OSPEDALE «A. Cardarelli»

Tiroide e Sport

DOTT.SSA GIORGIA ANNA GARINIS

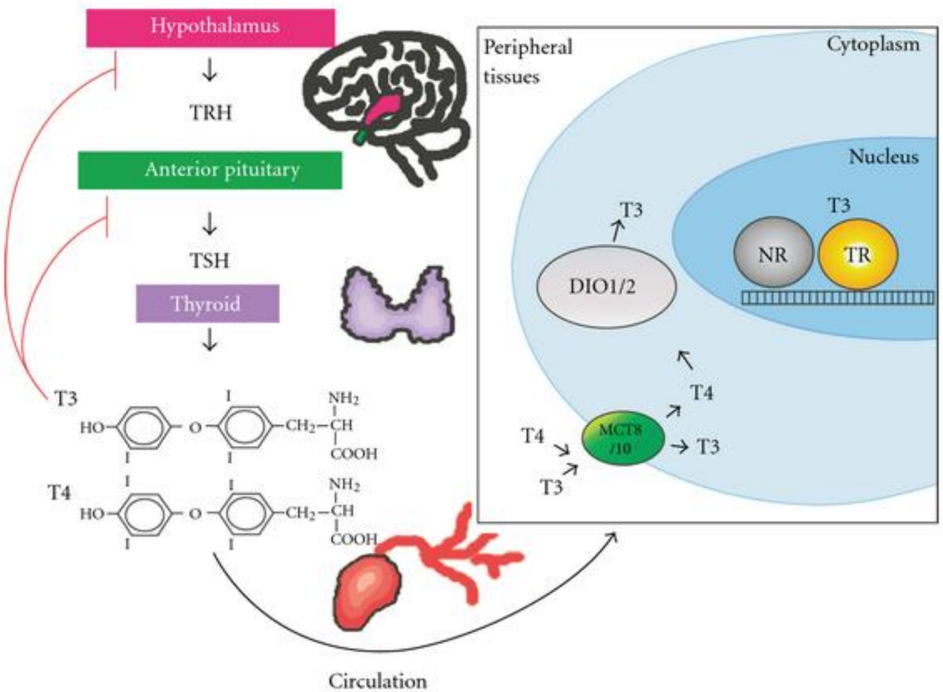
- Ruolo degli ormoni tiroidei nell’attività sportiva?

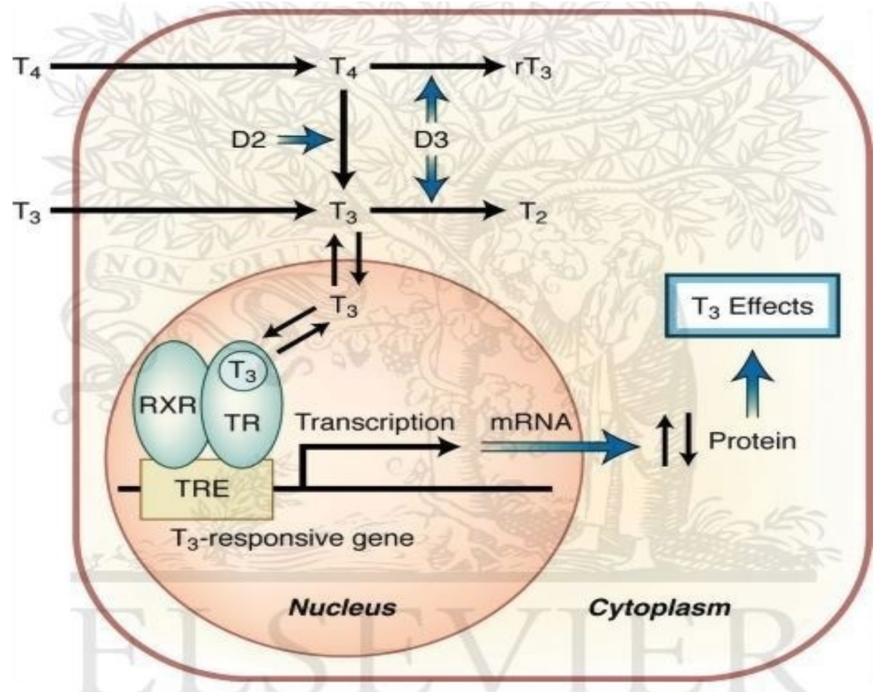
- Effetti dell’attività sportiva sugli ormoni tiroidei?

Succede durante l'esercizio fisico...

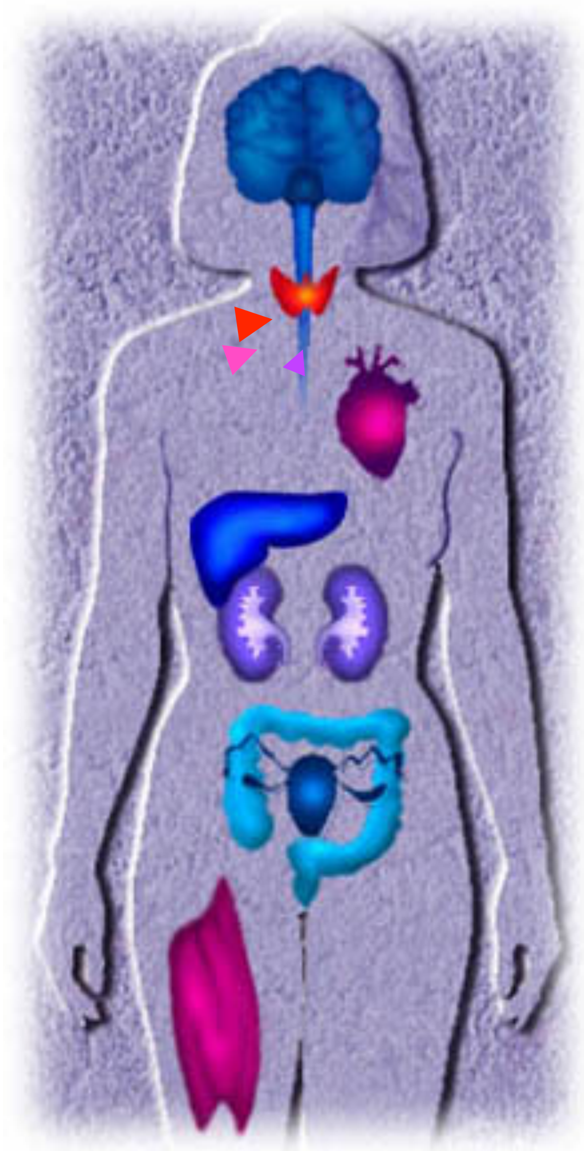
- Aumenta il lavoro muscolare
- Si modifica l'attività cardiaca
- Aumenta il consumo energetico

