Domen Tominec [1,*]
Tadej Debevec [1,2]

SPRINT INTERVAL TRAINING IN HYPOXIA AND EXERCISE PERFORMANCE – A SHORT REVIEW

UČINKI ŠPRINTERSKE INTERVALNE VADBE V HIPOKSIJI NA ŠPORTNO SPOSOBNOST – PREGLEDNI ČLANEK

ABSTRACT

Hypoxia is often used during training to augment metabolic load and heighten physiological adaptations with the aim of exercise performance improvements. The recently established altitude training method »sprint interval training in hypoxia« (SIH) requires individuals to perform multiple 30 s Wingate sprints under hypoxia, interspersed with 3–5 min recovery periods. As the execution of repeated supramaximal efforts in hypoxia does not seem to be compromised, it was hypothesized that SIH might further augment exercise performance compared to sprint interval training in normoxia (SIT). To elucidate the usefulness of hypoxia during sprint interval training for exercise performance a systematic review of the available literature was conducted. The PubMed, SportDiscus^{TM}, and Web of Science online databases were searched for original articles – published up to March 2023 – assessing changes in exercise performance following SIH and SIT. Six studies (randomized controlled trials (RCTs)) were identified, evaluating SIH interventions lasting 2–6 weeks. Currently, the available scientific literature does not suggest that SIH additively augments exercise performance in comparison to SIT. The potential changes in anaerobic thresholds after SIH, but not after SIT require further investigation to fully elucidate the subsequent effects on exercise performance. Nevertheless, there is evidence to support beneficial peripheral adaptations known to increase the oxidative and glycolytic capacity, especially in type II, fast-twitch fibers, following SIH, but not SIT. These local adaptations could potentially enable superior improvement in exercise performance after long enough SIH training protocols. Future RCTs on SIH and, particularly, on the performance-related underlying mechanisms seem warranted.

Keywords: altitude, sport, physiology, Wingate test

[1]Faculty of Sport, University of Ljubljana, Ljubljana, Slovenia

[2]Department for Automation, Biocybernetics, and Robotics, Jozef Stefan Institute, Ljubljana, Slovenia

IZVLEČEK

Z namenom izboljšanja športne sposobnosti se športniki danes poslužujejo predihovanja hipoksičnega zraka med športno vadbo, kar poveča presnovno obremenitev in potencialno vodi v večje fiziološke prilagoditve. Nedavno uveljavljena »šprinterska intervalna vadba v hipoksiji« (SIH) od posameznikov zahteva zaporedno izvajanje 30-sekundnih Wingatovih šprintov v hipoksiji, ki jim sledi 3–5 min odmora. Ker se je izkazalo, da izvajanje ponavljajočih se supra maksimalnih naporov v hipoksiji ni kompromitirano, je za pričakovati, da bo SIH v primerjavi s šprintersko intervalno vadbo v normoksiji (SIT) v večji meri izboljšala športno sposobnost. Da bi ugotovili učinkovitost dodajanja hipoksije k šprinterski intervalni vadbi za namene izboljšanja športne sposobnosti, smo opravili sistematičen pregled razpoložljive literature. Izvirne članke – objavljene do marca 2023 – na raziskovalno tematiko smo iskali v spletnih zbirkah podatkov PubMed, SportDiscus^{TM} in Web of Science. Vključitvenim kriterijem je ustrezalo šest raziskav (randomiziranih kontroliranih poskusov (RCT)), ki so raziskovale učinkovitost intervencij SIH in SIT v trajanju od 2 do 6 tednov. Trenutno razpoložljiva znanstvena literatura ne nakazuje, da SIH v primerjavi s SIT v večji meri izboljša športno sposobnost. Ugotovljeno povečanje anaerobnega praga po koncu SIH, zahteva nadaljnje preiskave, da lahko v celoti razjasnimo posledične učinke na športno sposobnost. Kljub temu obstajajo dokazi, da SIH privede do koristnih perifernih prilagoditev, ki povečujejo zmogljivost oksidativnih in glikolitičnih procesov, zlasti v hitrih mišičnih vlaknih tipa II. Tovrstne prilagoditve v mišični funkciji pa bi po dovolj dolgih protokolih SIH lahko rezulitarale v večjem izboljšanju športne sposobnosti. V prihodnosti se zahtevajo predvsem novi RCT, ki bodo ugotavljali temeljne mehanizme odgovorne za izboljšanje športne sposobnosti po koncu SIH.

Ključne besede: višina, šport, fiziologija, Wingate testiranje

Corresponding author:* Domen Tominec,

Faculty of Sport, University of Ljubljana, 1000 Ljubljana, Slovenia
E-mail: domen.tominec@fsp.uni-lj.si
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INTRODUCTION

Athletes and coaches are constantly looking for training innovations to help them augment performance. In recent years, in addition to endurance athletes (Millet et al., 2010), hypoxic training has also grown popular within team sports (Girard et al., 2017), which are characterized by the fact that their seasons are normally long incorporating numerous important competitions throughout the year. Implementing long-term altitude models such as "live high–train high" (LHTH) and "live high–train low" (LHTL) in-season is challenging, as weekly competitions do not allow for 2 week-long training blocks at altitude (Millet et al., 2010). Also, traveling to mountain regions is not always feasible (travel time, athlete engagement, expenses) and can be limited to top athletes or squads with sufficient time and resources. With the desire to minimize travel constraints and disruption to the athlete's usual training routine, the "live low–train high" (LLTH) method was developed over the last few decades (Girard et al., 2020). LLTH model enables the athletes to live at a low altitude (in "normoxia"), while they perform (part of) their training under continuous or intermittent hypoxic conditions lasting ≤3 h·day^{-1} (cumulative daily hypoxic dose ≤6 h·day^{-1}) for 2 to 5 exercise sessions per week (McLean et al., 2014). As the model is performed for only a short period of the day, exercise methods within the LLTH model can apply stronger hypoxic stimuli simulating altitudes up to 6000 m above sea level (Bartsch et al., 2008). At the same time, these exercise methods do not detrimentally affect sleep quality and regeneration, usually observed during prolonged living at higher altitudes (Millet et al., 2010).

