An optimal exercise protocol for improving endurance performance and health

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Abstract Recent evidence suggests that the underlying mechanisms involved in beneficial adaptations to aerobic exercise, which promote health and increase endurance capacity, may be due to exercise-induced transient gene responses. In this review, an efficient exercise protocol to promote health and increase endurance capacity is discussed in relation to exercise-induced changes in gene expression. Exercise-induced transient gene responses, which are associated with adaptations to aerobic exercise, have been suggested to be induced by metabolic stress. Exercise to increase aerobic capacity and improve health should aim to increase the expression of peroxisome proliferator-activated receptor- γ coactivator-1 α (PGC-1 α), which is the key gene to enhance the function of mitochondria. Training at the lactate threshold is suggested to be the threshold intensity for inducing gene expression of PGC-1 α . Analysis of training studies assessing the effect on $\dot{V}O_{2\max}$ suggests that individuals with varied baseline $\dot{V}O_{2\max}$ values obtain significant improvement in $\dot{V}O_{2\max}$ at the lactate threshold. High-intensity interval training (HIT), which can induce gene expression of PGC-1 α , may be as efficient and effective in increasing aerobic capacity as continuous exercise training, despite a substantial reduction in exercise volume. Exercise at times when muscle glycogen is low could be more effective at improving mitochondrial function. HIT consumes a large amount of muscle glycogen per unit of energy consumption, and studies suggest that longer recovery periods induce glycogen depletion with much lower amounts of exercise compared to continuous exercise. Exercise after HIT-induced glycogen depletion may be a beneficial exercise prescription for endurance capacity and health promotion.

Keywords : lactate threshold, peroxisome proliferator-activated receptor- γ coactivator-1 α , high-intensity intermittent training

Introduction

It is widely accepted that the beneficial effects of exercise, which promote health and endurance performance, are achieved by improving aerobic capacity via endurance training. Exercise therapy, consisting of endurance training for metabolic syndrome and all chronic diseases including cardiac rehabilitation, is well established. If exercise therapy is conducted correctly, even cardiac patients can achieve the high fitness levels required to complete a marathon¹⁾. Endurance training induces an increase in mitochondrial biogenesis and enhances muscle oxidative capacity. These adaptations contribute to endurance performance and reduce the risk of many chronic disorders. Recently, many studies have attempted to evaluate the efficacy of exercise protocols by assessing molecular markers for mitochondrial biogenesis just after a single session of exercise. From these studies, it is possible to delineate a practical and effective training strategy.

In this review, we discuss a practical and effective exer-

cise protocol, which people could use to improve health and endurance performance in, for example, marathon training.

Exercise-induced expression of skeletal muscle PGC-1 α

Aerobic capacity is dependent on the function of mitochondria in skeletal muscles. It is known that the function of mitochondria improves through appropriate training. Peroxisome proliferator-activated receptor- γ coactivator-1 α (PGC-1 α) is a transcriptional coactivator, which reinforces the transcriptional activity of the peroxisome proliferator-activated receptor, a transcription factor that increases the gene expression of enzymes in mitochondria. Rodent studies have demonstrated that PGC-1 α is a gene that is pivotal in causing skeletal muscle adaptation that determines aerobic capacity, and also promotes mitochondrial biogenesis, capillary angiogenesis, and fatty acid utilization^{2,3)}. If the exercise conditions that promote the PGC-1 α gene and protein expression in skeletal muscle are known, appropriate training regimens could be designed.

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Expression of PGC-1 α associated with muscle contraction is caused by the activation of calmodulin-dependent kinase accompanying [1] the release of calcium ions from the sarcoplasmic reticulum⁴⁾, [2] the activation of AMP-activated protein kinase (AMPK)^{5,6)}, [3] the activation of mitogen-activated protein kinase⁷⁾, and [4] catecholamine release⁸⁾. It is likely that [1] and [2] are intensity-dependent. Regarding [3], it has been shown that mitogen-activated protein kinase is activated within skeletal muscles after long-term spontaneous exercise in mice⁷⁾. Regarding [4], the lactate threshold is an index for catecholamine release, and the longer the duration of exercise, the higher the catecholamine concentration in the blood.