Ruolo degli ormoni tiroidei



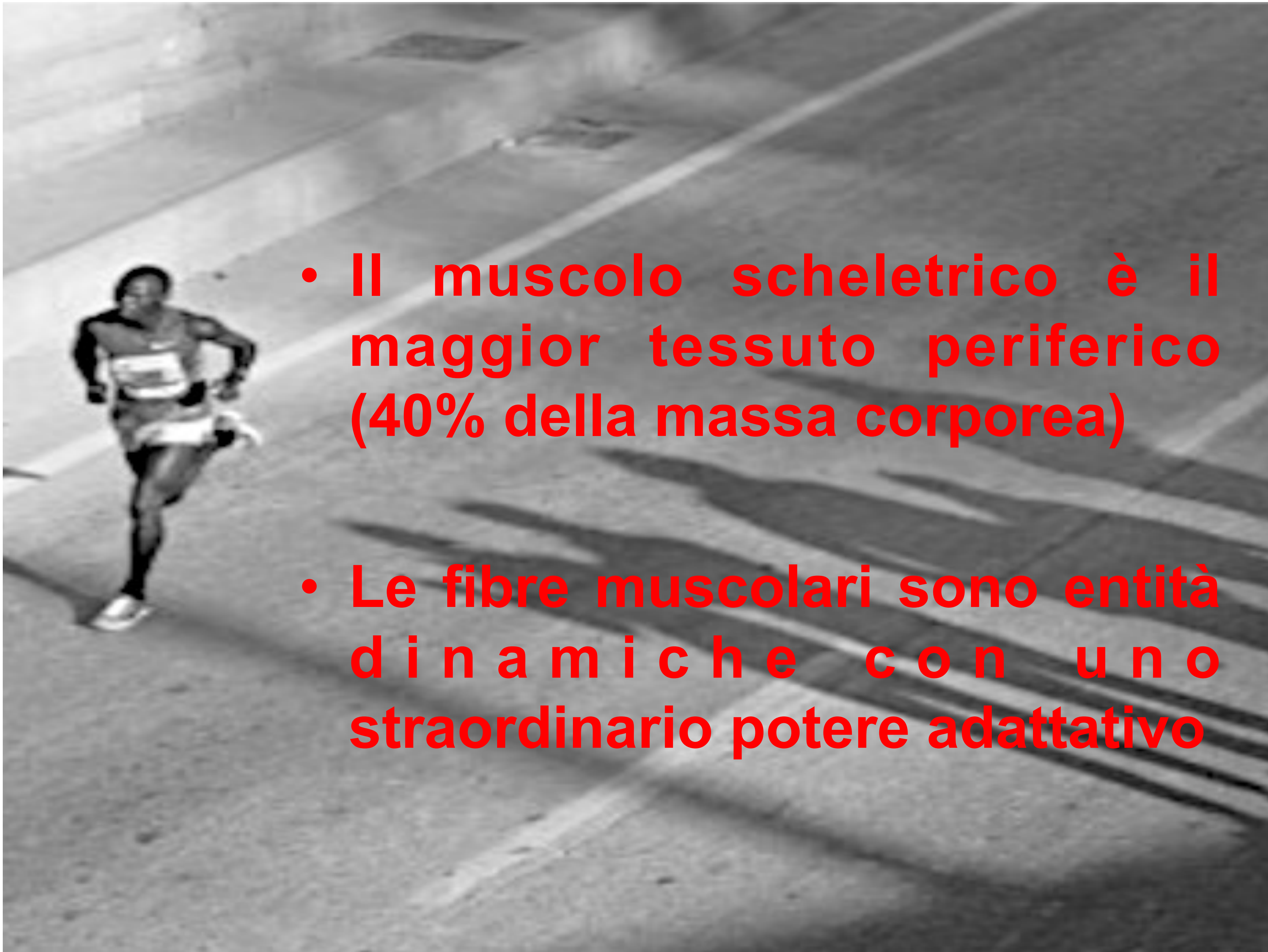


- **SNC**: TRß1 e TRß2 + *TRα1 TRα2*
- **Ipotalamo- Ipofisi:** TRß1 e TRß2
- **Cuore:** TRß1 e TRß2 + *TRα1*
- **Fegato**: TRß1 e TRß2
- **Rene:** *TRα1* + TRß1 e TRß2
- **Gonadi**: *TRα1*
- **Muscolo:** *TRα1*



Succede durante l’esercizio fisico...

- Si modifica l’attività cardiaca
- Aumenta il lavoro muscolare
- Aumenta il consumo energetico



- **Il muscolo scheletrico è il maggior tessuto periferico (40% della massa corporea)**
- **Le fibre muscolari sono entità dinamiche con uno straordinario potere adattativo**

Ormoni tiroidei e muscolo

- Influenzano il tipo e la composizione delle fibre muscolari.

- Regolano lo sviluppo e la maturazione.

- Regolano il profilo metabolico.

Table 1 Effects of thyroid hormone signalling on skeletal muscle properties

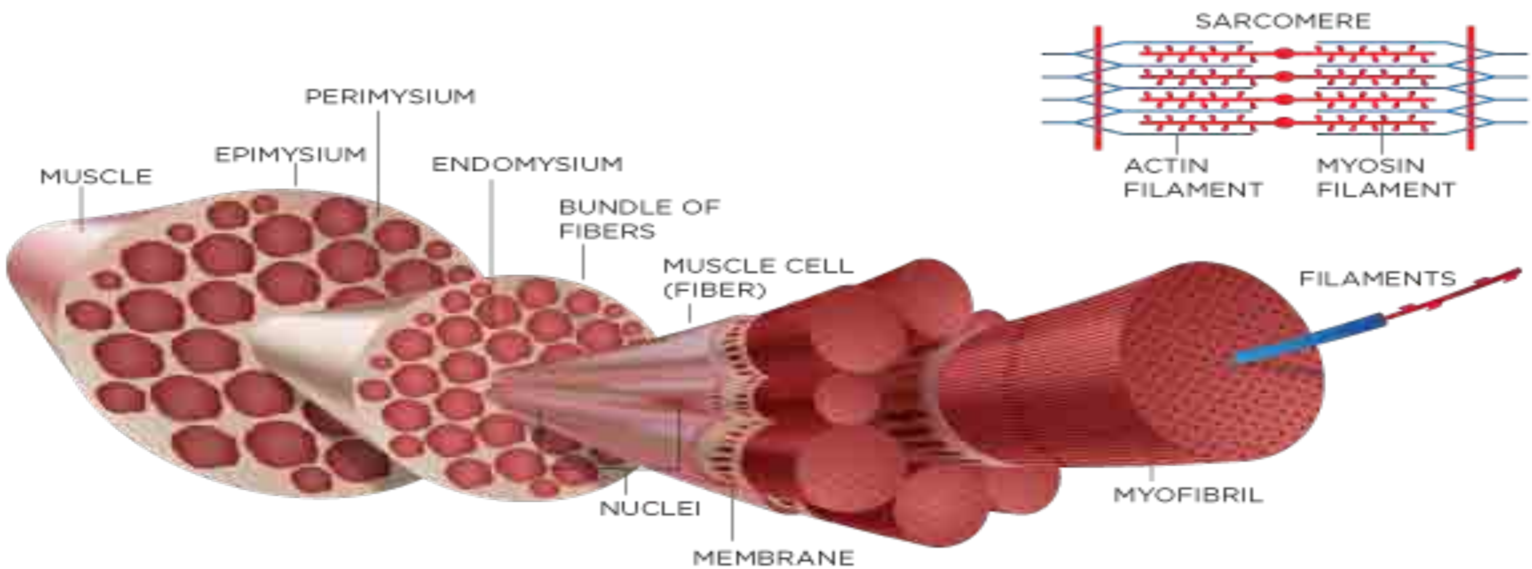
Table 1 | Effects of thyroid hormone signalling on skeletal muscle properties

Skeletal muscle feature	Key thyroid-hormone-regulated proteins	Associated effect
Contractility	Myosin-7 ↓, myosin-2 ↑, myosin-1 ↑, myosin-4 ↑	Increased rate of contraction
	SERCA1a ↑, SERCA2a ↑	Increased rate of relaxation
Metabolism	Na^+/K^+-ATPase ↑, SERCA1a ↑, SERCA2a ↑	Decreased energetic efficiency of contraction due to higher ATP consumption associated with fluxes of Na^+/K^+ and Ca^{2+} at rest and during activity
	GLUT-4 ↑, ME1 ↑	Increased glycolytic capacity leading to increased ATP generation
	PGC-1α ↑	Increased mitochondrial density leading to increased ATP generation
	UCP3 ↑, mGPDH ↑	Decreased mitochondrial efficiency

In addition to direct transcriptional regulation of a number of genes, thyroid hormone signalling has secondary effects, among them the action of muscle regulatory factors, such as MYOD1 and myogenin, as well as adaptive effects related to changes in energy metabolism and to modulation of Ca^{2+}-dependent signaling by the changes in intracellular Ca^{2+} handling during contractile activity. Because thyroid hormone signalling promotes expression of genes related with faster muscle fibre phenotypes, its effects are more pronounced in muscles with a higher content of slow fibres. Abbreviations: GLUT-4, glucose transporter 4; ME1, NADP-dependent malic enzyme; mGPDH, muscle glycerol-3-phosphate dehydrogenase; PGC-1α, peroxisome proliferator-activated receptor γ coactivator 1α; SERCA, sarcoplasmic-endoplasmic reticulum Ca^{2+}-ATPase; UCP3, uncoupling protein 3.

Salvatore, D. *et al.* (2013) Thyroid hormones and skeletal muscle—new insights and potential implications
Nat. Rev. Endocrinol. doi:10.1038/nrendo.2013.238

nature REVIEWS ENDOCRINOLOGY



- T_3 modula l'espressione dei fattori regolatori miogenici

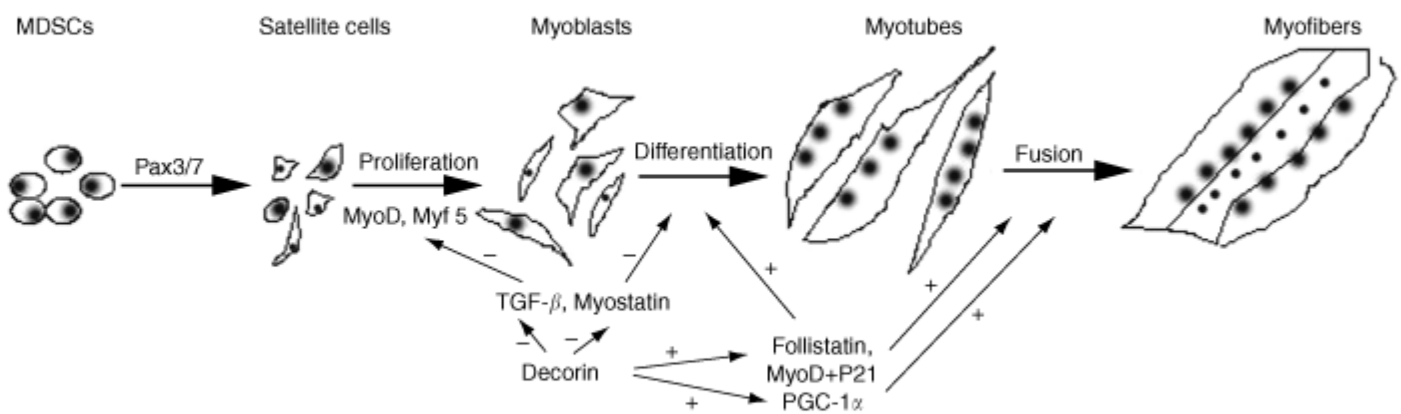
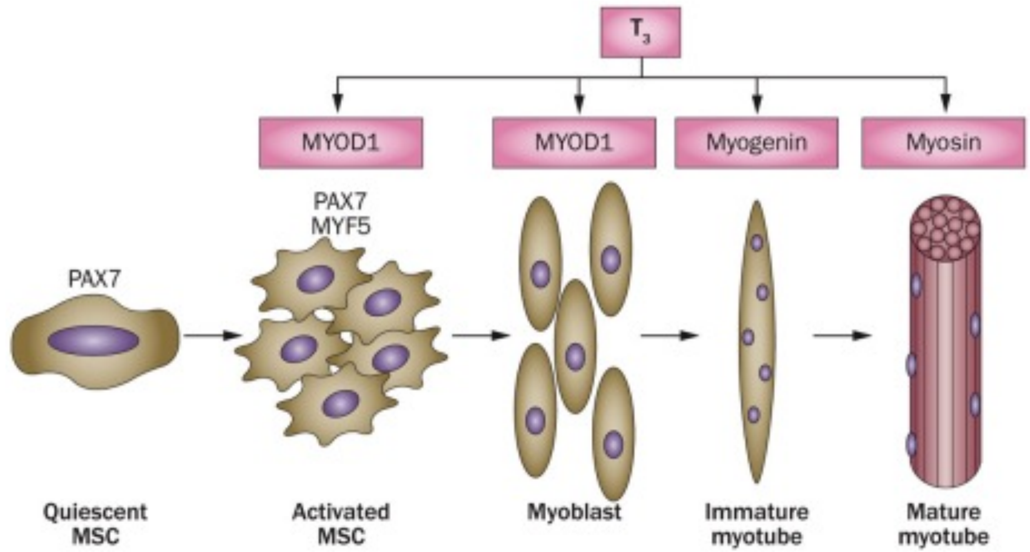


