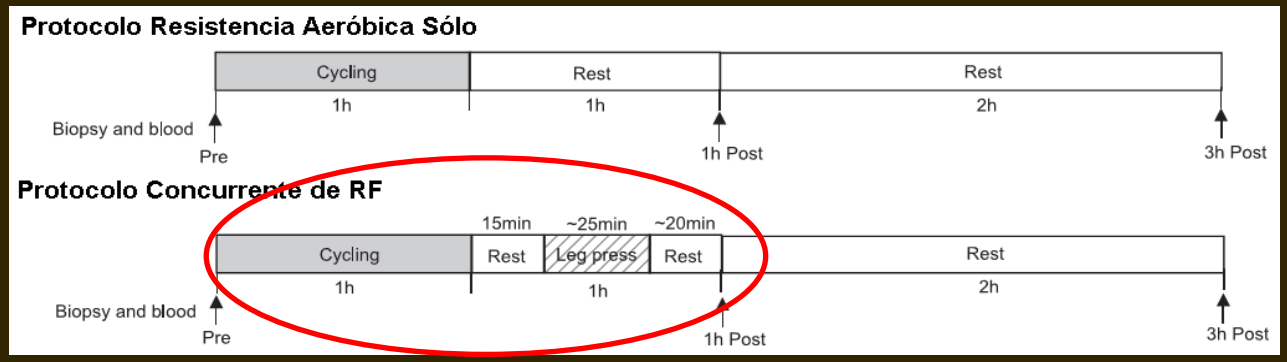
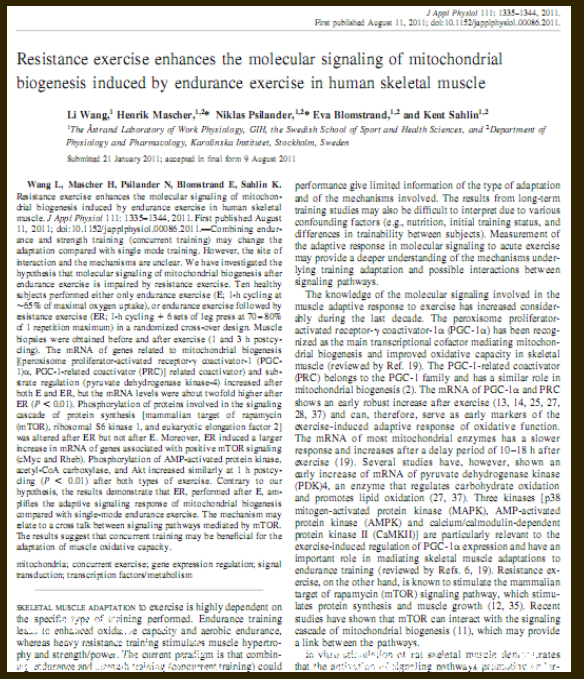
Mecanismos Moleculares del EC

10 sujetos sanos (V y M, recreativamente activos)
edad, 26±1.2 años; altura, 177±2.9 cm; peso, 72±3.5 kg
$VO_{2máx}$ 50±1.9 $ml \cdot min^{-1} \cdot kg^{-1}$
(1 MR) Press de piernas 336±22.3 kg

Efecto Agudo sobre Biogénesis Mitocondrial

R: 60' pedaleando al 65% de $VO_{2máx}$
R+F: 60' de pedaleo + 6 series de press de piernas al 70, 75, 80, 80, 75, y 70% de 1MR, al fallo (8-15rep), 3' pausa.





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Resistance exercise enhances the molecular signaling of mitochondrial biogenesis induced by endurance exercise in human skeletal muscle

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Wang L, Mascher H, Psilander N, Blomstrand E, Sahlin K. Resistance exercise enhances the molecular signaling of mitochondrial biogenesis induced by endurance exercise in human skeletal muscle. *J Appl Physiol* 111: 1335–1344, 2011. First published August 11, 2011; doi:10.1152/japplphysiol.00686.2011.—Combining endurance and strength training (concurrent training) may change the adaptation compared with single mode training. However, the site of interaction and the mechanisms are unclear. We have investigated the hypothesis that molecular signaling of mitochondrial biogenesis after endurance exercise is impaired by resistance exercise. Ten healthy subjects performed either only endurance exercise (E; 1-h cycling at ~65% of maximal oxygen uptake), or endurance exercise followed by resistance exercise (ER; 1-h cycling + 6 sets of leg press at 70–80% of 1 repetition maximum) in a randomized cross-over design. Muscle biopsies were obtained before and after exercise (1 and 3 h postcycling). The mRNA of genes related to mitochondrial biogenesis [peroxisome proliferator-activated receptor-γ coactivator-1 (PGC-1α, PGC-1-related coactivator (PRC)] related coactivator) and substrate regulation (pyruvate dehydrogenase kinase-4) increased after both E and ER, but the mRNA levels were about twofold higher after ER ($P < 0.01$). Phosphorylation of proteins involved in the signaling cascade of protein synthesis [mammalian target of rapamycin (mTOR), ribosomal S6 kinase 1, and eukaryotic elongation factor 2] was altered after ER but not after E. Moreover, ER induced a larger increase in mRNA of genes associated with positive mTOR signaling (cMyc and Rheb). Phosphorylation of AMP-activated protein kinase, acetyl-CoA carboxylase, and Akt increased similarly at 1 h postcycling ($P < 0.01$) after both types of exercise. Contrary to our hypothesis, the results demonstrate that ER, performed after E, amplifies the adaptive signaling response of mitochondrial biogenesis compared with single-mode endurance exercise. The mechanism may relate to a cross talk between signaling pathways mediated by mTOR. The results suggest that concurrent training may be beneficial for the adaptation of muscle oxidative capacity.