Results from studies examining skeletal muscle PGC-1 α gene expression, associated with exercise in humans, are summarized in Table 1⁹⁻³¹⁾. All studies with an exercise intensity greater than 70% $\dot{V}O_{2\max}$ showed an increase in gene expression. There were 11 research articles with exercise intensity less than 70% $\dot{V}O_{2\max}$. PGC-1 α gene expression was seen in most research articles (9 studies), even with an exercise intensity of 40% $\dot{V}O_{2\max}$. However, Schjerve et al. compared training at an intensity of 60 to 70% heart rate reserve (HRR) (duration: 47 minutes) with training at 85 to 95% HRR (exercise of 1 minute repeated 4 times by taking a recovery break at 50% HRR for 3 minutes at each interval)³²⁾, at the same level of energy consumption, and reported that PGC-1 α protein levels only significantly increased in the high intensity condition. Similarly, we compared the effects of two different exercise intensities with the same energy consumption, and showed that exercise at an intensity below the lactate threshold failed to increase gene expression³¹⁾. These studies suggest the presence of a training intensity threshold inducing PGC-1 α expression, similar to the improvement in $\dot{V}O_{2\max}$. As previously mentioned, PGC-1 α expression is related to metabolic demand. Activation of β -adrenergic receptors has been shown to be a major mechanism involved in exercise-induced increases in PGC-1 α expression in animals³³⁾. It is well documented that there is a catecholamine threshold exercise intensity, which corresponds to the lactate threshold. AMPK kinase is one of the main regulators of PGC-1 α , and is activated by a decrease in the ATP/AMP ratio and creatine phosphate concentration. During exercise, metabolic stress has been shown to be induced with exercise intensity above 50% $\dot{V}O_{2\max}$, which closely corresponds to the lactate threshold in individuals of average fitness. We confirmed that training at the lactate threshold can induce gene expression of PGC-1 α and an improvement in $\dot{V}O_{2\max}$ ²⁹⁾. Additionally, moderate training simultaneously induced the expression of a number of metabolic genes involved in the tricarboxylic acid cycle, oxidative phosphorylation, beta-oxidation, electron transport, antioxidant enzymes, contractile apparatus, and 233 novel transcripts²⁹⁾.

Relative exercise intensity in relation to baseline aerobic capacity

Unfit individuals can improve their aerobic capacity with a lower relative exercise intensity compared to fit individuals. The American College of Sports Medicine suggests that aerobic capacity is improved at a threshold intensity of 50% HRR or $\dot{V}O_{2\max}$ for most adults, and 40% HRR or $\dot{V}O_{2\max}$ for individuals with low aerobic fitness³⁴⁾. Swain and Franklin reviewed training studies to find the minimal training threshold³⁵⁾. They concluded that highly fit individuals with a $\dot{V}O_{2\max}$ greater than 40 ml.kg⁻¹.min⁻¹ could expect improvement in $\dot{V}O_{2\max}$ at training intensities of at least 45% of oxygen uptake reserve ($\dot{V}O_{2R}$), and those with a $\dot{V}O_{2\max}$ below 40 ml.kg⁻¹.min⁻¹ at 30% of $\dot{V}O_{2R}$. However, the reason why different threshold intensities exist for different baseline aerobic capacities is currently unknown.