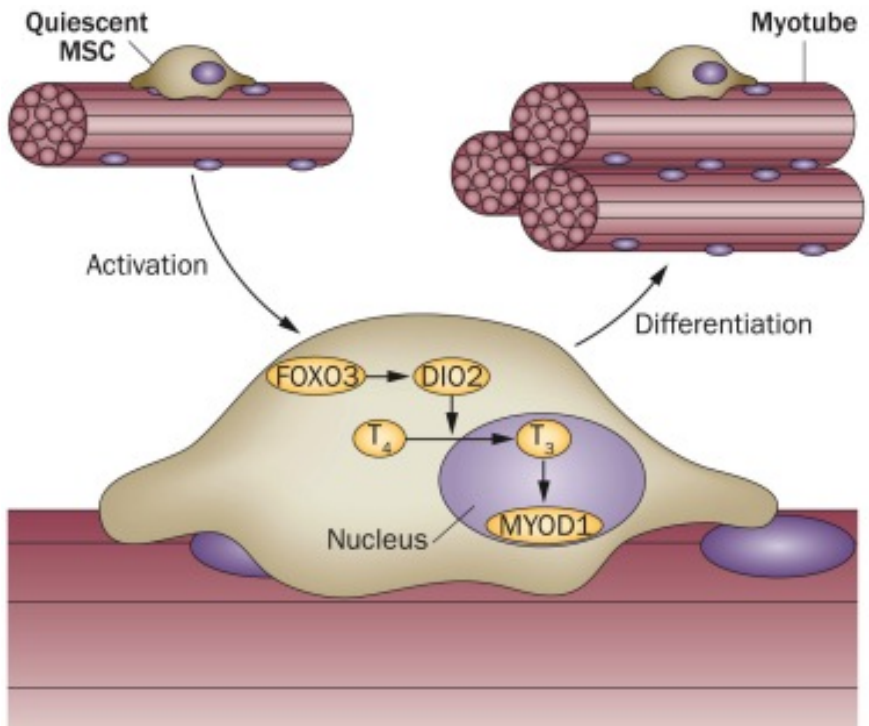
Figure 1 The role of thyroid hormone signalling in skeletal myogenesis



Salvatore, D. *et al.* (2013) Thyroid hormones and skeletal muscle—new insights and potential implications
Nat. Rev. Endocrinol. doi:10.1038/nrendo.2013.238

nature REVIEWS ENDOCRINOLOGY

Figure 2 The thyroid hormone signalling cascade in myotube differentiation



Salvatore, D. *et al.* (2013) Thyroid hormones and skeletal muscle—new insights and potential implications
Nat. Rev. Endocrinol. doi:10.1038/nrendo.2013.238

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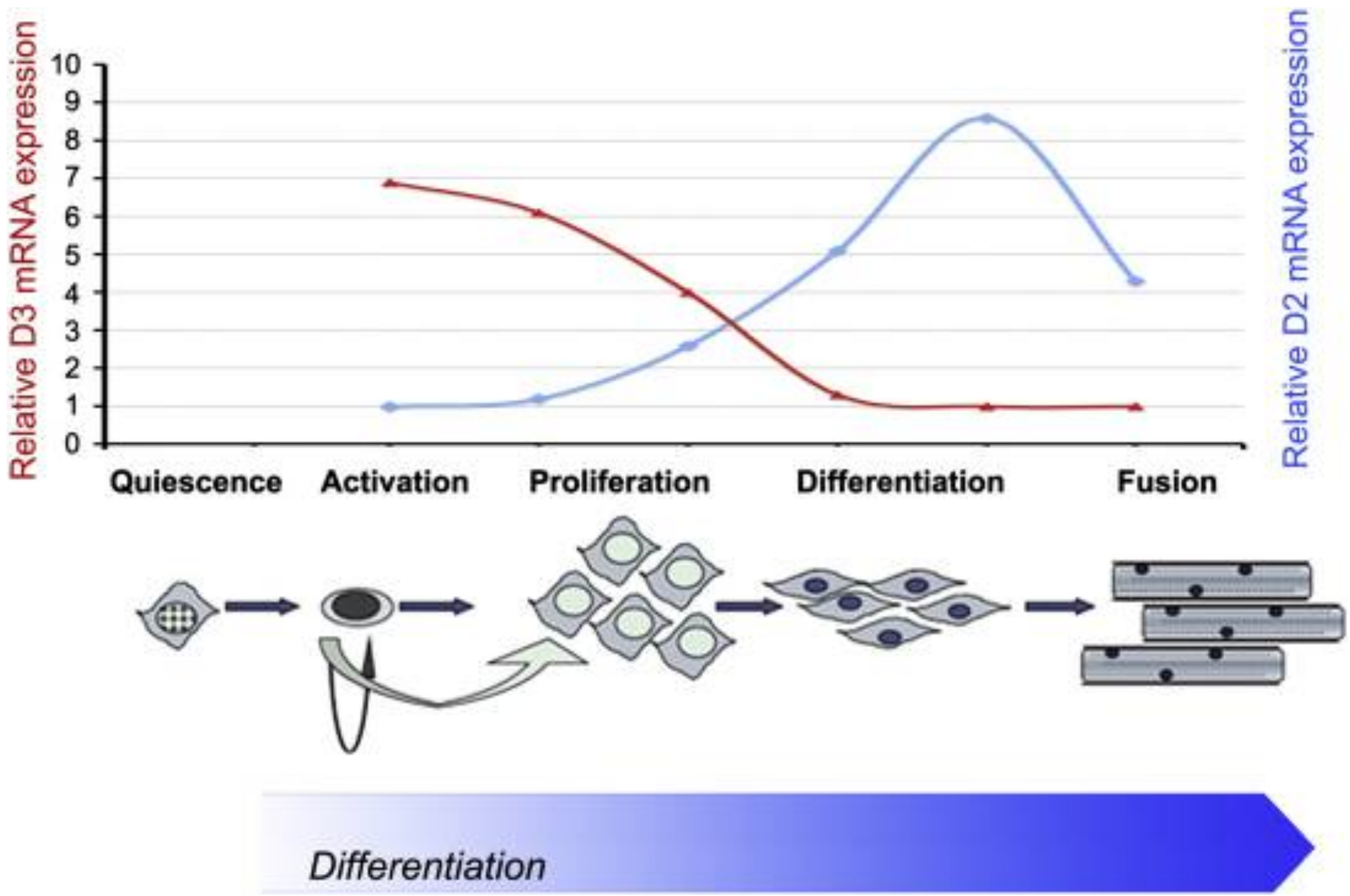
DESIODASI E MUSCOLO



In Vivo Regulation of Human Skeletal Muscle Gene Expression by Thyroid Hormone

Karine Clément,et al. Genome Res. 2002 Feb;12(2):281-91.

Table 4. Thyroid Hormone–Induced Up-Regulation of mRNA Expression for Genes of Protein Catabolism

UniGene no.	Encoded protein	Fold
Hs.9280	Proteasome (prosome, macropain) subunit, β type, 9	3.20
Hs.61153	Proteasome (prosome, macropain) 26S subunit, ATPase, 2	2.56
Hs.79137	Protein-L-isoaspartate (D-aspartate) *O*-methyltransferase	2.15
Hs.811	Ubiquitin-conjugating enzyme E2B (RAD6 homolog)	2.14
Hs.77578	Ubiquitin-specific protease 9, X chromosome	2.10
Hs.79357	Proteasome (prosome, macropain) 26S subunit, ATPase, 6	2.06
Hs.82159	Proteasome (prosome, macropain) subunit, α type, 1	2.04
Hs.4295	Proteasome (prosome, macropain) 26S subunit, non-ATPase, 12	2.02
Hs.12272	Beclin-1	1.95
Hs.76913	Proteasome (prosome, macropain) subunit, α type, 5	1.93
Hs.251531	Proteasome (prosome, macropain) subunit, α type, 4	1.88
Hs.86978	Prolyl endopeptidase	1.87
Hs.78950	Branched chain keto acid dehydrogenase E1, α polypeptide	1.85
Hs.167108	Proteasome (prosome, macropain) subunit, α type, 3	1.83
Hs.99819	Ubiquitin-specific protease 16	1.81
Hs.82919	Cullin 2	1.79
Hs.75981	Ubiquitin-specific protease 14 (tRNA-guanine transglycosylase)	1.74
Hs.79357	Proteasome (prosome, macropain) 26S subunit, ATPase, 6	1.68
Hs.15303	Protein similar to mouse ubiquitin-protein ligase E3-α	1.66
Hs.101408	Branched chain aminotransferase 2, mitochondrial	1.55

The fold increase represents the mean of the five comparisons.

