Obesità e scarsa attività fisica: un circolo vizioso tra epigenetica e psicologia

Dott. Domenico Meleleo

Cosa sono l’attività fisica e l’esercizio fisico ?

Esercizio fisico

E un'attività fisica programmata, strutturata e ripetitiva, finalizzata a migliorare o mantenere uno o più fattori del **fitness** fisico

- Esercizio aerobico

- Esercizio di Forza o di contro-resistenza

Esercizio aerobico

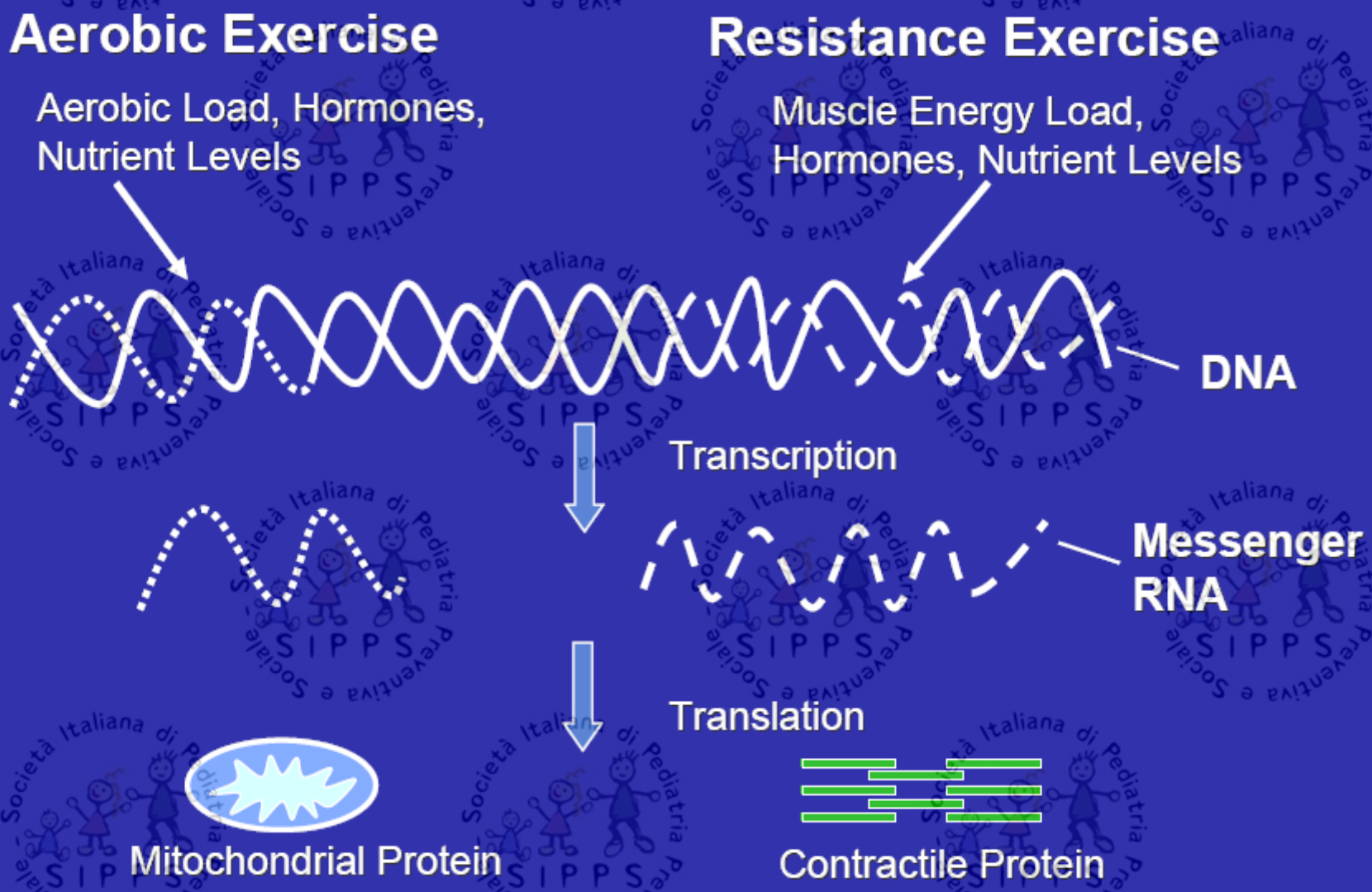
Consiste nella ripetizione di movimenti che coinvolgono la maggior parte dei gruppi muscolari per un periodo di almeno dieci minuti, come ad esempio, camminare, marciare, andare in bicicletta, nuotare, ecc.