Technological improvements enabled new tools and techniques for the implementation of different methods of the LLTH model at low altitudes and/or at sea level; with either decreasing atmospheric pressure (hypobaric hypoxia [HH]) for example in hyperbaric chambers or reducing the fraction of oxygen in the inspired air (F_IO_2; normobaric hypoxia [NH]) by nitrogen (N_2) dilution and/or oxygen (O_2) filtration such as within hypoxic rooms, tents, and corridors (Girard et al., 2013; Wilber, 2007). An interesting alternative to hypoxic exercise is also the technique of voluntary hypoventilation, in which by maintaining a low volume of air in the lungs during an exercise, O_2 diffusion from the lungs into the blood is reduced (Woorons et al., 2010). Additionally, with this technique, athletes can achieve similar hypoxic conditions within the body, as they normally experience at natural altitudes or under NH (Woorons et al., 2014).

A recent review of the LLTH altitude modalities outlined 6 new innovative hypoxic training methods as follows: (1) ischemic preconditioning (IPC), (2) blood flow restriction training

(BFR), (3) repeated sprint training in hypoxia (RSH), (4) voluntary hypoventilation training (VHL), (5) sprint interval training in hypoxia (SIH) and (6) resistance training in hypoxia (RTH) (Girard et al., 2020). While IPC, BFR, RSH, VHL, and RTH have already been reviewed elsewhere (Brocherie et al., 2017; Feriche et al., 2017; Holfelder & Becker, 2018; Incognito et al., 2016; Wortman et al., 2021), the SIH method did not receive much research interest.

Within the LLTH there are essentially two main sprint training protocols: RSH - characterized by repeated maximal exercise bouts of short duration (≤10 s) interspersed with brief recovery periods (≤60 s or exercise-to-rest ratio ≤1:4) and SIH comprised of longer sprints (usually 30-s Wingate sprints) with 2–5 min passive or active recovery (Buchheit & Laursen, 2013; Girard et al., 2017).

Up-to-date, sprint interval training (SIT) has been recognized as an effective and time-efficient training strategy for enhancing skeletal muscle oxidative capacity (Gist et al., 2014) and exercise performance (Koral et al., 2018; Sloth et al., 2013) to same or even larger extent than larger volume moderate-to-vigorous intensity continuous endurance training. Additionally, repeated SIT (8 × 30 s sprint training with 1.5 min recovery) is potentially more beneficial than 6 s sprint training (15 × 6 s sprints with 1 min recovery) in normoxia (Mohr et al., 2007). The training method induces a cascade of physiological adaptations, predominantly occurring in the muscle tissue – i.e. increased oxidative (Gibala et al., 2006) and glycolytic enzyme activity (Puype et al., 2013), muscle buffering capacity, glycogen content (Burgomaster et al., 2005) and increased skeletal muscle capillarization (De Smet et al., 2016) – all of which can augment exercise performance via enhanced O_2 uptake (VO_2) and O_2 transport capacity. Furthermore, improvements in exercise performance resulting from vascular and mitochondrial adaptations (Little et al., 2010; Rakobowchuk et al., 2008), improved growth hormone responses (Kon et al., 2015), and insulin sensitivity (Richards et al., 2010), have reinforced SIT as a powerful training stimulus in elite and recreational athletes (Gibala et al., 2006; Sloth et al., 2013) as well as in clinical populations (Whyte et al., 2010).

One of the earliest investigations on the potential benefits of SIH training indicated that exposure to moderate or severe hypoxia (F_IO_2=16.4–13.6 %) had no detrimental effects on the performance of repeatable 30-s Wingate tests, most likely due to sufficiently long 4–5 min recoveries between sprints (Kon et al., 2015). Additionally, highly-trained athletes could repeat 6 × 30 s Wingate tests (with only 1.5 min recoveries) in simulated hypobaric hypoxia up to 2150 m without compromising their mean or peak power outputs (Breenfeldt Andersen et al., 2020). So far, SIH was mostly performed in the form of Wingate sprints, which consist of 30 s maximal cycling sprints on a specialized bicycle ergometer with a resistance set to 7.5% of the participant's body mass (0.075 kg·kg bm^{-1}), while additional hypoxic air mixture during SIH exercise was supplied by using hypoxicators and/or altitude rooms (Wilber, 2007). In the case of specific requirements of team sports, special hypoxic marquees would also be feasible for athletes to perform 50–70 m running sprints, sports games and even swimming (Girard et al., 2013).

The addition of hypoxic stress during the high-intensity interval and repeated sprint training has already been proposed as a mechanism to further enhance exercise performance (Faiss, Girard, et al., 2013; Faiss, Leger, et al., 2013). Additionally, preliminary research supports the notion that performing SIT in hypoxia may further enhance the magnitude of physiological adaptation when compared to equivalent training performed in normoxia (Breenfeldt Andersen et al., 2020). Higher arterial deoxygenation and consequently reduced O_2 flux during sprinting in hypoxia provides additive stress, which results in increased metabolic demands during exercise, and increased relative stress during recovery, both potentially leading to greater exercise adaptations (Faiss, Leger, et al., 2013). It was shown that performing repeated supramaximal efforts in hypoxia requires an increased fraction of glycolytic ATP production due to a hypoxia-induced drop in oxidative energy turnover (Girard et al., 2017). To support this, a single session of SIH (3 × 30 s Wingate sprints) caused a greater decrease in muscle glycogen content compared with the same exercise under normoxia without interfering with the power output (Kasai et al., 2021). Furthermore, since each 30 s exercise bout of SIT requires a ~55% contribution from aerobic metabolism (Billaut & Bishop, 2009), this typically elicits greater performance decrements when training in hypoxia vs. normoxia. However, prolonged recovery periods (3–5 min) during SIH might reduce the stress on the anaerobic metabolism for energy restoration and facilitate near-complete recovery to maintain sprint training-specific stimuli (Millet & Faiss, 2012). This work-to-rest ratio (~1:8) enabled preserved specific training stimuli associated with SIT, e.g., upregulated O_2 signaling genes and fast twitch fiber recruitment (Millet & Faiss, 2012), whilst increasing the metabolic disturbances required for adaptations to glycolytic pathways (Puype et al., 2013).