In Vivo Regulation of Human Skeletal Muscle Gene Expression by Thyroid Hormone

Karine Clément,et al. Genome Res. 2002 Feb;12(2):281-91.

Table 5. Thyroid Hormone–Induced Up-Regulation of mRNA Expression for Genes Involved in Metabolism

UniGene no.	Encoded protein	Pathway	Fold
Hs.77837	UDP-glucose pyrophosphorylase 2	Glycogen synthesis	3.02
Hs.1691	Glycogen branching enzyme	Glycogen synthesis	2.82
Hs.169428	Cytochrome c[a]	Respiratory chain (complex IV)	2.68
Hs.2043	Adenine nucleotide translocase 1	Mitochondrial carrier	2.66
Hs.33084	Fructose transporter GLUT 5[a]	Glucose metabolism	2.66
Hs.78713	Adenine nucleotide translocase 2[a]	Mitochondrial carrier	2.58
Hs.74635	Dihydrolipoamide dehydrogenase (pyruvate dehydrogenase complex E3)	Citric acid cycle	2.58
Hs.80595	NADH dehydrogenase (ubiquinone) Fe-S protein 5	Respiratory chain (complex I)	2.54
Hs.8364	Pyruvate dehydrogenase kinase, isoenzyme 4[a]	Citric acid cycle	2.52
Hs.19236	NADH dehydrogenase (ubiquinone) 1 β subcomplex, 5	Respiratory chain (complex I)	2.50
Hs.131255	Ubiquinol–cytochrome c reductase binding protein	Respiratory chain (complex III)	2.46
Hs.155433	ATP synthase, F1 complex, γ 1	Respiratory chain (complex V)	2.35
Hs.101337	Uncoupling protein 3[a]	Mitochondrial carrier	2.30
Hs.81634	ATP synthase, F0 complex, subunit b, isoform 1	Respiratory chain (complex V)	2.26
Hs.109646	NADH dehydrogenase (ubiquinone) 1 β subcomplex, 6	Respiratory chain (complex I)	2.23
Hs.61255	Fructose-1,6-bisphosphatase 2[a]	Neoglucogenesis	2.13
Hs.1023	Pyruvate decarboxylase (pyruvate dehydrogenase complex E1-α)	Citric acid cycle	2.10
Hs.429	ATP synthase, F0 complex, subunit c, isoform 3	Respiratory chain (complex V)	2.09
Hs.79876	Steroid sulfatase, arylsulfatase C, isozyme S[a]	Steroid hormone synthesis	2.02
Hs.73851	ATP synthase, F0 complex, subunit F6	Respiratory chain (complex V)	2.02
Hs.78060	Phosphorylase kinase, β	Glycogenolysis	2.00
Hs.268012	Long-chain fatty acid–coenzyme A ligase 3	Lipid β oxidation	1.99
Hs.7043	Succinate-CoA ligase, GDP-forming, α subunit	Citric acid cycle	1.99
Hs.74823	NADH dehydrogenase (ubiquinone) 1 α subcomplex, 1	Respiratory chain (complex I)	1.96
Hs.3462	Cytochrome c oxidase subunit VIIc	Respiratory chain (complex IV)	1.90
Hs.76688	Carboxylesterase 1	Cholesterol metabolism	1.86
Hs.183435	NADH dehydrogenase (ubiquinone) 1 β subcomplex, 1	Respiratory chain (complex I)	1.82
Hs.74649	Cytochrome c oxidase subunit VIc[a]	Respiratory chain (complex IV)	1.74
Hs.77508	Glutamate dehydrogenase 1[a]	Citric acid cycle	1.72
Hs.177584	3-oxoacid CoA transferase	Citric acid cycle	1.64

The fold increase represents the mean of the five comparisons.
[a]Proteins that have been shown to be positively regulated by thyroid hormones in rodents.

Ormoni tiroidei e muscolo

- In aggiunta gli ormoni tiroidei hanno un ruolo importante nella riparazione del tessuto muscolare.

TIROIDE E MUSCOLO

- L'ipertiroidismo facilita l'aumento delle fibre rapide e aumento della velocità di contrazione.
- L'ipotiroidismo determina il cambiamento delle fibre muscolari da rapide a lente e riduce la massa muscolare.

Succede durante l’esercizio fisico…

Si modifica l’attività cardiaca

Aumenta il lavoro muscolare

Aumenta il consumo energetico

T3 aumenta:

1) β AR
2) Ca ATPasi
3) Na/K ATPasi
4) Canali K volt-dep.
5) ∝MHC

T3 diminuisce;

1) Fosfolambani
2) Na/Ca scambiatori
3) Adenilato ciclasi

Table 2. Effect of Thyroid Hormone on Cardiac Gene Expression

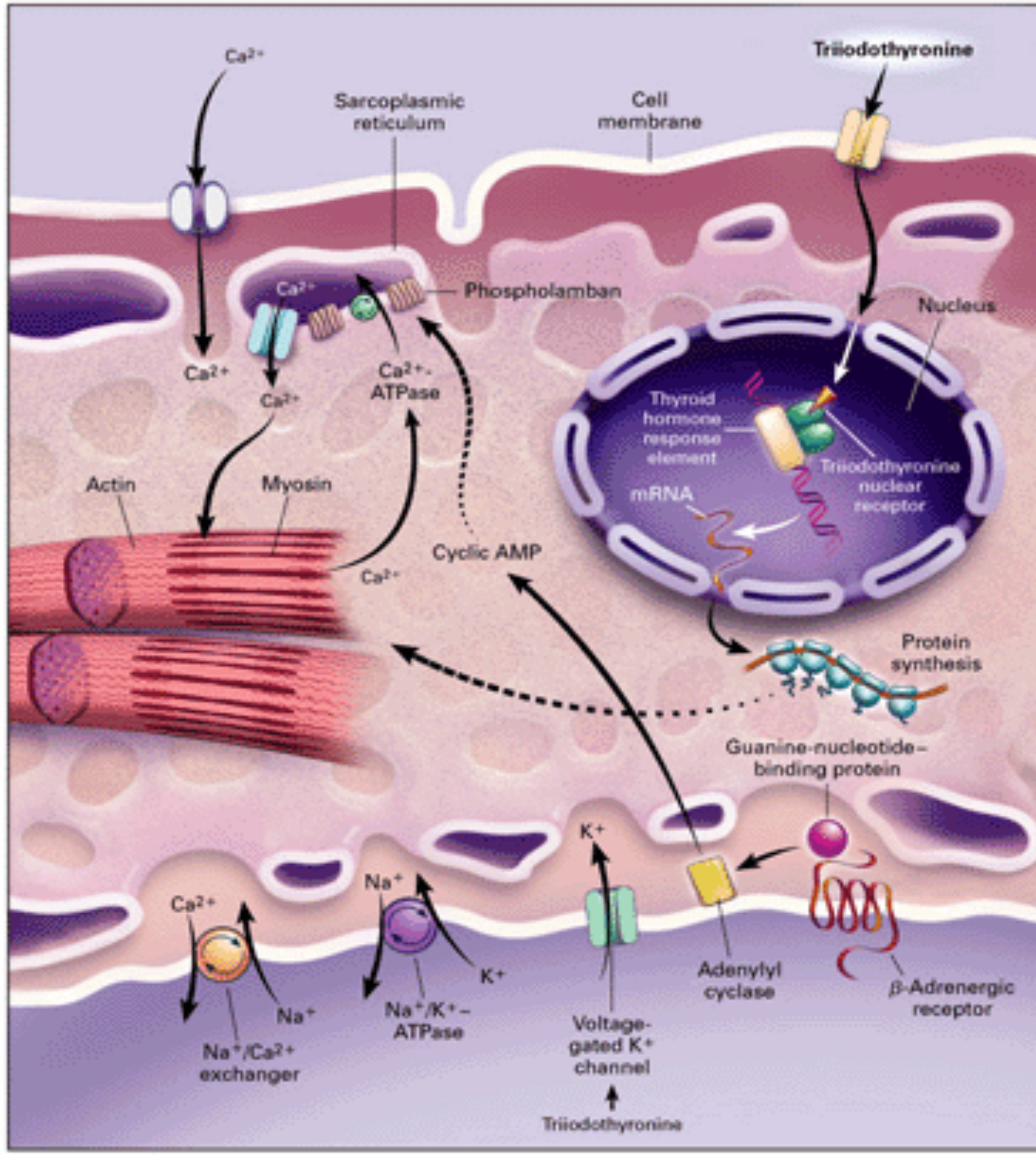
Positively Regulated	Negatively Regulated
α-Myosin heavy chain	β-Myosin heavy chain
Sarcoplasmic reticulum Ca^{2+}-ATPase	Phospholamban
Na^+/K^+-ATPase	Adenylyl cyclase catalytic subunits
β1-Adrenergic receptor	Thyroid hormone receptor α1
Atrial natriuretic hormone	Na^+/Ca^{2+} exchanger
Voltage-gated potassium channels (Kv1.5, Kv4.2, Kv4.3)	