There are many studies that have confirmed that training at the lactate threshold induces improvements in $\dot{V}O_{2\max}$, as well as in the lactate threshold itself, in young and elderly individuals^{29,36-48)}. The lactate threshold is between 40 and 60% of $\dot{V}O_{2\max}$ for most untrained individuals^{49,50)}, but between 60 and 80% $\dot{V}O_{2\max}$ in experienced distance runners⁵¹⁾. The relative intensity corresponding to the lactate threshold is also influenced by muscle fiber types⁵²⁾. Table 2 shows % $\dot{V}O_{2R}$ at the lactate threshold with $\dot{V}O_{2\max}$ levels from data from our laboratory. The mean % $\dot{V}O_{2R}$ is increased with increasing fitness level, but there is wide variation at all fitness levels. The same relative intensity expressed as % $\dot{V}O_{2R}$, % $\dot{V}O_{2\max}$, and %HRR may not induce the same metabolic stress and PGC1- α gene expression in all individuals.

Training intensity expressed as % $\dot{V}O_{2R}$ from previous training studies is shown in Table 3^{49,53-97)}. The training intensity of studies that were associated with improvement in $\dot{V}O_{2\max}$ is above the mean of % $\dot{V}O_{2R}$ minus one SD (standard deviation) corresponding to the lactate threshold of the fitness category. Conversely, most previous training studies, that examined the effectiveness of exercise intensity below the mean of % $\dot{V}O_{2R}$ minus one SD corresponding to the lactate threshold of the fitness category, failed to find improvement in $\dot{V}O_{2\max}$ (Fig. 1). In addition, only one study showed significant increases in $\dot{V}O_{2\max}$, and only a 4% increase at that. Thus, we have concluded that the lactate threshold is the minimum training intensity required to produce increases in $\dot{V}O_{2\max}$.

Minimum training intensity for trained individuals

Two studies have compared training intensity with PGC-1 α mRNA in trained subjects, based on the hypothesis that high-intensity interval training (HIT) results in greater metabolic stress and induces higher levels of PGC-1 α expression. Nordsborg et al. tested the hypothesis with fit subjects who had been performing regular exercise

Table 1. Exercise and PGC-1 α mRNA expression in human skeletal muscleExercise intensity $\geq 70\% \dot{V}O_{2\max}$

Authors	Year	Subjects	Exercise					Recovery		Result*
			Type		Intensity	Time (min)	set	Intensity	Time (min)	
Cluberton LJ et al.	2005	6 males	Cycling	Continuous	74% $\dot{V}O_{2\text{peak}}$	60	1	-	-	↑ 3-fold
Coffey VG et al.	2006	7 strength-trained, 6 endurance-trained males	Cycling	Continuous	70% $\dot{V}O_{2\text{peak}}$	60	1	-	-	↑ endurance-trained; ~8.5-fold strength-trained; ~10-fold
Sriwijitkamol A et al.	2007	12 type 2 diabetic, 8 obese & 8 lean	Cycling	Continuous	70% $\dot{V}O_{2\max}$	40	1	-	-	↑ about 10–15-fold
De Filippis E et al.	2008	7 lean and 9 obese	Cycling	Interval	54 & 84% $\dot{V}O_{2\max}$	10	4	0watt	2	↑ Lean; approximately 8-fold Obese; approximately 4-fold
Gibala MJ et al.	2009	6 young men	Cycling	Interval	maximal	0.5	4	Undescribed	4	↑ approximately 2-fold
Harber MP et al.	2009	8 male	Running	Continuous	~75% $\dot{V}O_{2\max}$	45	1	-	-	↑ & → Soleus; 5.5-fold Vastus lateralis; unchanged
Wang L et al.	2009	9 sedentary	Cycling	Interval	120% $\dot{V}O_{2\max}$	0.2	180	20% $\dot{V}O_{2\max}$	0.3	↑ 13-fold
Cochran AJ et al.	2010	10 healthy men	Cycling	Interval	90–95% $\dot{V}O_{2\max}$	4	5	Undescribed	2	↑ ~8-fold
Egan B et al.	2010	8 healthy, sedentary males	Cycling	Continuous	80% $\dot{V}O_{2\text{peak}}$	36	1	-	-	↑ approximately 10-fold
Psilander N et al.	2010	10 male elite cyclists	Cycling	Interval	maximal	0.5	7	50W	4	↑ 6–7-fold
					~87% $\dot{V}O_{2\max}$	20	3	50W	4	↑ 6–7-fold
					85% $\dot{V}O_{2\max}$	4	4	Undescribed	3	↑ 5–7-fold
Nordsborg NB et al.	2010	10 trained, 8 untrained	Cycling	Interval	70% $\dot{V}O_{2\max}$	4	4	Undescribed	3	↑ approximately 3-fold
Perry CG et al.	2010	9 male	Cycling	Interval	~90% $\dot{V}O_{2\text{peak}}$	4	10	Undescribed	2	↑ >10-fold
Petersen AC et al.	2012	8 healthy men	Cycling	Continuous	71% $\dot{V}O_{2\text{peak}}$	45	1	-	-	↑ 2-fold
Bartlett JD et al.	2012	10 active men	Running	Interval	90% $\dot{V}O_{2\max}$	3	6	50% $\dot{V}O_{2\max}$	3	↑ 4.2-fold
				Continuous	70% $\dot{V}O_{2\max}$	50	1	-	-	↑ 4.5-fold
Serpiello FR et al.	2012	10 healthy young adults (7 males, 3 females)	Running	Interval	maximal	(4sec)	3×5	Passive recovery	(20sec)	↑ 3-fold
Wang L and Sahlin K	2011	7 untrained	Cycling	Interval	120% $\dot{V}O_{2\max}$	0.2	180	20% $\dot{V}O_{2\max}$	0.3	↑ 5- to 8- fold