Cosiddetto perché da un punto di vista metabolico, utilizza prevalentemente il processo aerobico di produzione di energia (ciclo di Krebs).

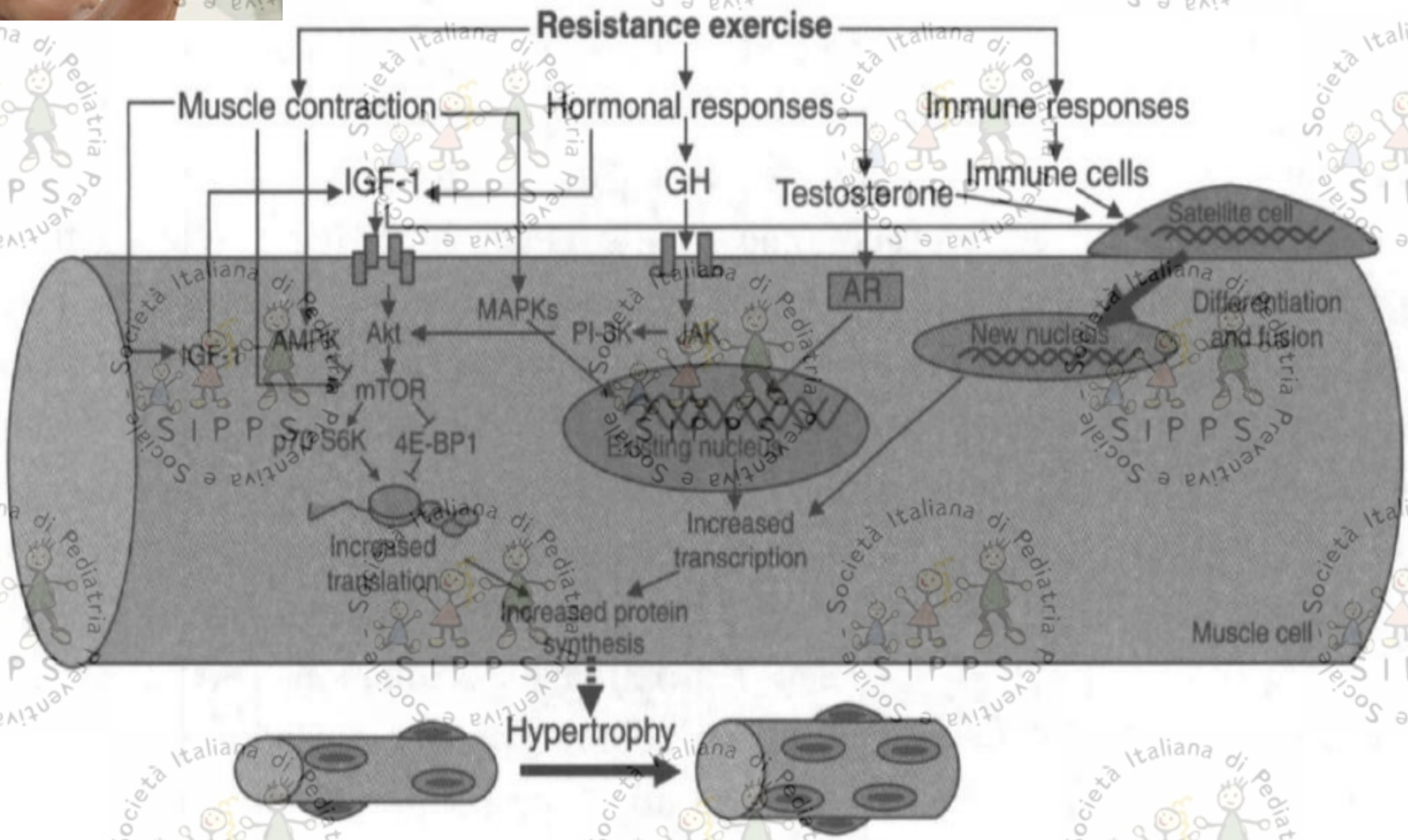
Esercizio di Forza o esercizio contro-resistenza

E’ l’esecuzione di esercizi che prevedono lo spostamento del corpo, in elevazione o in estensione, per mezzo di una contrazione muscolare volontaria (ad es. i salti da fermo in altezza o lunghezza; piegamenti del proprio corpo sugli arti inferiori o superiori; ecc), l’elevazione del busto da decubito supino o prono o esercizi che richiedono il superamento di una resistenza esterna (manubri e bilancieri di peso differente; elastici, lanci di palle zavorrate di peso differente, ecc.).