Circulation

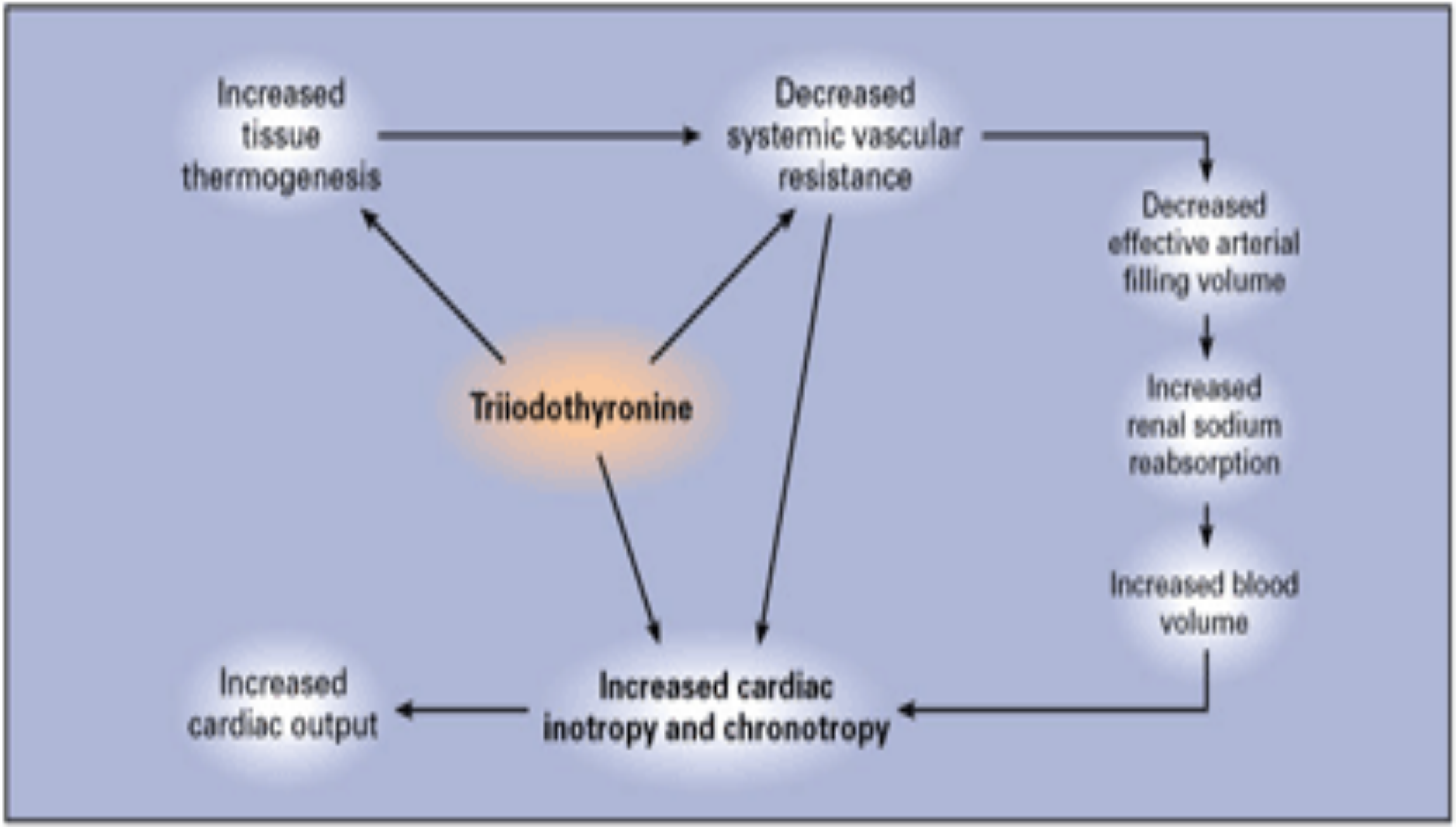
American Heart Association

Thyroid Disease and the Heart
Irwin Klein and Sara Danzi

Circulation. 2007;116:1725-1735
doi: 10.1161/CIRCULATIONAHA.106.678326



Effetti clinici di T3 sul Sistema cardio-vascolare



Cuore e tiroide

- **Aumenta battito cardiaco**
- **Aumenta forza di contrazione**
- **Aumenta volume sistolico**
- **Aumenta gittata cardiaca**
- **Up-regolano recettore catecolamine**

Succede durante l'esercizio fisico...

- Si modifica l'attività cardiaca
- Aumenta il lavoro muscolare
- Aumenta il consumo energetico

Effetti sul metabolismo

- **Aumenta l'assorbimento gastrointestinale di glucosio**
- **Aumenta il turnover dei carboidrati, lipidi e proteine**
- **Down-regola i recettori dell'insulina**
- **Aumenta la disponibilità di substrati**

Gli effetti dello sport sui livelli degli ormoni tiroidei non sono del tutto noti, sono oggetto di studio e rimangono controversi.

Cosa sappiamo???

- E' noto che l'esercizio fisico modifica la secrezione degli ormoni tiroidei

- La modifica avviene in base alla intensità dell'esercizio

Neuroendocrinology Letters No.6 December Vol.26, 2005
 ISSN 0172–780X **www.nel.edu**

Exercise intensity and its effects on thyroid hormones

Figen Ciloglu, Ismail Peker[1], Aysel Pehlivan[2], Kursat Karacabey[3], Nevin İlhan[4], Ozcan Saygin[5] & Recep Ozmerdivenli[3]

Lactate (mmol/l)		2.86 ± 0.658	4.59 ± 1.75	8.25 ± 2.74
TSH (μIU/ml)	0.5–8.9	1.69 ± 0.55	1.78 ± 0.60	1.89 ± 0.74
T3 (ng/ml)	0.8–2.1	1.47 ± 0.23	1.78 ± 0.42	1.48 ± 0.26
Free T3 (pmol/l)	3.4–7.2	5.30 ± 1.20	6.46 ± 1.62	6.17 ± 1.29
T4 (ng/ml)	42–120	71.10 ± 19.02	84.35 ± 24.86	86.35 ± 28.36
Free T4 (pmol/l)	11–24	16.97 ± 3.86	19.49 ± 3.82	20.16 ± 4.80

* Reference values of kits

Table 2: P-values of thyroid hormones changes in different exercise intensities

	45%–70% of max heart rate	45%–90% of max heart rate	70%–90% of max heart rate
TSH (μIU/ml)	0.200	0.045*	0.204
T3 (ng/ml)	0.025*	0.086	0.021*
Free T3 (pmol/l)	0.047*	0.063	0.038
T4 (ng/ml)	0.012*	0.008*	0.049
Free T4 (pmol/l)	0.023*	0.027*	0.311

Exercise intensity and its effects on thyroid hormones

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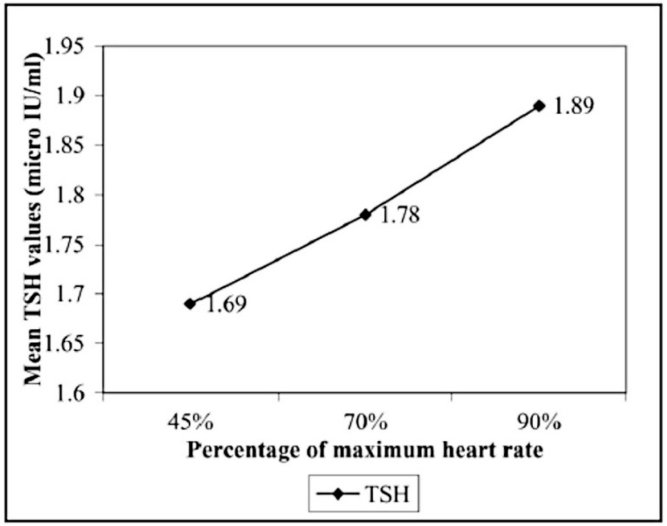


Fig. 1. Change in TSH values with exercise intensity

Incremento nei livelli di TSH, passando dal 45% al 90% della frequenza cardiaca massima (MHR - Maximum Heart Rate):

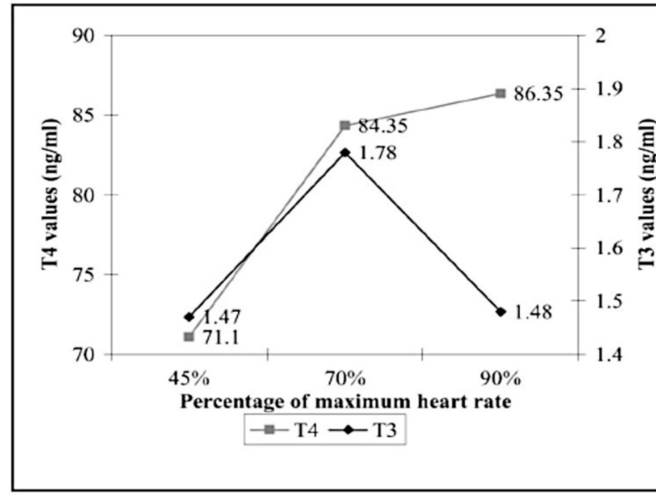


Fig. 2. Change in T4 and T3 values with exercise intensity

Passando dal 70% al 90% della MHR, T3 ed fT3 cominciano a diminuire fino ad un valore per T3 più o meno simile a quello osservato al 45% della MHR