Previous well-controlled studies provided some evidence that high-intensity training in hypoxia augmented blood perfusion, mitochondrial biogenesis, and hypoxia-inducible factor-1α (HIF-1α) mRNA content (Brocherie et al., 2017; Faiss, Leger, et al., 2013; Zoll et al., 2006). Since HIF-1α is of paramount importance in the regulation of the genes controlling the expression of proteins involved in glycolysis and pH regulation (Porporato et al., 2011), it can be hypothesized that SIH will induce a higher expression and activity of glycolytic enzymes, buffer capacity, and glycogen content, which in turn could enhance the performance in "glycolytic" exercise events such as a 400-meter dash, by contributing to a beneficial fiber-type shift (De Smet et al., 2016).

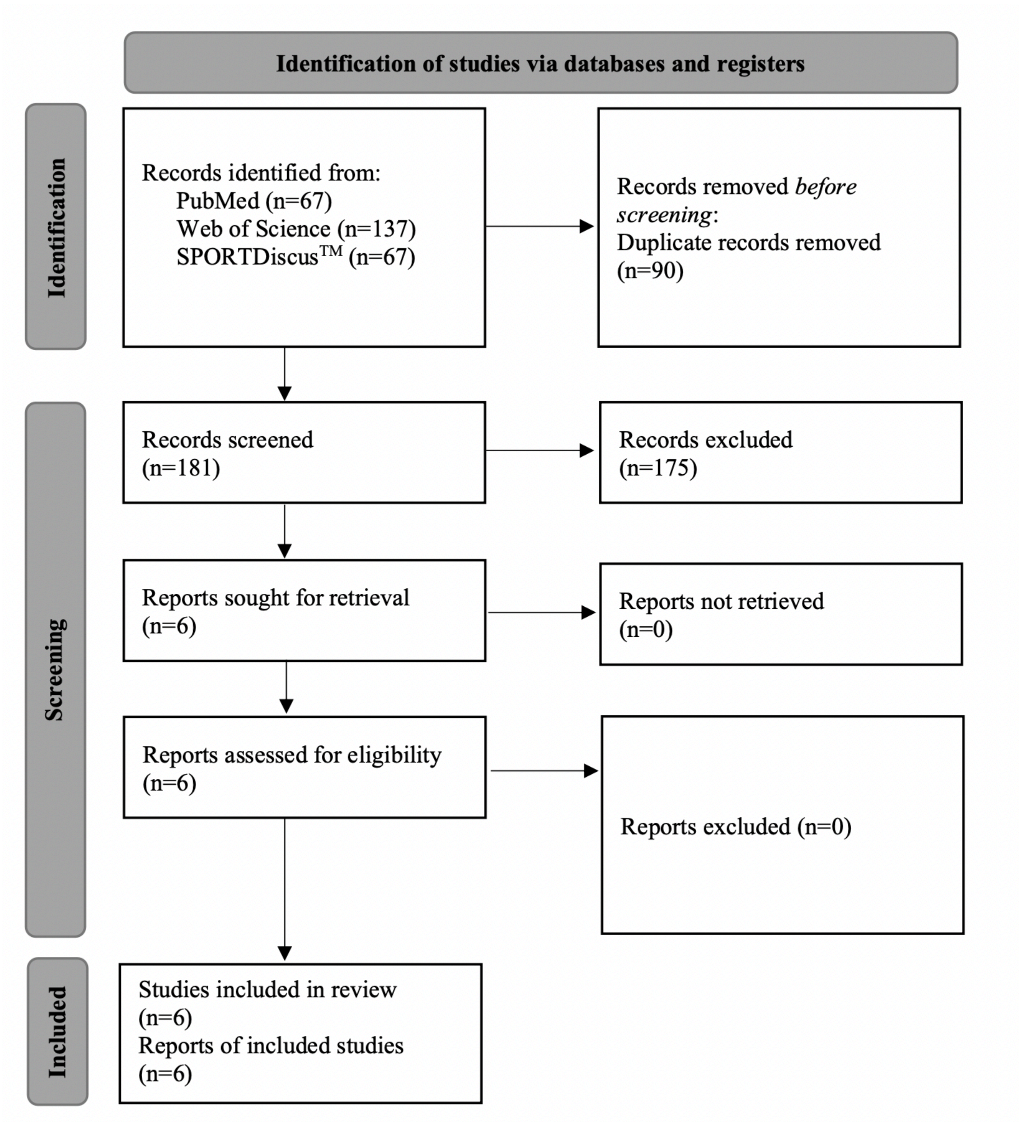
Based on previous studies conducted in normoxia it seems reasonable to speculate that SIH might be another potent exercise stimulus to boost exercise performance either at sea level or at different altitudes. Very few studies to date focused on the potential beneficial effects of SIH that could be modulated predominantly by increased metabolic stress in hypoxia. Past reviews (Girard et al., 2020; Millet et al., 2019) and one meta-analysis (Brocherie et al., 2017) provide some evidence of the potential use of innovative hypoxic training methods, and how these must be applied to enhance exercise performance. In this systematic review, we aimed to examine the SIH literature, assess evidence of its efficacy and subsequently provide guidelines on how SIT should be implemented to enhance exercise performance. The scope of this review has been limited to the inclusion of studies using the repeated Wingate protocol based on its recent frequent use and apparent impact despite the very low training volume.

METHODS

A systematic review of the available scientific literature was conducted in line with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines (Page et al., 2021) for studies evaluating the effects of SIH versus SIT interventions on exercise performance outcomes. An electronic literature search included articles published up to March 2023 using the following three online databases: Web of Science, PubMed, and SPORTDiscus™. The following terms were searched for: (hypoxi* OR altitude*) AND (sprint interval train* OR high-intensity intermittent train* OR Wingate test*), while the terms (patient* OR obes*) were excluded (using NOT). Also, the following filters were applied to each database: PubMed – *Text availability (Full text) OR Age (adult 19–44 years OR young adult 19-24 years)*; SPORTDiscus™ – *Academic Journals AND Language (English)*; Web of Science – *Document Type (Article) AND Category (Sport Science OR Physiology)*. Results were limited to full-text English papers only. The search was performed by two authors (DT and TD) with the EndNote reference manager (Clarivate™, London, United Kingdom). Articles were first screened by title and then by abstract using the eligibility criteria (mentioned below).

