688 207 3C), independently of condition. Breathlessness was rated globally higher in HYP vs. NOR
689
690 208 (+21.8%; $p < 0.05$), irrespective of time. Compared to interval 1, perceived limb discomfort
691
692 209 increased following intervals 2, 3 and 4 (+23.3%, +35.3% and +44.0%, respectively; $p < 0.01$;
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694 210 Figure 3D), independently of condition. Limb discomfort was rated globally higher in HYP vs.
695
696 211 NOR (+11.3%; $p = 0.01$), irrespective of time. The time-dependent decreases in perceived
697
698 212 pleasure across intervals (-14.7%, -25.4% and -32.3%, intervals 2, 3 and 4 vs. 1, respectively;
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700 213 $p < 0.01$; Figure 3E) tended to be larger in HYP vs. NOR (-31.3%, $p = 0.06$).

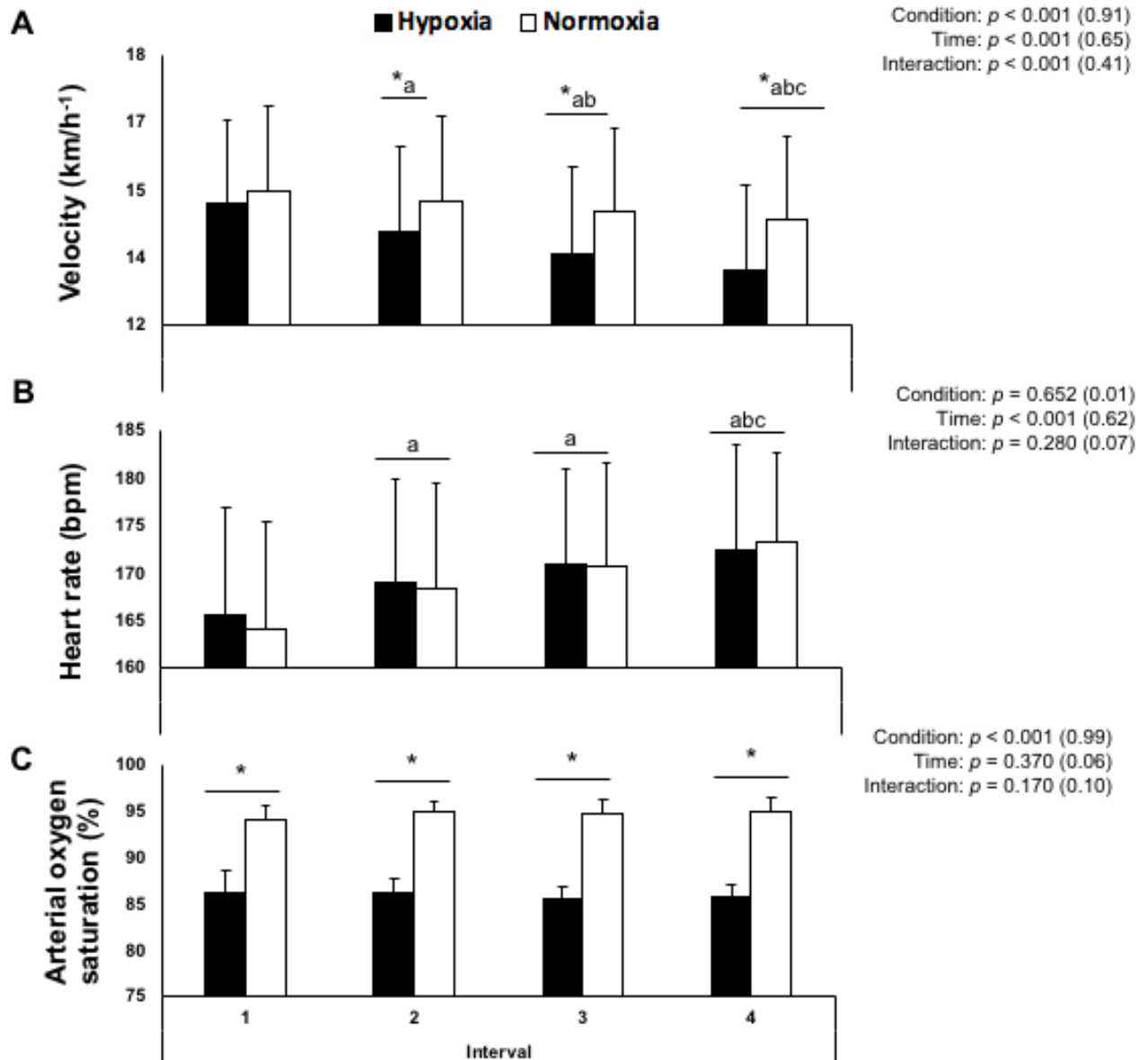


Figure 1 Changes in velocity (A), heart rate (B) and arterial oxygen saturation (C) during the high-intensity intermittent running protocol. Data are presented as mean \pm SD. ANOVA main effects of time, condition and interaction are presented along with partial-eta squared for effect size into brackets. 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 ($p < 0.05$).

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

222 The pre- to post-exercise increase in $[La^+]$ was larger ($p = 0.001$) in HYP (1.7 ± 0.8 vs. $13.1 \pm$
 223 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
 224 unaffected by condition and time (Figure 4A). Participants' reaction time was faster (+11%)
 225 post vs. pre HIIT ($p < 0.01$; Figure 4B), independently of condition.