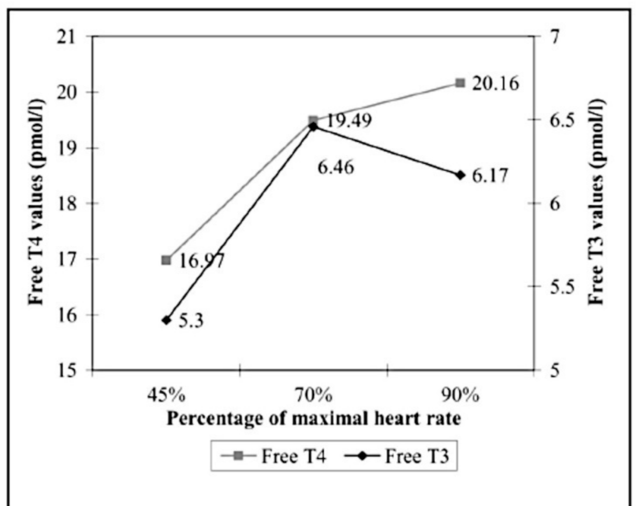


Fig. 3. Change in Free T4 and Free T3 values with exercise intensity

T4, fT4 continuano a crescere, passando dal 70% al 90% della MHR con una crescita statisticamente significativa se paragonata ai valori ottenuti al 45% della MHR

- **Il TSH aumenta durante tutto l'esercizio fisico**

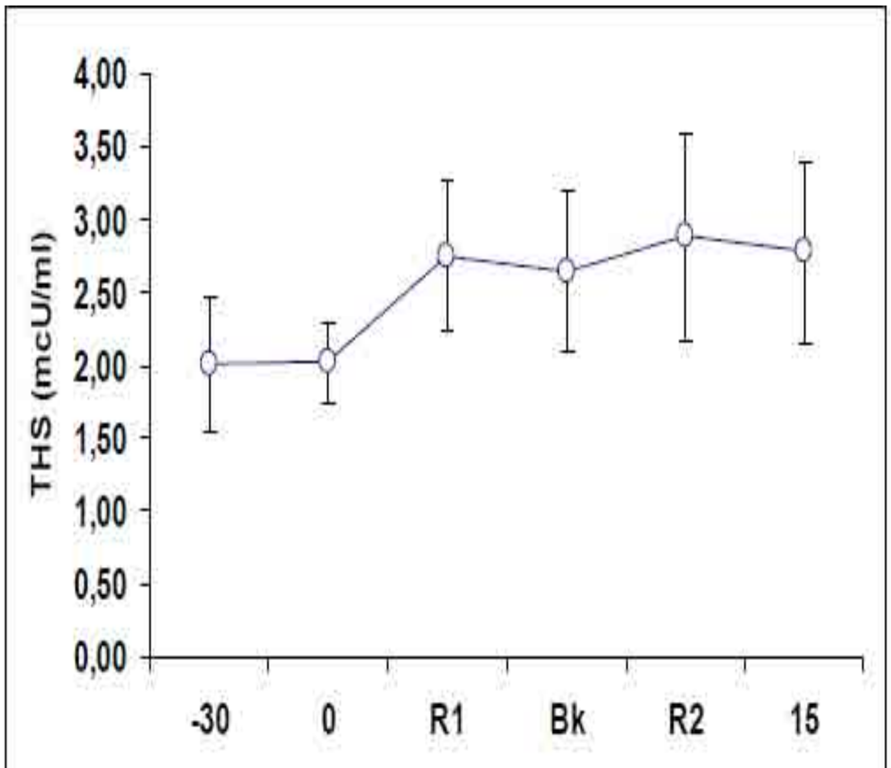
- **Il maggiore incremento degli ormoni tiroidei si verifica con l'esercizio fisico aerobico**

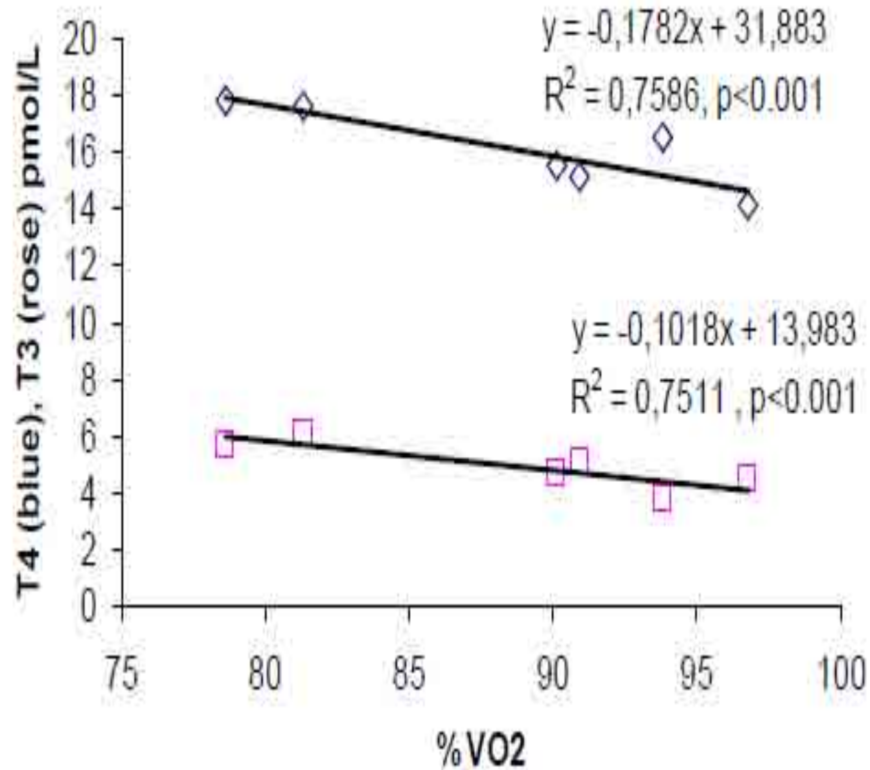
- **Alla massima intensità dell'esercizio fisico (esercizio anaerobico) si riducono FT_3 e T_3**

Thyroid hormones response in simulated laboratory sprint duathlon

JOSÉ RAMÓN ALVERO-CRUZ, MAURO RONCONI, MARGARITA CARRILLO DE ALBORNOZ GIL, JERÓNIMO C. GARCÍA ROMERO, DANIEL ROSADO VELÁZQUEZ, A. MARIO DE DIEGO ACOSTA

Exercise Physiology and Performance Laboratory. Sports Medicine School. Faculty of Medicine. University of Málaga. Spain.





Thyroid hormones response in simulated laboratory sprint duathlon

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Exercise Physiology and Performance Laboratory. Sports Medicine School. Faculty of Medicine. University of Málaga. Spain.

- **Si assiste ad una riduzione di T3 e T4 in relazione dell’intensità dell’esercizio fisico.**
- **La funzione tiroidea ha un ruolo fondamentale negli sport ad alta intensità**

Thyroid hormonal responses to intensive interval versus steady-state endurance exercise sessions

Anthony C. Hackney,[1] Ashley Kallman,[1] Karen P. Hosick,[1]
Daniela A. Rubin,[2] Claudio L. Battaglini[1]

Scopo dello studio:

Esaminare l'influenza di un esercizio ad elevata intensità (IE) rispetto ad uno di intensità sub-massimale o ad un esercizio regolare sui livelli di fT_3 ed fT_4 in 15 individui molto allenati

HORMONES 2012, 11(1):54-60

Thyroid hormonal responses to intensive interval versus steady-state endurance exercise sessions

Anthony C. Hackney,[1] Ashley Kallman,[1] Karen P. Hosick,[1]
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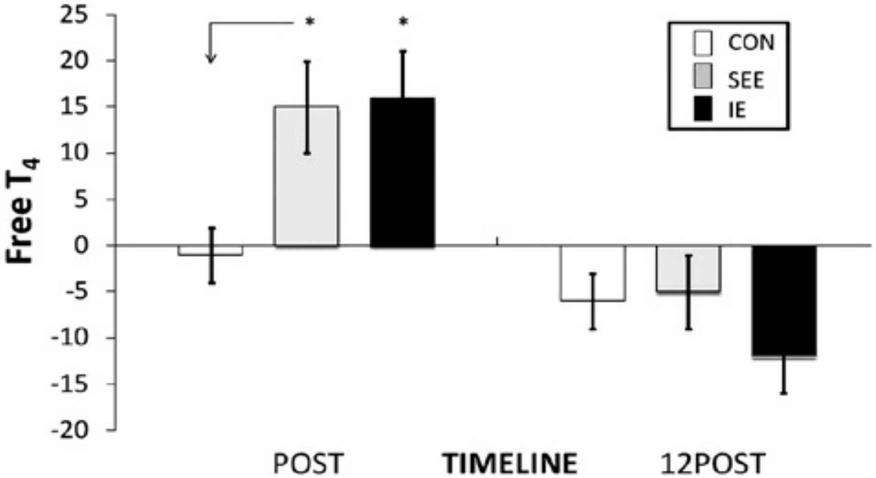
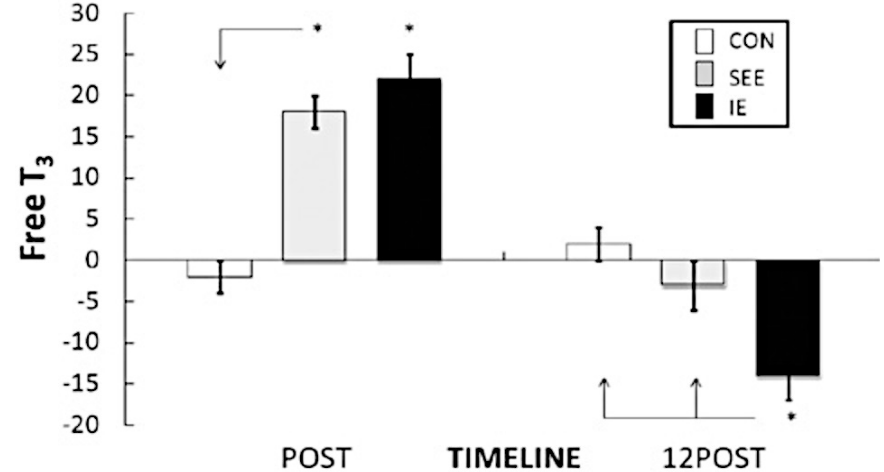
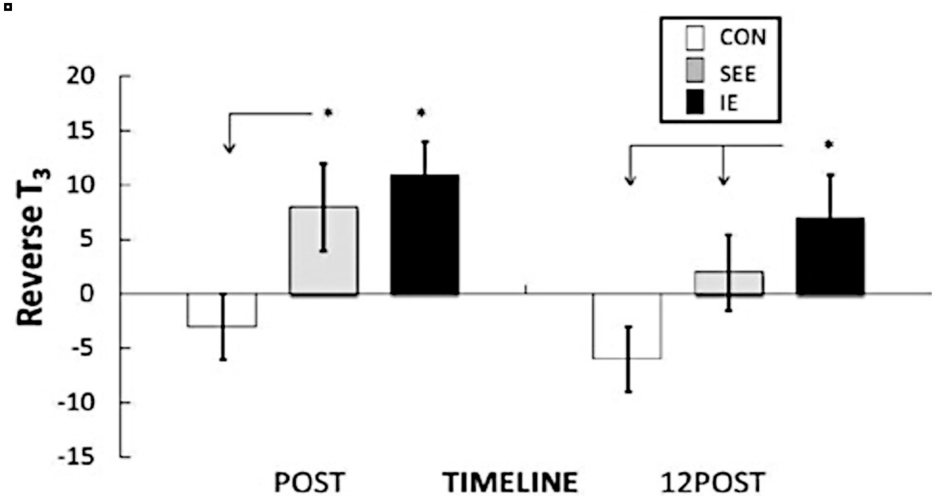