Impact of Exercise Type on Gene Expression



Resistance Training



quantità ma anche di qualità del movimento:

-Volume di allenamento
-Intensità di allenamento
-Tipo di allenamento (aerobico e/o anaerobico)

- In media un bambino di 8 aa è attivo solo per il 25% dell'ora canonica di allenamento (44% →10%)
(PAUSE !!!)

- Giornata tipo sogg. "sedentario" di 30 Kg
da 866 a 1455 Kcal/die VS sogg. "attivo" : da 1300 a 2110 Kcal

Donati ; CONI 2004

(circa 2000 bambini scuola elementare)

- **LARN 2012:**

LAF 25°/LAF 50°/LAF 75°

8 aa (peso 29,5 Kg): 1679 /1855/1996 kcal/die
9 aa (peso 33,2 Kg): 1799 /1988/2139 kcal/die

Kelli L. Cain, et al. Physical Activity in Youth Dance Classes . PEDIATRICS Volume 135, number 6, June 2015 ; 1066-73

17 private studios and 4 community centers in San Diego, California. A total of **264 girls** from 66 classes participated (n =154 children; n = 110 adolescents). Physical activity was measured with **accelerometers**

CONCLUSIONS: Overall, physical activity in youth dance classes was low; 8% of children and 6% of adolescents met the Centers for Disease Control and Prevention 30-minute guideline for afterschool physical activity during dance. To increase physical activity in dance classes, teaching methods could be employed to increase activity in all types, or emphasis could be placed on greater participation in more active dance types.

Eur J Sport Sci. 2017 Mar 20:1-10. doi: 10.1080/17461391.2017.1291750. [Epub ahead of print]

Evaluation of body composition with bioimpedence. A comparison between athletic and non-athletic children.

Meleleo D[1,2], Bartolomeo N[3], Cassano L[1,2], Nitti A[1,2], Susca G[1,2], Mastrototaro G[1,2], Armenise U[1,2], Zito A[4], Devito F[4], Scicchitano P[4], Ciccone MM[4].

At t0, the weekly hours dedicated to physical activity by **non-competitive** individuals ranged from a **minimum of 0 to a maximum of 10 h (median = 2),** while **competitive** individuals practiced sports from a **minimum of 2 to a maximum of 20 h (median = 6.5).** The differences between two groups is statistically significant ($p < .0001$).

At t1, the **non-competitive** maintained a range of hours/week of physical activity between **0 to 12 h (median = 2**), while **competitive** constantly **practiced 2–20 h/week (median increased to 8 h per week)** and the differences between two groups is statistically significant ($p < .0001$)

Meleleo D et al.

Evaluation of body composition with bioimpedence. A comparison between athletic and non-athletic children.

	All subjects		Non-competitive		Competitive	
	Estimation	Pr > | t |	Estimation	Pr > | t |	Estimation	Pr > | t |
FFMH at *t0*	0.11	0.0186	0.11	0.2050	−0.01	0.9108
• Hours/week	0.51	0.0484	0.20	0.4943	1.55	0.0026
• Age	0.79	0.0058	0.62	0.0430	1.30	0.0670
• Sex (male)	0.46	<.0001	0.44	<.0001	0.71	<.0001
• BMI						
FFMH at *t2*	0.11	0.0044	0.09	0.2076	0.08	0.2697
• Hours/week	2.69	<.0001	2.74	<.0001	2.31	<.0001
• Age	0.71	0.0036	0.59	0.0263	1.22	0.0276
• Sex (male)	0.51	<.0001	0.49	<.0001	0.78	<.0001
• BMI						

Meleleo D et al.

Evaluation of body composition with bioimpedence. A comparison between athletic and non-athletic children.