Exercise intensity $< 70\% \dot{V}O_{2\max}$

Authors	Year	Subjects	Exercise					Recovery		Result
			Type		Intensity	Time (min)	set	Intensity	Time (min)	
Tunstall RJ et al.	2002	3 male & 4 female	Cycling	Continuous	63% $\dot{V}O_{2\max}$	60	1	-	-	→ -
Watt MJ et al.	2004	7 active males	Cycling	Continuous	60% $\dot{V}O_{2\text{peak}}$	180	1	-	-	↑ about 13-fold
Russell AP et al.	2005	7 healthy, untrained male	Cycling	Continuous	Approximately 50% $\dot{V}O_{2\max}$	120	1	-	-	↑ 12-fold 1 h post-exercise
Sriwijitkamol A et al.	2007	12 type 2 diabetic, 8 obese & 8 lean	Cycling	Continuous	50% $\dot{V}O_{2\max}$	40	1	-	-	↑ about 3–5-fold
Mathai A et al.	2008	7 male	Cycling	Continuous	65% $\dot{V}O_{2\max}$	until exhaustion (~120min)	1	-	-	↑ ~6.2-fold
Wang L et al.	2009	9 sedentary	Cycling	Continuous	60% $\dot{V}O_{2\max}$	90	1	-	-	↑ 10-fold
Egan B et al.	2010	8 healthy, sedentary males	Cycling	Continuous	40% $\dot{V}O_{2\text{peak}}$	69.9	1	-	-	↑ approximately 4-fold
Nishida Y et al.	2010	6 healthy men	Cycling	Continuous	36.8% $\dot{V}O_{2\max}$	60	1	-	-	↑ approximately 4-fold
Wang L et al.	2011	10 healthy	Cycling	Continuous	~65% $\dot{V}O_{2\max}$	60	1	-	-	↑ 10-fold
Tobina T et al.	2011	6 young men	Cycling	Continuous	48% $\dot{V}O_{2\text{peak}}$	60	1	-	-	↑ approximately 5-fold
			Cycling	Continuous	37% $\dot{V}O_{2\text{peak}}$	88.5	1	-	-	→ -
Wang L and Sahlin K	2012	7 untrained	Cycling	Continuous	60% $\dot{V}O_{2\max}$	90	1	-	-	↑ 5- to 8- fold