After screening titles and abstracts, the full text was retrieved for all potentially relevant articles and assessed according to the selection criteria. Reference lists for all selected articles were then screened and searches were supplemented by reviewing the reference lists of recent reviews on the broader area (Brocherie et al., 2017; Girard et al., 2020; Millet et al., 2019). A flow diagram of the search is presented in Figure 1.

Figure 1. The PRISMA flowchart on studies evaluating the effects of SIH compared to SIT on exercise performance.



To assess the effects of SIH versus SIT the following inclusion criteria were considered: (1) randomized controlled trials (RCTs) or matched control trials; (2) short-term ($\leq$3 h·day^{-1}) hypoxia exposure throughout a training period $\geq$5 days; (3) training intensity was classified as »all out«, »maximal« or »supramaximal« or »$\geq$100% VO_{2max}«; (4) SIT in the work-to-rest ratio of 30 s:3–5 min was completed; (5) exercise performance was assessed in normoxic or hypoxic conditions; and (6) subjects were trained and adults, aged between 18 and 45 years. Studies were excluded according to the following criteria: (1) hypoxic exposures lasted for >3 $h \cdot day^{-1}$; (2) subjects were previously acclimatized to hypoxia (e.g. high-altitude natives); (3) submaximal training intensity and (4) animal/clinical subjects. “Exercise performance” was defined as any physical test leading to several outcomes, as follows: maximal incremental exercise test (MAXInc) assessing maximal oxygen uptake (VO_{2max}), time to exhaustion during MAXInc (T_{lim}), power output at VO_{2max} (P_{max}), aerobic (AT) and anaerobic threshold (AnT), power output at AT (P_{AT}) and AnT (P_{AnT}), power output at a lactate (La^-) concentration of 4 mmol $La^- \cdot L^{-1}$ (P_{LT4}), Wingate anaerobic test (WAnT) assessing maximal (PPO) or mean (MPO) power output, fatigue index (FI) and sprint decrement score (SDS), time to exhaustion (TTE) tests, time trials (TT), and repeated sprint ability (RSA) tests.

RESULTS

A search of electronic databases revealed 271 relevant records (Figure 1). Electronic searches returned 67, 137, and 67 results for PubMed, Web of Science, and SPORTDiscus^{TM}, respectively. Out of all 271 relevant records, 90 duplicate records were removed. Based on a review of the title or abstract or lack of any inclusion criterion, 175 articles were dismissed. Six full-text articles were evaluated and included in the present review. Each study was read and coded for descriptive variables (Table 1): reference, participants (training status and sex), training protocol (intervention [weeks × $sessions \cdot week^{-1}$], training protocol [sets × reps × duration, recovery between sprints], training mode), type of hypoxia used (NH or HH), experimental groups and design of the study, performance measures and meaningful differences.

SIT studies carried out in hypoxia used a wide variety of training modalities, including differences in exercise mode, degree of hypoxia, number of exposures per week, weeks of training, and performance outcome variables. Four studies included recreationally active participants (De Smet et al., 2016; Puype et al., 2013; Richardson & Gibson, 2015; Richardson, Reif, et al., 2016), while two studies included well-trained athletes (Takei et al., 2020; Warnier et al., 2020). Out of 6 studies, only two included female participants (Richardson & Gibson, 2015; Richardson, Reif, et al., 2016). SIH training protocols of the included studies lasted from 2–6 weeks with 2 or 3 exercise $sessions \cdot week^{-1}$. The SIT training units were consistently performed on a cycle ergometer, including 4–9 × 30 s Wingate sprints, with 4–4.5 min intermediate recoveries. For the simulation of a hypoxic environment, all of the included studies used NH facilities, where participants were exposed to simulated altitudes ranging from 2000 m to 4000 m (F_IO_2=16.7–13.0 %). All trials used a randomized controlled design, while three studies also included a control group, performing regular daily recreational activities (Puype et al., 2013; Richardson & Gibson, 2015; Richardson, Reif, et al., 2016). One study included a group in which participants combined SIH training with the ingestion of exogenous nitrates (De Smet et al., 2016), while one study included groups performing SIH training at different altitudes (Warnier et al., 2020).

Due to the disparity in the performance tests used, a comparison is difficult to make. Performance tests based on time, i.e. MAXInc exercise tests (De Smet et al., 2016; Puype et al., 2013; Richardson & Gibson, 2015; Richardson, Reif, et al., 2016; Warnier et al., 2020), 10 min and 30 min TT (De Smet et al., 2016; Puype et al., 2013), ~10 min submaximal TTE at 80% of VO_{2max} (Richardson & Gibson, 2015; Richardson, Reif, et al., 2016) or power output, single and multiple 30-s Wingate sprints (De Smet et al., 2016; Richardson, Reif, et al., 2016; Takei et al., 2020) have been used. Maximal incremental tests asessed several differents variables as follows: VO_{2max}, T_{lim}, P_{max}, P_{LT2}, P_{LT4}, AT, AnT, P_{AT} and P_{AnT} (De Smet et al., 2016; Puype et al., 2013; Richardson & Gibson, 2015; Richardson, Reif, et al., 2016; Warnier et al., 2020). During the TTs, the time to accomplish 600 kJ (Warnier et al., 2020), or total work produced during 10-min (Puype et al., 2013) and 30-min TT (De Smet et al., 2016) were measured. The TTE test required participants to insist on cycling at a corresponding power output of 80% VO_{2max}, until volitional exhaustion when determined as when cadence fell below 40 rpm (Richardson & Gibson, 2015; Richardson, Relf, et al., 2016). Furthermore, one study tested subjects performing MAXInc and 10-min TT under both hypoxic and normoxic environmental conditions (Puype et al., 2013). Detailed characteristics of the included studies are presented in Table 1.

Table 1. Detailed characteristics of the studies evaluating changes in exercise performance following SIH and SIT training periods.