•Sport ad elevata intensità determinano una ridotta conversione di T4 in T3.

•Sport di elevata intensità e protratti nel tempo o di bassa-moderata intensità per periodi più estesi determinano uno stato di ipotiroidismo non patologico transitorio che persiste dalle 24 alle 72 ore.

- **Aumento dell’uptake a livello dei tessuti target**

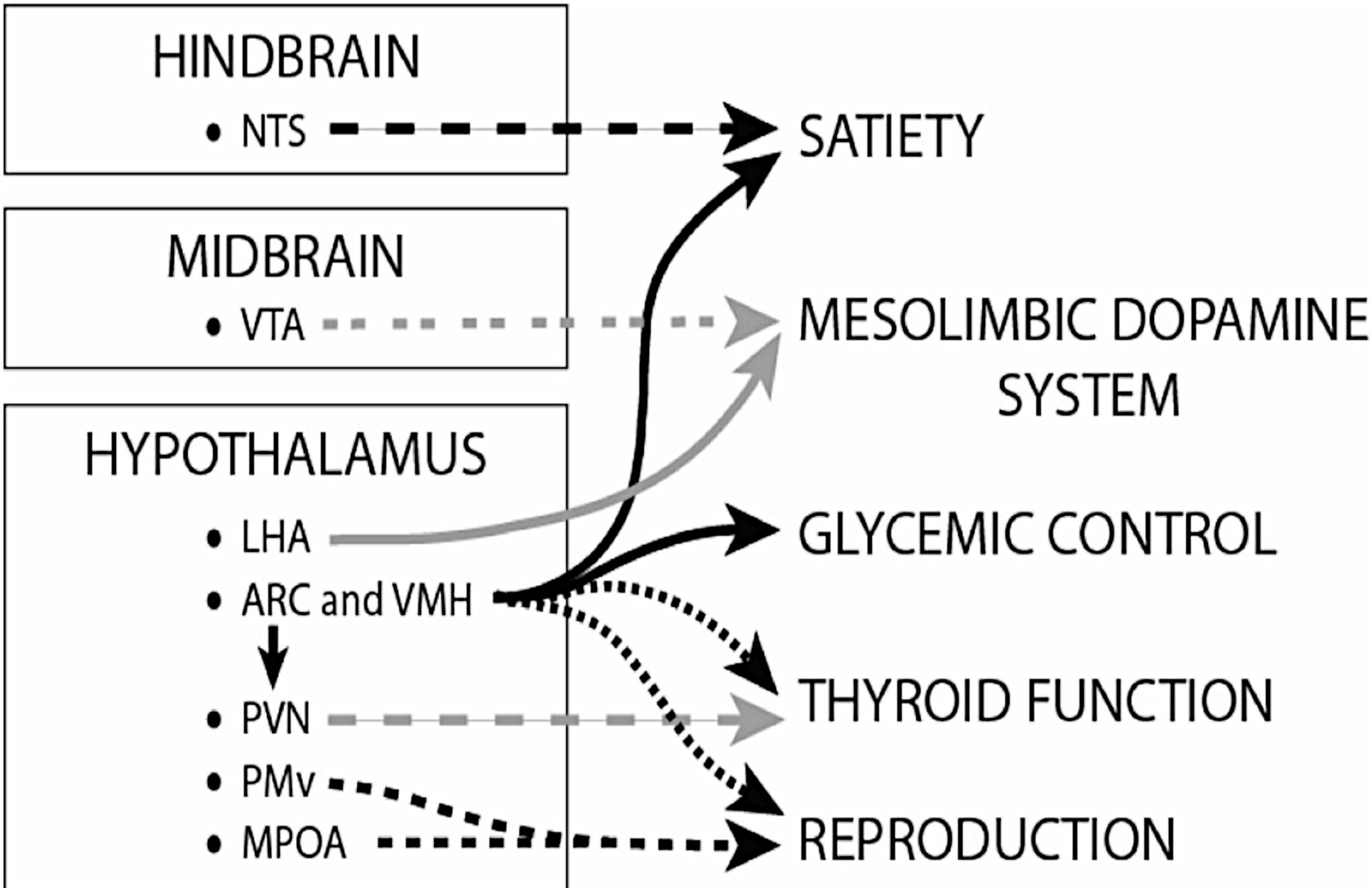
- **Ridotta conversione periferica di T_4 in T_3 (ruolo di D2)**

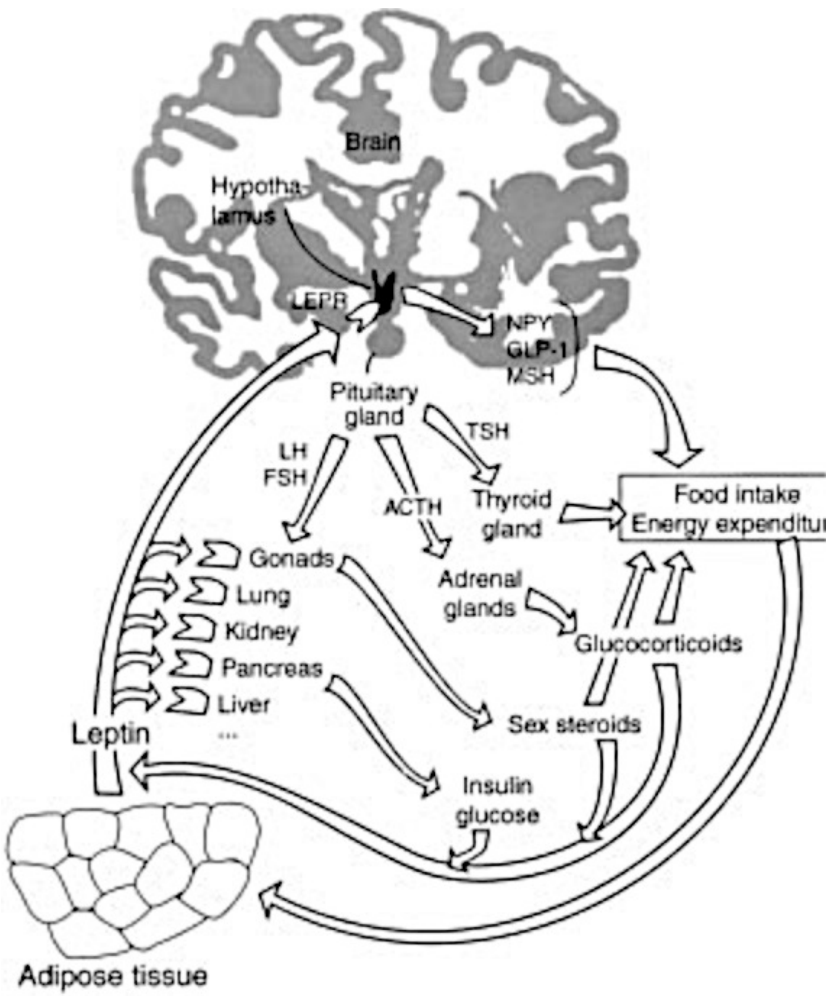
- **Ridotta secrezione di T_4 dalla ghiandola per fattori inibitori**

I livelli di **leptina** biologicamente attiva sono determinanti nella risposta adattativa della funzione tiroidea in individui molto allenati es. atleti????

La Leptina è un ormone proteico di 167-amino-acidi prodotto dagli adipociti e anche dallo stomaco, tessuto scheletrico e placenta.

Regola l'appetito, la spesa energetica e il peso corporeo attraverso l'azione a livello del sistema nervoso centrale.