*↑ means significant increase, and → means unchanged in PGC-1 α mRNA abundance.**Table 2.** Range of % $\dot{V}O_{2R}$ at lactate threshold intensity

$\dot{V}O_{2\max}$ range (ml/kg/min)	n	% $\dot{V}O_{2R}$ at Lactate threshold(%)			<i>p</i> for trend
		mean	min	max	
<30	n=70	39.7 ± 7.8	34.9	54.0	<i>p</i> <0.001
30~39.9	n=44	44.6 ± 11.0	32.2	62.9	
40~49.9	n=42	47.9 ± 8.8	34.1	68.8	
50<=	n=25	55.6 ± 7.6	44.8	73.9	

Data are given as mean ± SD.

Table 3. Summary of aerobic training study converted into % $\dot{V}O_2R$.

Aauthor	yrs	n	age	Initial $\dot{V}O_{2max}$	Frequency	Time	duration	Training Intensity				$\dot{V}O_{2max}$	% $\dot{V}O_2R$
				ml/kg/min	times/wk	min/session	week	% $\dot{V}O_{2max}$	%HRR	%MHR	% $\dot{V}O_2R$	%change	at LT -1SD*
Davies and Knibbs	1971	9	18-38	50.8	1,3,5	5,10,20	8	80			79	3.0	+
		9		47.0				50			46	ns	+
Gledhill and Enyon	1972	8	18-22	39.4	5	20	5				55	14.0	+
		8		38.9							43	13.0	+
Edwards	1974	6	17-21	26.2	7	15	4		63		63	34.0	+
		6		27.3					47		47	26.0	+
Burke and Franks	1975	4	16-18	44.6	3	15	10			85	72	9.0	+
		4		44.1		22	10			75	55	9.0	+
Kearney et al.	1976	13	17-22	38.5	3	14	9		65		65	23.0	+
		14		38.4		18			50		50	14.0	+
Blair et al.	1980	5	18-26	43.5	5	19	10	80			78	9.0	+
		8		43.5		35		50			46	8.0	+
Badenhop et al.	1983	14	60-	20.6	3.1	25	9		60		60	15.0	+
		14		21.1					38		38	16.0	+
Gaesser and Rich	1984	7	20-30	43.3	3	25	18	83			81	20.0	+
		9		37.7		50		45			39	17.0	+
Seals et al.	1984	11	60-69	25.4	4.6	27	26		40		40	11.0	+
Seals et al.	1985	10	62	28.0	3-4	30-45	24			80-90	72	17.9	+
Gossard et al.	1986	23	40-60	32.2	5	37	12	72			69	17.0	+
		21		33.3		52		51			45	8.0	+
Foster et al.	1989	9	67-89	13.7	3	25	10		60		60	15.0	+
		7		12.6		34			40		40	13.0	+
Hagberg et al.	1989	16	70-79	22.5	3	40	13	60			53	15.0	+
Panton et al.	1990	17	71.8	22.5	3	35-45	26		80		80	20.4	+
Belman and Gaesser	1991	8	65-75	24.3	4	30	8		75		75	7.0	+
		9		25.4	4	30	8		35		35	7.0	+
Blumenthal et al.	1991	32	67	19.5	3	30	16		70		70	9.7	+
Duncan et al.	1991	16	20-40	30.6	5	36	24				49	16.0	+
		12		32.4		45					37	9.0	+
King et al.	1991	40	50-65	28.7	6	40	24			73-88	65	5.2	+
		34	50-65	24.3		40				73-88	65	0.4	+
		42	50-65	30.1	3	40	24			73-88	65	3.0	+
		35	50-65	23.1		40				73-88	65	4.3	+
		45	50-65	30.8	5	30	24			60-73	44	1.6	+
		29	50-65	22.4		30				60-73	44	2.2	+
Probart et al.	1991	10	72	21.2	3	20	26			70	49	8.4	+
Carroll JF et al.	1992	14		25.4	3	40	12		60-65		63	9.8	+
		23		26.1		40			60-65		63	6.9	+
		14		27.9		45			65-70		68	6.1	+
		23		27.9		35			80-85		83	15.8	+
Hill et al.	1993	87	64	24.5	3-5	50	48			80	64	24.3	+
Braith et al.	1994	19	66	25.0		40	24		70		70	16.0	+
		14	66	26.0		35	24		85		85	26.9	+
Suter et al.	1994	28	40	38.1	2.4	38	26	75			72	8	+
		28	42	35.3	3	40					44	7	+
Ready et al.	1996	19	61.3	23.2	3	60	24	60			53	12.1	+
		17	61.3	22.3	5	60	24	60			53	13.9	+
Gillett et al.	1996	76	64.4	23.8	3	60	16		60-80		70	31.9	+
Hepple et al.	1997	20	65-74	25.3	3	30	18		60-70		65	22.5	+
King et al.	1997	10	60.2	22.6	7	40	16		60-75		68	3.1	+
Engels HJ et al.	1998	18	66	20.4	3.3	45	44		79		56	22.5	+
Kohrt et al.	1998	10	68.6	20.5	3	60	10		50-70		60	9.3	+