Reference (year)	**Participants (Training status [M or F])**	**Training Protocol**	**Hypoxia (NH [F_IO_2[a]]/HH (m))**	**Groups (Design)**	**Performance measures**	**Meaningful differences (SIH vs. SIT)**
(De Smet et al., 2016)	Recreationally active M	5 weeks × 3 sessions·week^{-1} 4–6 × 30 s, 4.5 min recovery Cycling on a cycle ergometer	F_IO_2=15% NH	SIH: 9 SIH+N[b]:9 SIT: 9 (RCT)	MAXInc	
					VO_{2max}	No difference
					T_{lim}	No difference
					P_{max}	No difference
					P_{LT2}	No difference
					P_{LT4}	No difference
					30-min cycling TT	
					MPO	No difference
					WAnT	
					MPO	No difference
(Puype et al., 2013)	Recreationally active M	6 weeks × 3 sessions·week^{-1} 4–9 × 30 s, 4.5 min recovery Cycling on a cycling ergometer	F_IO_2=14.5% NH	SIH: 10 SIT: 9 CON: 10 (RCT)	MAXInc HYP	
					VO_{2max}	No difference
					T_{lim}	No difference
					P_{LT4}	*9% increase in SIH*
					MAXInc NOR	
					VO_{2max}	No difference
					T_{lim}	No difference
					P_{LT4}	*7% increase in SIH*
					10-min TT HYP	
					MPO	No difference
					10-min TT NOR	
					MPO	No difference
(Richardson & Gibson, 2015)	Recreationally active M (n=15) F (n=12)	2 weeks × 3 sessions·week^{-1} 4–7 × 30 s, 4 min recovery Cycling on a cycling ergometer	F_IO_2=15% NH	SIH: 14 SIT: 14 CON: 14 (RCT)	MAXInc	
					VO_{2max}	No difference
					TTE (80% VO_{2max}) time	No difference
(Richardson, Reif, et al., 2016)	Recreationally active M (n=27) F (n=15)	2 weeks × 3 sessions·week^{-1} 4–7 × 30 s, 4 min recovery Cycling on a cycling ergometer	F_IO_2=15% NH	SIH: 14 SIT: 14 CON: 14 (RCT)	MAXInc	
					VO_{2max}	No difference
					P_{max}	No difference
					AnT	*9.5% increase in SIH*
					P_{AnT}	No difference
					TTE (80% VO_{2max}) time	No difference
					WAnT	
					PPO	No difference
					MPO	No difference
					FI	No difference

Reference (year)	**Participants (Training status [M or F])**	**Training Protocol**	**Hypoxia (NH [F_IO_2[a]]/HH (m))**	**Groups (Design)**	**Performance measures**	**Meaningful differences (SIH vs. SIT)**
(Takei et al., 2020)	University sprinters M	2 weeks × 3 sessions·week^{-1} 3 × 30 s, 4.5 min recovery Cycling on a cycling ergometer	F_IO_2=14.5% NH	SIH: 6 SIT: 6 (RCT)	3 × 30 s WAnT PPO MPO Total work SDS[d]	 No difference No difference No difference No difference
(Warnier et al., 2020)	Well-trained endurance athletes M	6 weeks × 2 sessions·week^{-1} 4–9 × 30 s, 4.5 min recovery Cycling on a cycling ergometer	2000 m (F_IO_2=16.7%) 3000 m (F_IO_2=14.5%) 4000 m (F_IO_2=13.0%) NH	SIH (2000 m): 8 SIH (3000 m): 8 SIH (4000 m): 7 SIT (sea-level): 7 (RCT)	MAXInc P_{max} P_{AnT} 600 kJ TT time WAnT PPO MPO FI	 No difference No difference No difference No difference No difference No difference

Notes. Published studies on SIH (n=6). The significantly ($p<0.05$) greater benefits of SIH vs. SIT are presented in italics. F: females, M: males, HYP: hypoxia, NOR: normoxia, NH: normobaric hypoxia; HH: hypobaric hypoxia, F_IO_2: fraction of inspired oxygen, SIH: sprint interval training in hypoxia, SIT: sprint interval training in normoxia, CON: control group without SIT training, RCT: randomized controlled trial, MAXInc: maximal incremental exercise test, VO_{2max}: maximum oxygen uptake, P_{max}: power output at VO_{2max}, T_{lim}: time to exhaustion during MAXInc, AT: aerobic threshold, AnT: anaerobic threshold, P_{AT}: power output at AT, P_{AnT}: power output at AnT, LT_2: lactate concentration of 2 mmol $La^-·L^{-1}$, LT_4: lactate concentration of 4 mmol $La^-·L^{-1}$, P_{LT2}: power output at LT_2, P_{LT4}: power output at LT_4, WAnT: Wingate anaerobic test, PPO: maximal power output, MPO: mean power output, FI: fatigue index, SDS: sprint decrement score, TT: time trial, TTE: time to exhaustion test.

[a]Where (simulated) altitude was not reported, we estimated it according to the fraction of inspired oxygen (F_IO_2)

[b]nitrate supplementation (6.45 mmol $NaNO_3$ administered 3 h before each session)

[c](Bangsbo et al., 2008)

[d](Girard et al., 2011)

DISCUSSION

Compared to the studies evaluating similar innovative hypoxic methods – RSH (Brocherie et al., 2017) and VHL (Holfelder & Becker, 2018) – studies on SIH, in general, did not demonstrate significant improvements in exercise performance compared to equivalent training methods conducted under normoxic conditions. Although SIT training in normoxia is a time-efficient and effective training method for increasing both aerobic and anaerobic exercise performance (Hazell et al., 2010; Sloth et al., 2013) the addition of hypoxic stimulus to SIT exercise does not seem beneficial for further augmenting exercise performance. Nevertheless, it is important to emphasize that the completion of 30-s Wingate sprints in oxygen-deprived environments during SIH was not associated with larger performance decrements – lower PPO and MPO, total work produced, or increased FI – when compared to SIT.