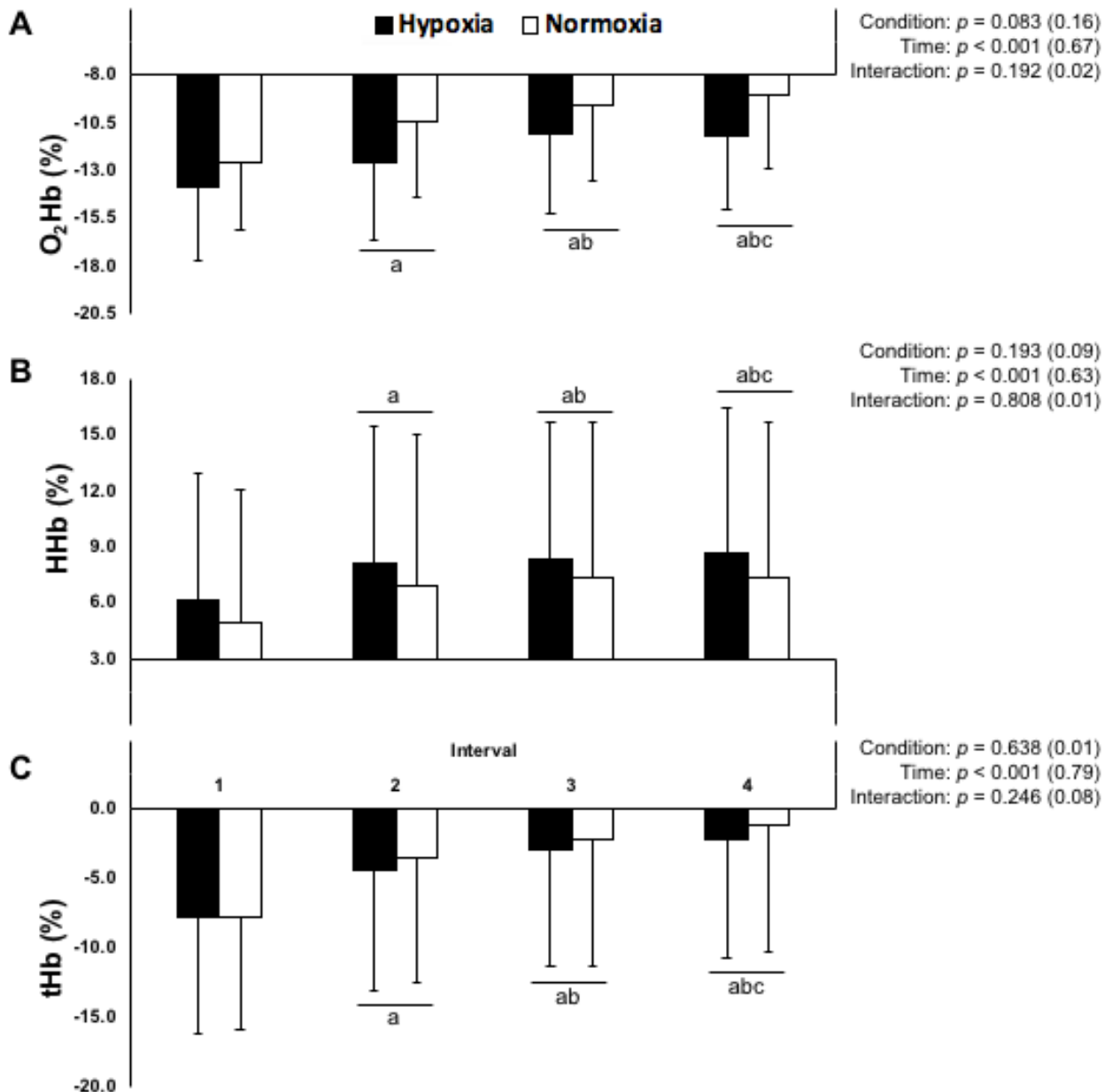