Schuit et al.	1999	65.1	67	27.9	3	45	24	60-80	66	8.6	+	
Shin	1999	27	60-75	20.3	3	60	8	40-60	50	26.6	+	
Sunami et al.	1999	20	67	29.8	4	60	20	50	43	7.0	+	
Branch et al.	2000	10	20-40	29.2	3.4	39	12	80	77	21.0	+	
		8		29.8	3.3	62	12	40	32	17.0	+	
Fahlman et al.	2000	15	76	19.0	3	50	10	70	70	36.8	+	
Tsuji et al.	2000	31	67.3	23.7	2	25	25	60	60	15.5	+	
Kim et al.	2001	45	55	23.3	3	60	48	50	41	7.3	+	
		55	53	24.0	3	60	48	85	82	12.5	+	
Donnelly et al.	2003	25	22	32.8	~5	45	48	55-70	60-75	58	18.3	+
		16	24	39.2	~5	45	48	55-70	60-75	59	22.2	+
Prior et al.	2003	50	57.7	28.3	3	40	14	70	66	15.5	+	
		76	57.6	22.3	3	40	14	70	64	16.6	+	
		11	58.5	25.1	3	40	14	70	65	31.5	+	
		18	57.6	21.6	3	40	14	70	64	6.0	+	
Chaouachi et al.	2005	9	21.4	50.7	2	5.8	12	100	100	8.3	+	
		11	21.4	56.4	2	5.1	12	100	100	12.8	+	
		12	21.4	54.2	2	5.0	12	100	100	15.3	+	
		9	21.4	48.5	2	4.7	12	100	100	7.4	+	
Goodman et al.	2005	8	19.4	47.8	6	120		65	62	7.5	+	
Dolan et al.	2006	20	43	16.9	3	30	14		60	35	8.9	+
Audette et al.	2006	8	71.3	23.7	3	30	12		70	49	1.7	+
Heilbronn et al.	2007	8	37	47.1	4	45	6	55-70	59	17.0	+	
		7	38	45.3	4	45	6	55-70	59	10.9	+	
Ferrara et al.	2006	19	63	28.2	3	45-50	24		75-80	78	17.6	+
Fearheller et al.	2009	94	58.4	24.8	3	60	24	70	65	16.1	+	
Timmons et al.	2010	24	young	47.0	5	45	6	70	68	14.0	+	
Davies and Knibbs	1971	9	18-38	47.0	1,3,5	5,10,20	8	30	24	—	—	
Gledhill and Enyon	1972	8	18-22	41.5	5	20	5		30	—	—	
Burke and Franks	1975	4	16-18	41.4		35	10		65	38	—	—
Duncan et al.	1991	16	20-40	31.8	5	60	24		28	4.0	—	

$\dot{V}O_2\text{max}$ indicates maximum oxygen consumption; %HRR (% heart rate reserve); %MHR (% max heart rate); LT (lactate threshold); % $\dot{V}O_2\text{R}$ (% $\dot{V}O_2$ reserve).