Studies on SIH generally examined whether the addition of hypoxic stimuli to SIT sessions enables any further improvements in aerobic performance. The present studies analysis revealed that SIH did not enable any significant increase in VO_{2max}, T_{lim} or P_{max} during maximal incremental exercise test (De Smet et al., 2016; Puype et al., 2013; Richardson & Gibson, 2015; Richardson, Reif, et al., 2016; Warnier et al., 2020), the performance of 10-min, 30-min, and 600 kJ cycling TTs (De Smet et al., 2016; Puype et al., 2013; Warnier et al., 2020), and TTE at an intensity of 80% VO_{2max} (Richardson & Gibson, 2015; Richardson, Reif, et al., 2016) when compared to SIT, both in normoxic and hypoxic testing conditions (Puype et al., 2013). Both SIH and SIT equally increased VO_{2max} and P_{max} by about 10% after 5 weeks of training (De Smet et al., 2016), while a smaller specific block of SIH had the potential to improve aerobic capacity by slightly more than 10% (Richardson & Gibson, 2015). Contrary to the general trend of no additional effect on aerobic performance compared to SIT, SIH resulted in a significantly increased AnT (Richardson & Gibson, 2015; Richardson, Reif, et al., 2016) and the P_{LT4} (Puype et al., 2013), which indicates up-regulation of muscular aerobic capacity and suggests that improved oxidative phosphorylation after SIH had occurred. In support of these findings, 6 weeks of SIH increased the estimated AT from the pre-test at 2000 m and 4000 m, while no such changes were observed after SIT (Warnier et al., 2020). Importantly, it was also observed that both SIH and SIT augmented VO_{2max} by about 6.5% in normoxic, but not in hypoxic testing conditions (Puype et al., 2013), which suggests that SIH would be potentially beneficial for improving aerobic performance in normoxic conditions only.

Since SIT also targets the improvement of anaerobic exercise performance, studies included in this review investigated the effects of SIH on the ability to perform individual or repeatable 30-s Wingate tests (De Smet et al., 2016; Richardson, Reif, et al., 2016; Takei et al., 2020; Warnier et al., 2020). Using SIH compared to SIT failed to provide any significant increase in PPO, MPO, total work, or decrease in FI or SDS during the single or repeatable 30-s Wingate tests in recreationally active participants (De Smet et al., 2016; Richardson, Reif, et al., 2016), as well as in endurance and sprint athletes (Takei et al., 2020; Warnier et al., 2020). Despite relative gains in PPO and MPO for each of the three sprint bouts being greater in the hypoxic compared to the normoxic training group after 2 weeks of training, differences were still non-significant (Takei et al., 2020). Interestingly, De Smet and colleagues observed about a 6% larger increase in MPO of the 30-s Wingate test in the hypoxic group which ingested exogenous nitrates compared to normoxic and hypoxic groups, although differences were non-significant (De Smet et al., 2016). This finding suggests that short-term oral nitrate supplementation in conjunction with SIH may be a valid strategy to further augment anaerobic performance, due to nitrate-induced effects on increased blood flow, improved contractility of fast-glycolytic muscle fibers (Ferguson et al., 2013; Hernandez et al., 2012), and increased rate of post-exercise muscle phosphocreatine (PCr) resynthesis (Vanhatalo et al., 2014). Furthermore, Warnier et al. observed a main time effect for the Wingate PPO only in the group which trained at the altitude of 4000 m, while no effect was observed for groups training at altitudes of 2000 m, 3000 m, and sea level, respectively (Warnier et al., 2020). Similar observations were also observed after RSH periods (Kasai et al., 2015). It was hypothesized that muscle PCr content may be increased in response to repeated sprinting in hypoxia, and turn, induce a greater improvement in PPO (Faiss, Girard, et al., 2013), but later studies did not support that hypothesis, observing a similar increase in muscle PCr content between RSH and RSN (Kasai et al., 2017). Warnier et al., therefore, hypothesized that the greater increase in PPO observed during the Wingate test after training at 4000 m altitude (F_IO_2=13.0%) is probably not related to changes in energy metabolism, but to changes in muscle structure or recruitment (Warnier et al., 2020). Additionally, hypoxic conditions were already shown to induce a higher expression of fast-twitch fibers (De Smet et al., 2016), increased spinal excitability, and also the number of recruited motor units (Delliaux & Jammes, 2006). Since a study using less severe hypoxic conditions (F_IO_2=14.5%) did not detect any change in PPO during a Wingate test (Takei et al., 2020), it is reasonable to speculate that higher hypoxic stimuli during SIH protocols might provoke greater adaptations in muscle contractility and energy metabolism and consequently augment anaerobic performance.

Due to the non-fulfillment of the inclusion criteria, we did not include one study (Gatterer et al., 2018), which performed a trial comparing the effects of SIH (4 sprints × 30 s, 4.5 min recovery) with the effects of RSH (3 sets × 5 sprints × 10 s, 20 s and 5 min recovery between repetitions and sets) on running and cycling performance in team athletes. After 3 weeks of training (3 sessions·week^{-1}) at an altitude of 2200 m, no significant differences in performance of the Yo-Yo IR2 test, 6 × 17 m back and forth running sprints, 30-s Wingate test, and 5 × 6 s repeated cycling sprints, were observed between the experimental groups, although both training methods significantly improved performance from the baseline values. The study revealed that both RSH and SIH training improve sea-level performance to a similar extent, without observed significant differences. Nevertheless, considering the medium to large effect size observed, cycling power output and La^- concentrations data indicate that RSH compared to SIH might be favorable for performance improvements and increases in anaerobic contribution, respectively. The somewhat higher overall training volume during RSH compared to SIH (overall sprinting time: 1350 s vs. 1080 s for RSH and SIH, respectively) might have underlined these differences. Based on the results of the study, it seems that the two training regimes can interchangeably be used to achieve superior training adaptations in exercise performance. However, as this study lacked a normoxic control group it is impossible to speculate the exact additive and independent effect of hypoxia.