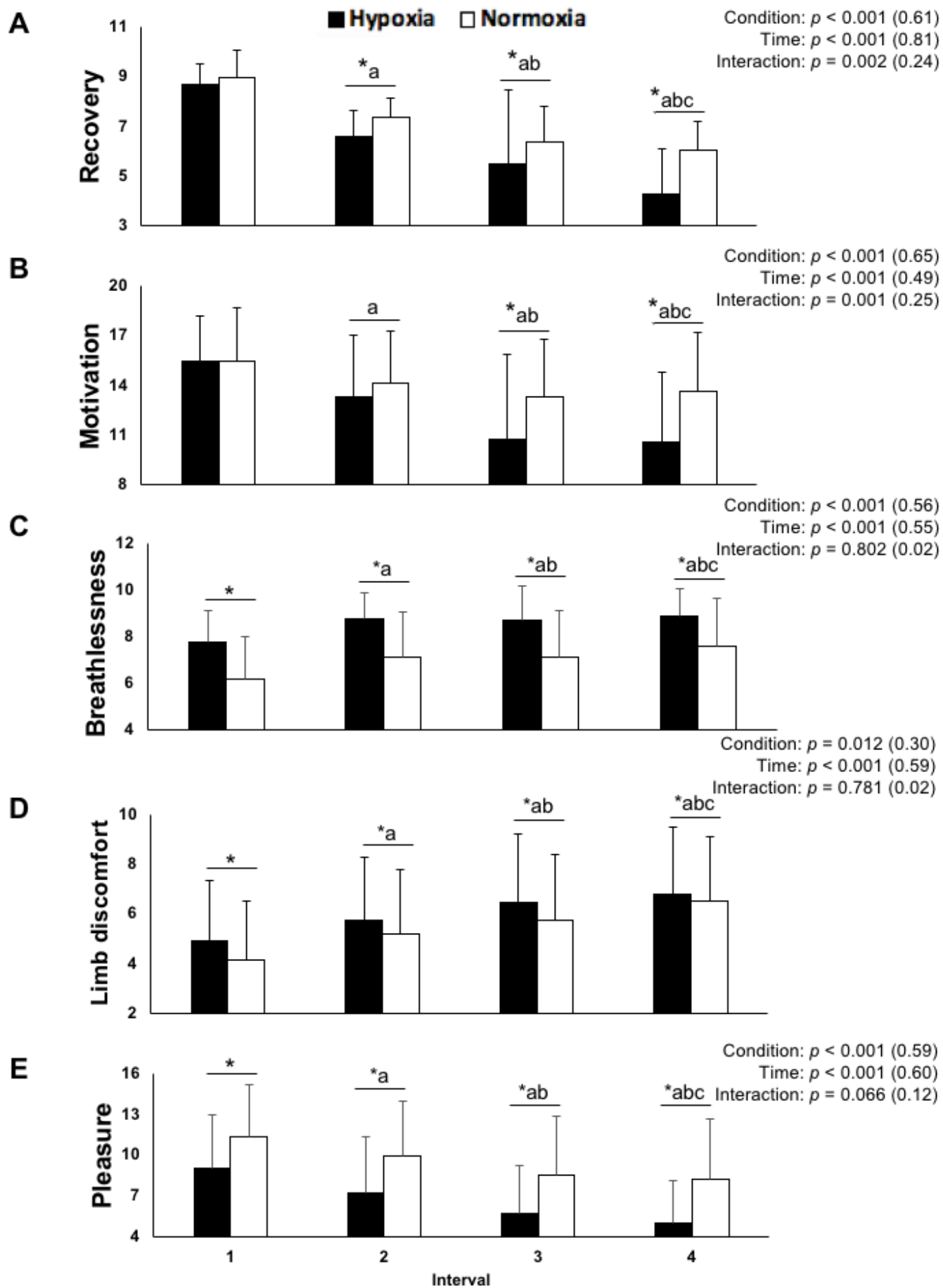