mitochondria; concurrent exercise; gene expression regulation; signal transduction; transcription factors/metabolism

SKELETAL MUSCLE ADAPTATION to exercise is highly dependent on the specific type of training performed. Endurance training leads to enhanced oxidative capacity and aerobic endurance, whereas heavy resistance training stimulates muscle hypertrophy and strength/power. The current paradigm is that combining endurance and strength training (concurrent training) could

performance give limited information of the type of adaptation and of the mechanisms involved. The results from long-term training studies may also be difficult to interpret due to various confounding factors (e.g., nutrition, initial training status, and differences in trainability between subjects). Measurement of the adaptive response in molecular signaling to acute exercise may provide a deeper understanding of the mechanisms underlying training adaptation and possible interactions between signaling pathways.

The knowledge of the molecular signaling involved in the muscle adaptive response to exercise has increased considerably during the last decade. The peroxisome proliferator-activated receptor-γ coactivator-1α (PGC-1α) has been recognized as the main transcriptional cofactor mediating mitochondrial biogenesis and improved oxidative capacity in skeletal muscle (reviewed by Ref. 19). The PGC-1-related coactivator (PRC) belongs to the PGC-1 family and has a similar role in mitochondrial biogenesis (2). The mRNA of PGC-1α and PRC shows an early robust increase after exercise (13, 14, 25, 27, 28, 37) and can, therefore, serve as early markers of the exercise-induced adaptive response of oxidative function. The mRNA of most mitochondrial enzymes has a slower response and increases after a delay period of 10–18 h after exercise (19). Several studies have, however, shown an early increase of mRNA of pyruvate dehydrogenase kinase (PDK)4, an enzyme that regulates carbohydrate oxidation and promotes lipid oxidation (27, 37). Three kinases [p38 mitogen-activated protein kinase (MAPK), AMP-activated protein kinase (AMPK) and calcium/calmodulin-dependent protein kinase II (CaMKII)] are particularly relevant to the exercise-induced regulation of PGC-1α expression and have an important role in mediating skeletal muscle adaptations to endurance training (reviewed by Refs. 6, 19). Resistance exercise, on the other hand, is known to stimulate the mammalian target of rapamycin (mTOR) signaling pathway, which stimulates protein synthesis and muscle growth (12, 35). Recent studies have shown that mTOR can interact with the signaling cascade of mitochondrial biogenesis (11), which may provide a link between the pathways.

In vitro stimulation of rat skeletal muscle demonstrates that the activation of signaling pathways promoting or in-

Ejercicio de Fuerza	*Serie 1*	*Serie 2*	*Serie 3*	*Serie 4*	*Serie 5*	*Serie 6*
Peso (kg)	235 ± 15	249 ± 16	264 ± 17	264 ± 17	249 ± 16	235 ± 15
% de 1MR	70.2 ± 0.5	74.4 ± 0.8	78.7 ± 0.8	78.7 ± 0.8	74.4 ± 0.8	70.2 ± 0.8
Repeticiones (número)	14.4 ± 1.0	11.1 ± 0.6	9.5 ± 0.7	8.7 ± 0.8	10.1 ± 0.9	10.7 ± 0.6

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Mecanismos Moleculares del EC

Efecto Agudo sobre Biogénesis Mitocondrial

*Los mRNA de los genes relacionados a la biogénesis mitocondrial y a la regulación del sustrato **aumentaron** después e R y R+F, pero los niveles de mRNA fueron superiores casi el doble después de R+F.*
*La fosforilación de las proteínas involucradas en la cascada de la señalización de la síntesis de proteínas **fue alterada** después de R+F pero no después de R.*

	Tipo	Pre	1h Post	3h Post
AGL, mmol/l	R	0.07 ± 0.01	0.21 ± 0.04*	0.22 ± 0.03*
	R+F	0.07 ± 0.03	0.20 ± 0.04*	0.22 ± 0.02*
Glucosa, mmol/l	R	5.18 ± 0.07	5.02 ± 0.21	4.89 ± 0.24*
	R+F	5.42 ± 0.21	5.24 ± 0.14	5.00 ± 0.15*
Lactato, mmol/l	R	1.14 ± 0.17	1.15 ± 0.08	0.89 ± 0.05
	R+F	1.20 ± 0.18	6.64 ± 0.83*†	1.15 ± 0.14
Glucógeno, mmol/kg	R	460 ± 21	194 ± 35*	224 ± 31*
	R+F	434 ± 26	146 ± 20*	176 ± 19*

* Post vs Pre. † R+F vs R

✓Contrariamente a varios trabajos científicos anteriores, los resultados demuestran que el R+F, realizado después de R, **amplifica** la respuesta adaptativa de señalización de la biogénesis mitocondrial comparado con R de único modos.

✓El mecanismo puede relacionarse a **una interferencia** entre las vías de señalización mediados por el mTOR.

✓Los resultados indican que el **EC** puede ser **beneficioso** para la adaptación de la **capacidad oxidativa** del músculo.

→ No hubo interferencia en las adaptaciones del entrenamiento.

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