As SIT is a particularly potent variation of interval training, performed at intensities ≥100% of the power output or speed at an individual's VO_{2max} (Weston et al., 2014), training effort, in particular, requires substantially higher absolute power outputs. Such intensities, however, require higher recruitment of type II, fast-twitch fibers and extensive use of non-oxidative substrate metabolism; fueled exclusively by intramuscular substrates (PCr and glycogen) with little or no contribution from fat-based fuels (Gibala & Hawley, 2017). The addition of hypoxia to SIT exercise results in the slowing of VO_2 kinetics at the beginning of the maximal 30-s sprint, increasing the magnitude of the O_2 deficit incurred during each sprint and placing even more demand on anaerobic sources and the activation of type-II, fast-twitch muscle fibers to maintain ATP production and quickly provide sufficient power outputs, respectively (Girard et al., 2017). Because of these characteristics, 6 weeks of SIH provided a significant 59% increase in phosphofructokinase (PFK) enzyme activity, while no such effect was observed after SIT (Puype et al., 2013). Additionally, both SIT and SIH elevated monocarboxylate transporter 1 protein (MCT-1) – membrane transporters responsible for co-transport La^- and hydrogen (H^+) ions (Girard et al., 2011) – content by ~70% compared to the baseline levels (Puype et al., 2013). De Smet et al. also observed increased muscle carnosine content (physicochemical buffer capacity of muscle) by ∼13% only in hypoxic groups, although differences were non-significant. Additionally, 5 days of combined RSH and SIH markedly augmented muscle glycogen content in a hypoxic group only (Kasai et al., 2017). In addition to earlier findings, SIH training with simultaneous supplementation of exogenous nitrates, compared to SIH and SIT alone, significantly increased the proportion (+45–56%) and fiber-specific cross-sectional area (+11%) of type IIa, fast-twitch oxidative muscle fibers in *m. vastus lateralis* (De Smet et al., 2016). Since anaerobic glycolysis accounts for about 50% of the total ATP production during a 30-s all-out exercise bout (Putman et al., 1995). De Smet et al., therefore postulated that a higher proportion of type IIa muscle fibers, providing a higher capacity for glycolytic ATP production, should be ergogenic during a 30-s sprinting exercise (De Smet et al., 2016). Mechanistically, observed adaptations after SIH only, can in combination increase the anaerobic breakdown and muscle buffering capacity, enabling potentially greater exercise adaptations after SIH periods.

It was hypothesized that superior adaptations after SIT compared to continuous endurance exercise is a reflection of stimulation of various signaling pathways – greater AMP-activated protein kinase (AMPK) phosphorylation, increased gene expression of peroxisome proliferator-activated receptor δ coactivator 1 α (PGC-1α) (Gibala & Hawley, 2017). Since exposure to hypoxia and interval high-intensity exercise stimulates similar signaling pathways (Faiss, Leger, et al., 2013; Zoll et al., 2006), the combination of physiological stressors experienced within SIH would potentially contribute to greater adaptations connected with the above-mentioned signaling pathways.

During a maximal 30-s sprint aerobic energy production to ATP resynthesis count up to 55% of the whole energy supply (Billaut & Bishop, 2009), with its significantly increasing role towards the end of individual 30-s sprints and repeated trials (Gastin, 2001; Parolin et al., 1999). Because of the decreased oxygen availability for aerobic energy production during exercising in hypoxia, it is expected that sprinting in hypoxia would induce greater physiological adaptations in aerobic metabolism. It was already found that RSH enhances muscle perfusion (Faiss et al., 2015), while the same hypoxic training method can result in a decrease (Faiss, Leger, et al., 2013) or an increase (Brocherie et al., 2017) in factors involved in mitochondrial biogenesis. The study evaluating SIH-induced mitochondrial function reported that SIH training did not affect changes in muscular O_2 extraction and mitochondrial function of peripheral blood mononuclear cells (a measure estimating physical ability similar to skeletal muscle mitochondrial function (Tyrrell et al., 2015)). Authors proposed that O_2 flow per cell count seems to be less affected by SIH training (Gatterer et al., 2018). Nevertheless, it seems that SIH still provides some increase of aerobic capacity with which muscles can increase the oxidation of produced La^- within mitochondria. This is supported by observations of increased La^- clearance from the blood after the end of each consecutive 30-s sprint interval (~9–17% decrease in blood La^-) after a two-week-long SIH exercise protocol (Takei et al., 2020). Additionally, these findings can be supported by the practical finding of increased power outputs at an AnT, which reflects lower synthesis or higher oxidation of La^- in muscle fibers at a given submaximal exercise intensity (Puype et al., 2013; Richardson, Relf, et al., 2016).

Although some beneficial findings encourage the use of SIH for further improving aerobic capacity, De Smet et al. found that maximal citrate synthase (CS) activity after 5 weeks of SIT exercise increased by 54% in the normoxic group and by just under half that (22–25%) in the hypoxic groups (De Smet et al., 2016). This is in line with previous reports, where SIT in normoxic conditions increased CS activity (Sloth et al., 2013), while SIH did not augment adaptations in muscle oxidative capacity (Faiss, Leger, et al., 2013). Additionally, Gatterer et al., observed improved de- and re-oxygenation during repeated sprinting, indicating enhanced O_2 extraction and restoration of O_2 levels for the RSH group only (Gatterer et al., 2018). Since the major benefit of increased re-oxygenation during short recovery periods is a faster resynthesis of PCr (McMahon & Jenkins, 2002), the mechanism could contribute to performance improvements. It was purposed, that the generation of peak power during the first few seconds of an all-out sprint might be more likely responsible for the adaptations to SIT, than the total work completed during a 30-s bout (Hazell et al., 2010). Consequently, the availability of PCr during repeated sprints might be the most important factor because it is mainly responsible for the high power output during the initial 10 s of maximal exercise (Bogdanis et al., 1996). Currently, available literature did not evaluate if SIH in comparison whit SIT increases muscle oxygenation and PCr restoration, which would potentially improve exercise performance. Therefore, future studies should examine SIHs effects on muscle oxygenation status during the repetition of high-intensity efforts, since SIT in normoxia was shown to improve the slope of slow VO_2 component, which authors associated with greater O_2 extraction (Bailey et al., 2009).

As expected, only minor hematological changes were observed after SIH training periods, as such short durations and a relatively low altitude dosage were not likely to induce erythropoiesis (Richardson, Relf, et al., 2016; Warnier et al., 2020). After two weeks of SIH training (3 sessions$\cdot$week^{-1}) hemoglobin concentration was significantly different from pre to post-training, however, this increase was not different between training groups. In contrast to this, hematocrit values were not different from pre to post-training or between groups (Richardson, Relf, et al., 2016). To further support these findings, 6 weeks of SIH training (2 sessions$\cdot$week^{-1}) resulted in unchanged hemoglobin mass, hemoglobin concentrations, hematocrit, and plasma volume, while there were also no differences between hypoxic and sea-level groups (Warnier et al., 2020). Additionally, red blood cell volume increased after both the SIH and SIT training program, but none of the group increases was significant. The common cumulative hypoxic dose of SIH training periods is sufficiently too low (~40–50 hours) to increase hematological adaptation since 100 hours of cumulative exposure to hypoxia (real or simulated altitude of ~2500 m) increases the hemoglobin mass by about 1% (Garvican et al., 2012). In a practical sense, it follows that for a meaningful 2,5% increase in hemoglobin mass, it is necessary to aim for at least 250 cumulative hours of hypoxic exposure, e.i. 20–25 days spent at a (simulated) altitude between 2000 m and 2500 m (Garvican-Lewis et al., 2016).