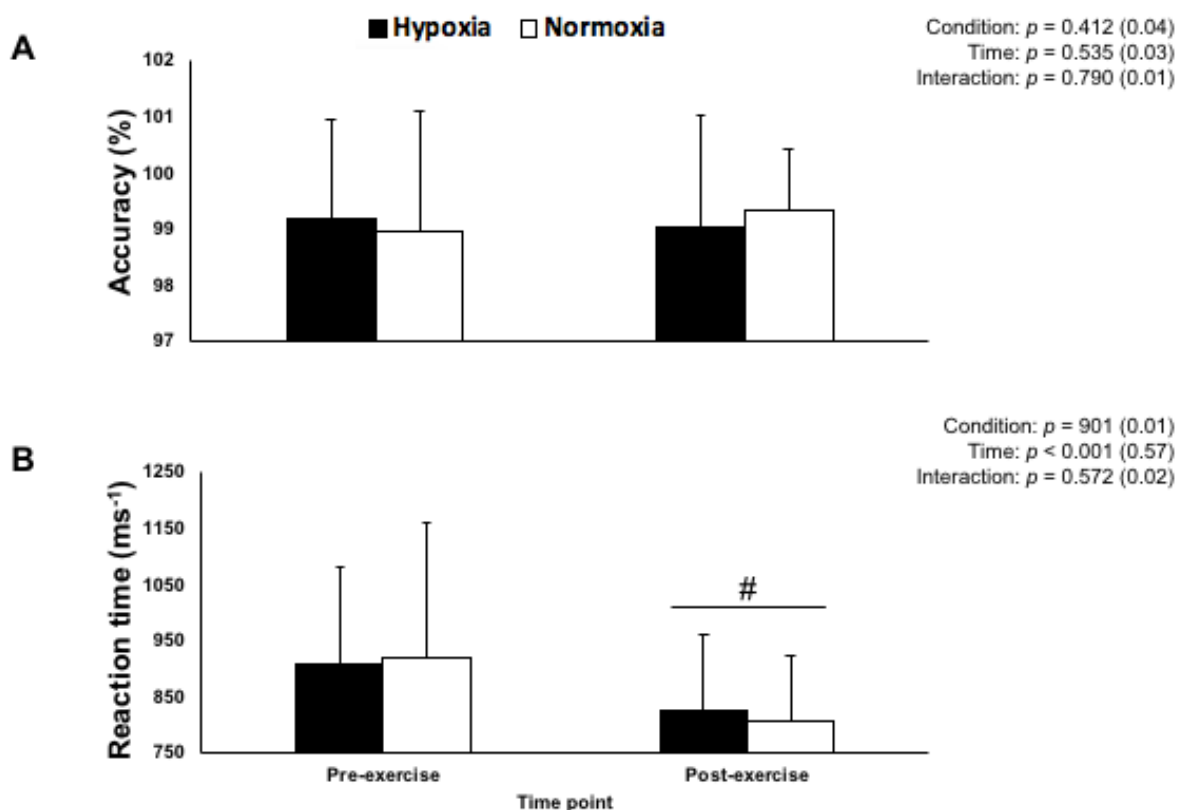
Figure 2 Changes in Oxygenated (A; O₂Hb), deoxygenated (B; HHb) and total hemoglobin (C; tHb) during the high-intensity intermittent running protocol. Data are calculated as a percentage difference from baseline (%) and presented as mean \pm SD. ANOVA main effects of time, condition and interaction are 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 ($p < 0.05$).