*++ means that it is above the mean of % $\dot{V}O_2\text{R}$ minus one SD corresponding to the lactate threshold.

training for more than 1 year, and who showed a $\dot{V}O_2\text{peak}$ greater than $52 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ on a cycle ergometer¹⁹). They compared the effect of exhaustive intermittent cycling exercise (4×4 min at 85% of $\dot{V}O_2\text{peak}$, interspersed with 3-min recovery periods) with light intermittent cycling exercise (4×4 min at 70% of $\dot{V}O_2\text{peak}$, interspersed with 3-min recovery periods). PGC-1 α mRNA increased significantly in both exercise conditions, but increased approximately 4- to 5-fold after exercise at 85% $\dot{V}O_2\text{max}$, and approximately 3-fold less after exercise at 70% $\dot{V}O_2\text{max}$ compared with 85% $\dot{V}O_2\text{max}$. However, because the total amount of exercise volume was lower with exercise at 70% $\dot{V}O_2\text{max}$, it could not be concluded that HIT induces greater increases in PGC-1 α mRNA. Bartlett et al. have unexpectedly shown that high-intensity running (6×3-min at 90% $\dot{V}O_2\text{max}$ interspersed with 3-min recovery periods at 50% $\dot{V}O_2\text{max}$, and with a 7-min warm-up and cool-down period at 70% $\dot{V}O_2\text{max}$) and moderate-intensity continuous running (50-min continuous running at 70% $\dot{V}O_2\text{max}$), matched for work done amount, induce

similar activation of molecular pathways associated with regulation of mitochondrial biogenesis in recreationally active subjects at $52 \pm 7 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ of $\dot{V}O_2\text{max}$ ²²).

As mentioned above, 70% $\dot{V}O_2\text{max}$ is within the range of the lactate threshold in trained subjects. Thus, we hypothesize that, even in athletes, the minimal training intensity to induce PGC-1 α gene expression, for improving aerobic capacity, is their lactate threshold, as it is in sedentary subjects.

Minimum volume of training

A recent study showed that low-volume anaerobic interval training (4-6×30 s supramaximal sprint cycling Wingate tests) has a similar effect on improvement of mitochondria functions and endurance performance as aerobic endurance exercise (40-120 min exercise per session at 65% of $\dot{V}O_2\text{peak}$)⁹⁸. The weekly training volume of anaerobic HIT was ~90% lower in continuous training. It was also confirmed that this type of low volume HIT can

Fig. 1 Relationship between the initial $\dot{V}O_2\text{max}$ and the mean of $\% \dot{V}O_2R$ corresponding to the lactate threshold, and training intensity expressed as $\% \dot{V}O_2$ from previous training studies. The “●” indicates the mean of $\% \dot{V}O_2R$ corresponding to the lactate threshold. The “○” indicates that $\dot{V}O_2\text{max}$ was improved, and the “▲”, indicates no improvement in $\dot{V}O_2\text{max}$.

activate signaling pathways associated with mitochondrial biogenesis. Psilander et al. demonstrated, in elite cyclists, that 7×30 s “all-out” bouts and 3×20 min bouts at approximately 87% of $\dot{V}O_2\text{peak}$ could induce a similar increase in PGC-1 α ¹⁸. The volume of performed work in the anaerobic exercise was 88% lower than in the aerobic exercise. However, too much metabolic stress, associated with severe exercise, may not be practical for non-athletic individuals. Little et al. demonstrated that exercise at 100% $\dot{V}O_2\text{max}$, but continued for 1 min and interrupted for 75 s (repeated 8-12 times, which is double the total amount of anaerobic HIT), could induce mitochondrial biogenesis in skeletal muscle and improve functional exercise performance⁹⁹. Furthermore, Hood et al. demonstrated that practical aerobic HIT (10×1 min at 85-95% HRR interspersed with 1 min of recovery) could improve insulin sensitivity and increase markers of skeletal muscle mitochondrial contents and glucose transport capacity in sedentary middle-aged adults¹⁰⁰.