HINDBRAIN
• NTS
MIDBRAIN
• VTA
HYPOTHALAMUS
• LHA
• ARC and VMH
• PVN
• PMv
• MPOA
SATIETY
MESOLIMBIC DOPAMINE SYSTEM
GLYCEMIC CONTROL
THYROID FUNCTION
REPRODUCTION



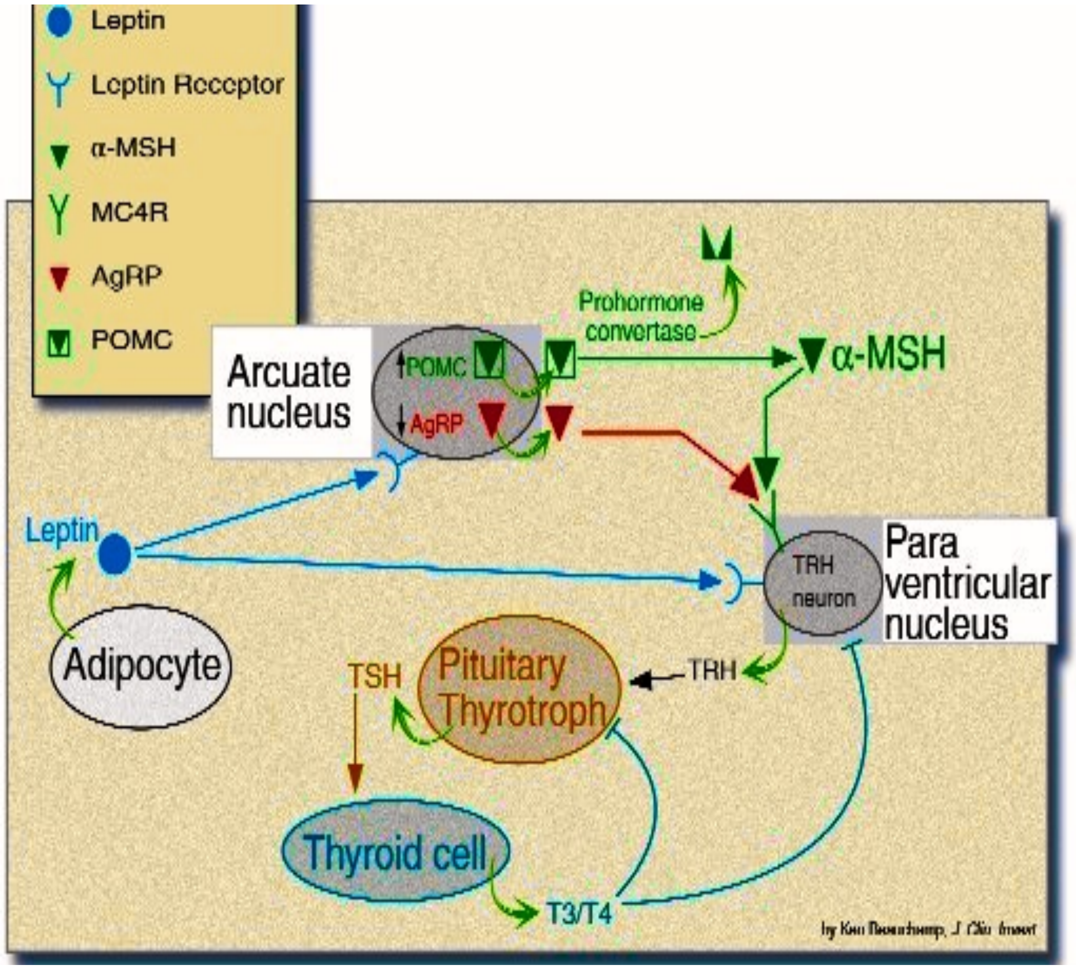
La Leptina modula la secrezione di TSH, ACTH e gonadotropine a livello ipotalamico.

La leptina stimola la secrezione di TSH e pertanto degli ormoni tiroidei.

European Journal of Endocrinology (2000) 143 293±311 ISSN 0804

Leptin, nutrition, and the thyroid: the why,the wherefore, and the wiring

Jeffrey S. Flier, Mark Harris, and Anthony N. Hollenberg



Conclusioni:

• L'attivazione del segnale della leptina è necessario per la regolazione a livello ipotalamico-ipofisario della funzione tiroidea

The Journal of Clinical Investigation | April 2000 | Volume 105 | Number 7

Free leptin index and thyroid function in male highly trained athletes

Gianluca Perseghin[1,2], Guido Lattuada[2], Francesca Ragogna[2], Giampietro Alberti[1], Antonio La Torre[1] and Livio Luzi[1,2]

Table 1 Anthropometric, laboratory, and metabolic characteristics of study subjects.

	Athletes	Normals
Number	27	27
Age (years)	28±11	30±6
Body weight (kg)	68±7	68±5
Height (cm)	178±6	177±6
BMI (kg/m^2)	21.5±1.1	21.8±1.2
Body fat (%)	8.1±0.4*,a	11.6±0.8
Plasma glucose (mg/dl)	85±7	85±7
Serum insulin (μU/ml)	7.7±4.2†	10.6±4.9
Serum C-peptide (ng/ml)	1.24±0.65*	1.96±0.91
HOMA2-%S	113±51†	83±41
HOMA2-%B	114±42†	143±55
Serum FFA (mmol/l)	0.63±0.24	0.53±0.22
Total cholesterol (mg/dl)	152±38	164±31
HDL-cholesterol (mg/dl)	57±10	55±13
Triglycerides (mg/dl)	62±22	72±38
hsCRP (mg/dl)	1.11±0.96	0.82±0.77
Free T_3 (pg/ml)	5.4±0.9	5.3±0.9
Free T_4 (pg/ml)	18.2±3.9	18.5±3.4
TSH (μU/ml)	0.90±0.65†	1.27±0.76
TSH/freeT_3 ratio	0.16±0.11†	0.25±0.17
REE (kcal/die)	1903±324	1796±214
Percentage of predicted REE (%)	112±16	107±11
RQ	0.77±0.06†	0.83±0.11

*$P<0.01$ versus normals; †$P<0.05$ versus normals (2-tails independent *t*-test). REE, resting energy expenditure; RQ, respiratory quotient.
[a]Assessment of body fat was obtained in 19 athletes.

Scopo del lavoro:

Verificare la relazione che intercorre tra: funzione tiroidea, metabolismo energetico totale e adipochine in 27 atleti molto allenati e 27 individui sedentari - entrambi i gruppi in buone condizioni di salute

Conclusioni:

- *Gli atleti hanno mostrato un rapporto basso TSH/FT3 rispetto ai controlli.*

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Free leptin index and thyroid function in male highly trained athletes

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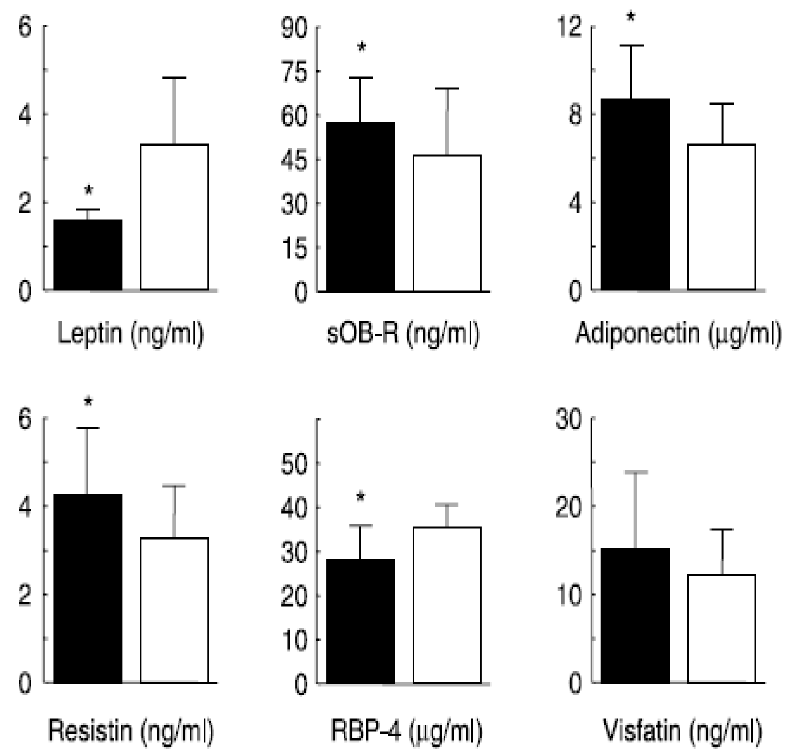

Figure 1 Serum adipokines and sOB-R concentrations in study groups. Fasting serum concentrations of leptin, sOB-R, adiponectin, resistin, RBP-4, and visfatin are summarized. Black columns represent the athletes, white columns the sedentary control subjects. Mean ± S.D. *$P<0.05$ versus normal sedentary controls (two-tailed independent samples *t*-test).

Conclusioni:

- Gli atleti hanno mostrato un valore dell'indice FLI (Free Leptin Index) basso rispetto ai controlli.

- Il livello di leptina biologicamente attiva è correlato alla risposta adattativa della funzione tiroidea, in soggetti atleticamente allenati.

TIROIDE E SPORT

- Gli ormoni tiroidei hanno un ruolo fondamentale nello sport.
- La secrezione ormonale è modulata dalla intensità dell' attività sportiva.
- Sono necessari ulteriori studi per identificare le cause delle modifiche e dell'adattamento degli ormoni tiroidei.

Conclusioni

Proposta di introdurre test di screening della tiroide per chi pratica attività sportiva agonistica al fine di una precoce diagnosi e terapia


Grazie per l’attenzione