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



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

250 Discussion

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

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947 255 motivation and pleasure scores were stated during recovery between HYP vs. NOR, and 4)
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949 256 blood lactate concentration was larger after HYP vs. NOR. Overall, using a manipulation of
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951 257 oxygen availability, reduced external workload (i.e., running velocity) during perceptually-
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953 258 regulated interval running is associated with a similar internal load (i.e., physiological
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955 259 responses). Although no cognitive function differences were found between conditions, this is
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957 260 achieved with less favourable exercise-related sensations. A matched internal workload for a
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959 261 decreased external workload during perceptually-regulated HIIT in hypoxia *versus* normoxia
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961 262 may assist athletes to reach intended session goals with minimal over-induced physiological
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963 263 stress. However, perceptually-regulated HIIT exacerbates exercise-related sensations and
964
965 264 blood lactate concentrations in hypoxia compared to normoxia. This may then have negative
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967 265 carry-over effects on training responsiveness in the following days.
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972 266 *Exercise intervals*

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975 267 The velocity deemed equal to RPE 16 (PRV) was as expected for trained runners (~15 km/h⁻¹)
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977 268 (28). Interestingly, running velocity did not differ between conditions during the first HIIT
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979 269 interval, despite lower SpO₂ in hypoxia *versus* normoxia. Smith & Billaut (29) found
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981 270 maintained SpO₂ during repeated-sprinting in normoxia (20 × 5-s all out, 25-s recovery) until
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983 271 after the fifth sprint in national-level soccer players, whereby peak power significantly
984
985 272 decreased compared to sprint one. Overall, it seems that initial decreases in SpO₂ (within
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987 273 interval one) do not necessarily impact on HIIT compared to sprint intervals.
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990 274 We found that participants selected a progressively slower running velocity during HIIT in
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992 275 both conditions. In highly-trained middle to long-distance runners, a 6% reduction in $\dot{V}O_{2MAX}$
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994 276 when running in hypoxia *versus* normoxia is acceptable to match the acute physiological stress
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996 277 induced (5). It can be suggested that self-selected velocity adjustments found in the current
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998 278 study to maintain RPE 16 are matched with modifications in hypoxic *versus* normoxic training
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1006 279 sessions employed by coaches and sport scientists for athletes (30). Decreased external
1007
1008 280 workloads have been reported by Pramsöhler et al. (31) during continuous cycling (seven 30-
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1010 281 min sessions over 3-wk), whereby participants cycled at -28% lower power output in hypoxia
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1013 282 ($\text{FiO}_2 = 15.3\%$) *versus* normoxia for a similar HR. Differences in these findings and ours may
1014
1015 283 be due to the inclusion of geriatric patients completing pre-set (in normoxia) fixed-intensity
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1017 284 cycling compared to trained runners self-regulating HIIT in the current study. However,
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1019 285 Fernández-Menéndez et al. (10) reported preferred walking velocity (RPE of 10) in hypoxia
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1021 286 ($\text{FiO}_2 = 15.3\%$) was 7% slower than normoxia in obese adults over 3 weeks. Using a self-paced
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1023 287 model, irrespective of RPE target, population demographics and training block duration, lower
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1025 288 external workloads are selected in hypoxia compared to normoxia. Overall, decreases in self-
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1027 289 paced running velocity occurred to a greater extent in hypoxia than normoxia to maintain RPE