Based on the findings we can summarize that although both SIH and SIT improve aerobic and anaerobic performance compared to baseline values, the addition of hypoxic stimuli to SIT does not seem to further augment exercise performance, therefore the alternative implementation of SIH in athlete's training routines may not be as meaningful as the implementation of RSH method (Brocherie et al., 2017; Millet et al., 2019). Nevertheless, the use of SIH may be more effective in improving submaximal aerobic performance, since SIH provided lactate-related adaptations that were not observed after identical training in normoxia (Puype et al., 2013; Warnier et al., 2020). Despite these observations, it is important to bear in mind that these adaptations did not reflect further improvements in submaximal exercise performance, i.e. improved performance during the TT (De Smet et al., 2016; Puype et al., 2013; Warnier et al., 2020), or TTE test (Richardson & Gibson, 2015). The evidence though suggests that a SIH-related increase in anaerobic threshold is probably not sufficient enough to enhance submaximal exercise performance.

It was suggested, that observed non-significant differences in exercise performance after SIH, can be attributed to a low hypoxic stimulus, added to SIT since most studies simulated altitudes from 2000–3000 m (Warnier et al., 2020). Future studies should therefore determine if high altitudes (≥4000 m) can elicit greater physiological stress and therefore larger adaptations in aerobic and anaerobic exercise performance than the SIH training performed at moderate altitudes.

Several limitations have to be addressed when interpreting the results of the identified studies. First, only three studies included a control group, though it is difficult to conclude if observed changes are the result of SIT, hypoxic exposure, or its combination. Second, a lack of prescribing a blinding procedure for the hypoxic condition was evident and some of the studies. Thirdly, articles included in this review investigated the effects of SIT on subjects characterized as “healthy recreationally active adults or top athletes”. However, the potential for SIH to elicit exercise improvements can be also observed in other populations. Included studies used the various durations of training interventions, which leaves much to be determined regarding the impact of participation in SIH on not only improvements in exercise performance but also on the time course of physiological adaptations, participant adherence, and injury rates. The time course of physiological adaptations may be further elucidated through testing different lengths of training interventions that specifically examine central and peripheral changes at various time points throughout the trials. Also, alterations in the gene expression level can explain the underlying regulatory mechanism responsible for the muscular adaptations induced by SIH, therefore, it is desired that future studies investigate its effects on the aforementioned adaptations.

It can be identified that SIT in hypoxia augments adaptation during a 6-week training period (Puype et al., 2013) however SIT in hypoxia over a 2-week training intervention may offer little additional benefit when compared to equivalent training in normoxia (Richardson & Gibson, 2015; Richardson, Relf, et al., 2016). In this training modality, the dose-response relationship remains to be fully determined in hypoxia, though it is known that 2 weeks is a sufficient period to elicit adaptations in normoxia (Burgomaster et al., 2008; Burgomaster et al., 2005).

Future studies should determine whether SIH can be similarly an effective and time-efficient training method compared to continuous exercise methods performed in hypoxia (continuous training in hypoxia, interval training in hypoxia (McLean et al., 2014)) as observed in normoxia (Gist et al., 2014; Sloth et al., 2013). Additionally, it should be explored if SIH is a feasible training strategy for acclimatization to real altitude, since acclimatization periods due to a reduced aerobic capacity at altitude, require reduced training volumes to be to avoid overtraining. Furthermore, the majority of included RCTs required participants to perform sprints on a cycle ergometer, while no SIH study included any other exercise type, such as running, rowing, double-polling, etc. Despite stationary cycling being a non-weight-bearing activity, coupled with the minimal eccentric contraction of leg muscles, which seems to mitigate the risk of injury and discomfort; new well-designed RCTs using various modes of SIH are needed to increase the knowledge of effects across different exercise types. Nevertheless, studies of various populations and all age ranges are necessary to determine the impact of SIH in clinical and older populations.

CONCLUSION

The hypothesis driving the current review – that performing SIT in hypoxic conditions might yield specific physiological adaptations to boost exercise performance was not fully confirmed. In particular, this systematic review indicates that SIH does not further augment exercise performance in healthy recreationally active, or top athletes when compared to SIT performed in normoxia. Accordingly, it seems that SIH is not a superior training method for improving exercise performance compared to its normoxic counterpart, therefore, the training method does not appear as meaningful as other new LLTH training methods (RSH, VHL, BFR, RTH). However, SIH did show some potential for inducing beneficial physiological adaptations which could potentially facilitate aerobic and anaerobic energy turnover in skeletal muscles and are usually not expressed to the same extent after the SIT exercise periods. Observed cellular and molecular adaptation might augment oxidative and glycolytic capacity, especially of fast-twitch muscle fibers, and could, therefore, contribute to the improvement in explosive, high-intensity, and submaximal endurance efforts. The use of longer recovery periods in SIH would potentially allow for more complete PCr resynthesis, myoglobin saturation, higher muscle La^- and H^+ ions efflux as well as the re-establishment of ion-homeostasis (which are all important fatigue-modulating factors (Girard et al., 2011)) before the start of consecutive sprints, which can augment the activation of fast-twitch muscle fibers, and prolong the maintenance of high muscle forces during exercise in hypoxia. With these properties, athletes can achieve a complete restoration of sprinting performance during exercising in hypoxia, which enables them to exert greater metabolic load and consequential improvements in aerobic and anaerobic performance. The finding of our review is of particular interest for disciplines requiring longer high power outputs, such as in very explosive sports (400 m sprints, cycling, skiing, etc.). Additionally, our findings reinforce SIH for athletes sojourning to moderate altitude and aiming to maintain training quality and avoid overtraining, by reducing the volume and increasing the intensity of training.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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