In conclusion, HIT can induce similar adaptations as endurance training despite a lower total exercise volume.

Training with low muscle glycogen

The important training adaptation for enhancing performance and muscle insulin sensitivity is a shift in substrate metabolism from carbohydrates to lipids. Recent studies show that exercise in individuals with lower muscle glycogen induces a greater increase in the transcriptional activity of several metabolic genes¹⁰¹⁻¹⁰⁴.

Hansen et al. demonstrated that training in individuals with low muscle glycogen increases the time to exhaustion and citrate synthase activity, and tends to increase

3-hydroxyacyl-CoA dehydrogenase activity compared to training in individuals with high muscle glycogen¹⁰⁵. Yeo et al. demonstrated that, in well-trained persons, training with low muscle glycogen resulted in greater fat utilization, during 30-min exercise at 70% $\dot{V}O_2\text{max}$, and greater increases in 3-hydroxyacyl-CoA dehydrogenase activity¹⁰⁶. Hulston et al. confirmed the findings of Yeo et al. and, using an isotope tracer, found that muscle-derived triacylglycerol oxidation increased after training in individuals with low muscle glycogen¹⁰⁷. Taken together, these studies indicate that exercise in individuals with low muscle glycogen improves the capacity for lipid oxidation to a greater degree compared with training in individuals with normal muscle glycogen levels.

In the studies above, the level of muscle glycogen in the low muscle glycogen group was 50% lower compared with the normal muscle glycogen group. Additionally, subjects performed 90-100 min of exercise at approximately 70% $\dot{V}O_2\text{max}$ prior to the main training. Since the glycogen utilization rate is highly dependent on exercise intensity, exercise at higher intensities can induce greater glycogen utilization. Data from Gollnick et al. showed that 50% glycogen utilization could be estimated with exercise for 9 min at 120% $\dot{V}O_2\text{max}$ (3×3 min exercise interspersed with 10-min recovery periods) or 4 min of exercise at 150% $\dot{V}O_2\text{max}$ (4×1 min exercise interspersed with 10-min recovery periods)¹⁰⁸. The total amount of exercise needed to consume 50% of available muscle glycogen would be drastically reduced if supramaximal, but intermittent, exercise was done instead of endurance-type exercise. However, supramaximal exercise is often too stressful. We hypothesized that short HIT at 100% $\dot{V}O_2\text{max}$, with longer durations of recovery to restore pH (which inhibits glycolysis) to physiological levels would result in muscle glycogen decreases. We showed that practical aerobic HIT (12×1 min at 100% $\dot{V}O_2\text{max}$ interspersed with 4-min recovery periods) could reach 60% lower glycogen levels. With this type of HIT, we were able to manipulate the glycogen level easier, and with a lower exercise volume (about 1/5), compared to submaximal endurance exercise¹⁰⁹.

In summary, the optimal exercise protocol to improve health and endurance performance was discussed in relation to exercise-induced gene expression of PGC-1 α , which is a critical regulator of mitochondrial biogenesis, angiogenesis, and fiber-type switching. Training intensity is a critical factor in PGC-1 α gene expression. Exercise at the lactate threshold is recommended as the minimum training intensity to improve aerobic capacity. HIT can be used to reduce training volume while achieving the same endurance adaptations and lower the muscle glycogen level, similar to submaximal continuous exercise training.

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