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1029 290 16, suggesting of a lower external workload. This finding may be of benefit to athletes who are
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1031 291 unable or advised by their coach not to be training at a full intensity. Completing perceptually-
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1033 292 regulated HIIT in hypoxia that requires slower running velocities compared to normoxia may
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1035 293 in turn minimise mechanical constraints and eventually injury risk.
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1039 294 Our data show HR increased progressively during HIIT, irrespective of condition. This matches
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1041 295 our hypothesis that HR will be comparable between hypoxia and normoxia, even though
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1043 296 running velocity was lower in hypoxia. Other studies employing moderate continuous-intensity
1044
1045 297 exercise have also found matched HR responses between hypoxic and normoxic training
1046
1047 298 interventions (~4 weeks) when cycling at a -21.0% power output in healthy males (32) and
1048
1049 299 walking/running at a -17.5% velocity in obese adults (33) in hypoxia *versus* normoxia. Although
1050
1051 300 exercise intensities in these studies were fixed, we believe similar increases in HR between
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1053 301 conditions occur due to the environmental stressor (hypoxia) augmenting autonomic cardiac
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1055 302 regulation (34). Overall, it seems self-paced exercise in hypoxia provides an added
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1065 303 environmental stressor that is able to mimick HR responses in normoxia for a lower external
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1067 304 load.
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1070 305 Lower [O₂Hb] and [tHb], and greater [HHb] of the *vastus lateralis* were recorded across HIIT,
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1072 306 irrespective of condition. Decreases in [O₂Hb] and increases in [HHb] were expected during
1073
1074 307 HIIT as oxygen delivery is outweighed by utilisation, whilst decreases in [tHb] reflect a lower
1075
1076 308 localised blood flow (35). Active musculature oxygenation is negatively impacted during
1077
1078 309 fixed-intensity exercise in hypoxia compared to normoxia due to a lower FiO₂ (7). In support
1079
1080 310 of this, Chacaroun et al. (11) reported lower [O₂Hb] and greater [HHb] with maintained [tHb]
1081
1082 311 of the *vastus lateralis* during fixed, relative high-intensity cycling in hypoxia (85% maximal
1083
1084 312 power output in normoxia; FiO₂ = 13.5%) *versus* normoxia. Where we employed a self-paced
1085
1086 313 exercise model, similar [O₂Hb] and [HHb] responses are achieved between conditions. This is
1087
1088 314 likely explained through the decreased workload (i.e., slower running velocity) in hypoxia
1089
1090 315 compared to normoxia, subsequently lowering oxygen utilisation. Discrepant findings in [tHb]
1091
1092 316 may be due to different exercise modalities (cycling *versus* running) modifying blood flow
1093
1094 317 regulation (36). Similar to HR responses (central) previously discussed, it can be suggested
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1096 318 here that local (tissue oxygenation) physiological stress is matched between conditions during
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1098 319 HIIT in hypoxia at a slower velocity compared with normoxia.
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1103 320 Elevations in [La⁺] following HIIT were higher in HYP than NOR. Values in the current study
1104
1105 321 (10–13 mmol/l⁻¹) are somewhat higher than those (5–6 mmol/l⁻¹) reported elsewhere following
1106
1107 322 a single HIIT session (6 × 4-min intervals at a RPE ~17, 4-min recoveries) (19). This maybe
1108
1109 323 due to a 1:0.75 work:rest ratio implemented during our protocol compared to 1:1 employed by
1110
1111 324 Seiler & Sjursen (19). [La⁺] normalization during shorter recovery periods may not occur to
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1113 325 the extent following longer recovery periods due to excess pyruvate accumulation (37). This
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1115 326 suggests that HIIT in hypoxia *per se* leads to increased [La⁺] at slower running velocities
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1117 327 compared to normoxia for similar physiological stress amounts. Practitioners should be aware
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328 that perceptually-regulated HIIT in hypoxia is a viable method for matching indices of
329 physiological stress to normoxia. However, the blood lactate concentration increases after
330 exercise were larger in hypoxia compared to normoxia. This may have negative implications
331 on the muscle fatigue recovery process.

332 *During recovery*

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

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

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1183 352 et al. (5) reported that 3-min absolute-intensity running intervals (84% $v\dot{V}O_{2MAX}$) in hypoxia
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1185 353 ($FiO_2 = 15.4\%$) led to larger perceived limb discomfort compared to a lower absolute intensity
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1187 354 in normoxia (90% $v\dot{V}O_{2MAX}$). We expected exercise-related sensations to be similar between
1188
1189 355 conditions as participants could adjust their velocity where necessary. However, this was not the
1190
1191 356 case. Similar responses have been shown elsewhere (42), with greater perceived overall
1192
1193 357 discomfort, breathlessness and limb discomfort following progressive, sub-maximal, self-
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1195 358 paced cycling intervals (RPE = 3; modified CR10 Borg scale) in hypoxia ($FiO_2 = 13.0\%$)
1196
1197 359 compared to normoxia at a similar power output. Perceived breathlessness, limb discomfort
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1199 360 and pleasure are exercise-related sensations contributing to overall RPE during exercise (16).
1200
1201 361 However, there is a detachment between these when immediately assessed after HIIT intervals.
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1203 362 We suggest that self-paced HIIT in hypoxia leads to unfavourable exercise-related sensations
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1205 363 before and after running intervals, compared to normoxia.

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1210 364 *Pre- and post-exercise*

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1212 365 During the Stroop test, alertness increased (i.e., faster reaction time) whilst accuracy was
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1214 366 maintained following HIIT, irrespective of condition. It is well known that HIIT in normoxia
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1216 367 generally increases cognitive performance *versus* rest (i.e., faster reaction time, better
1217
1218 368 accuracy) (43). However, during fixed-intensity exercise in hypoxia, cognitive performance
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1220 369 (i.e., attention and executive function) is worsened compared to normoxia (17,18). We report
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1222 370 that even though exercise-related sensations were worsened during HIIT, cognitive
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1224 371 performance (assessed post-HIIT) was not negatively affected. Ochi et al. (18) reported
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1226 372 decreased Stroop performance 15 mins after 10 mins of moderate-continuous intensity exercise
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1228 373 (50% peak oxygen uptake) in hypoxia ($FiO_2 = 13.5\%$) *versus* normoxia. Our results likely
1229
1230 374 differ to the aforementioned study due to cognitive testing performed in normoxia and
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1232 375 following different exercise modalities. Our data show that alertness is increased following
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1234 376 HIIT, and not negatively impacted by hypoxia.

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1242 377 *Limitations and perspectives*
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1245 378 During self-paced exercise at a perceptually-regulated intensity in hypoxia, HR and muscle
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1247 379 oxygenation responses are similar to normoxia for a lower running velocity. However, we used
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1249 380 a single “hypoxic dose” (i.e., hypoxic severity and duration), target RPE and exercise duration
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1251 381 during HIIT. Further investigations should refine self-selected protocols in hypoxia, such as
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1253 382 the “hypoxic dose”, target RPE and exercise duration to minimise the negative side effects of
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1255 383 worsened exercise-related sensations found under the present circumstances. In addition,
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1257 384 whether there are gender differences in response to hypoxic exposure during perceptually-
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1259 385 regulated HIIT should be investigated, given that our final sample size (n = 19) included only
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1261 386 three females.
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1268 388 **Conclusion**
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1271 389 When carrying out HIIT at a perceptually-regulated intensity (RPE equal to 16), larger running
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1273 390 velocity decreases are needed in hypoxia than normoxia. This is accompanied by similar
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1275 391 physiological stress (i.e., HR and muscle oxygenation) during HIIT, and cognitive function
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1277 392 adjustments after. In hypoxia, exercise-related sensations and blood lactate concentrations were
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1279 393 higher-than-normal with larger peripheral oxygen desaturation. Overall, perceptually-regulated
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1281 394 running velocity in hypoxia compared to normoxia may be an effective alternative, at the
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1283 395 expense of less favourable exercise-related sensations. Our results suggest that athletes under
1284
1285 396 the influence of hypoxia require lower external workloads to reach a perceptually-regulated
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1287 397 target during HIIT than normoxia. If employed in a practical setting, coaches should consider
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1289 398 the potential of negatively implicated exercise-related sensations and blood lactate
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1291 399 concentrations which may have further negative carry-over effects on training responsiveness
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1293 400 in the following days.
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407 Conflict of interest

408 The authors have no conflicts of interest or financial ties to disclose and no current or past
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