	All subjects		Non-competitive		Competitive	
	Estimation	Pr > |t|	Estimation	Pr > |t|	Estimation	Pr > |t|
FMH at *t0*	−0.13	0.0093	−0.09	0.3215	−0.03	0.6991
• Hours/week	0.39	0.1289	0.66	0.0252	−0.45	0.2972
• Age	−0.57	0.0489	−0.43	0.1643	−0.91	0.1524
• Sex (male)	1.05	<.0001	1.08	<.0001	0.79	<.0001
• BMI						
FMH at *t2*	−0.12	0.0008	−0.12	0.0875	−0.06	0.2743
• Hours/week	−1.75	<.0001	−1.86	<.0001	−1.05	0.0007
• Age	−0.49	0.0362	−0.37	0.1503	−1.06	0.0093
• Sex (male)	1.05	<.0001	1.08	<.0001	0.79	<.0001

Perché l’esercizio fisico fa dimagrire ?

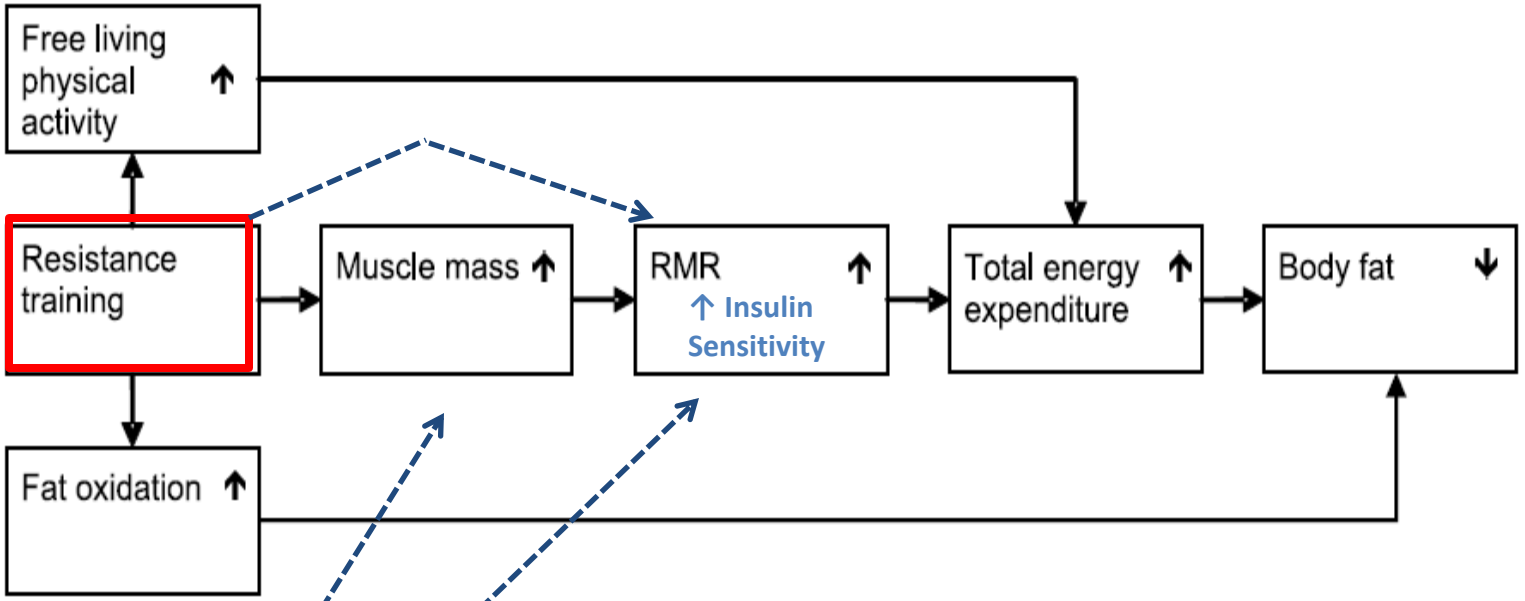


FIGURE 1—Conceptual model of resistance training and the potential effect on energy expenditure. A conceptual model that includes both the energy expenditure from increased muscle mass and the potential energy expenditure from increased activities of daily living. RMR, resting metabolic rate.

Endurance training; Cardiorespiratory ; Aerobic

Med Sci Sports Exerc. 2009 Feb;41(2):459-71 (modificato).

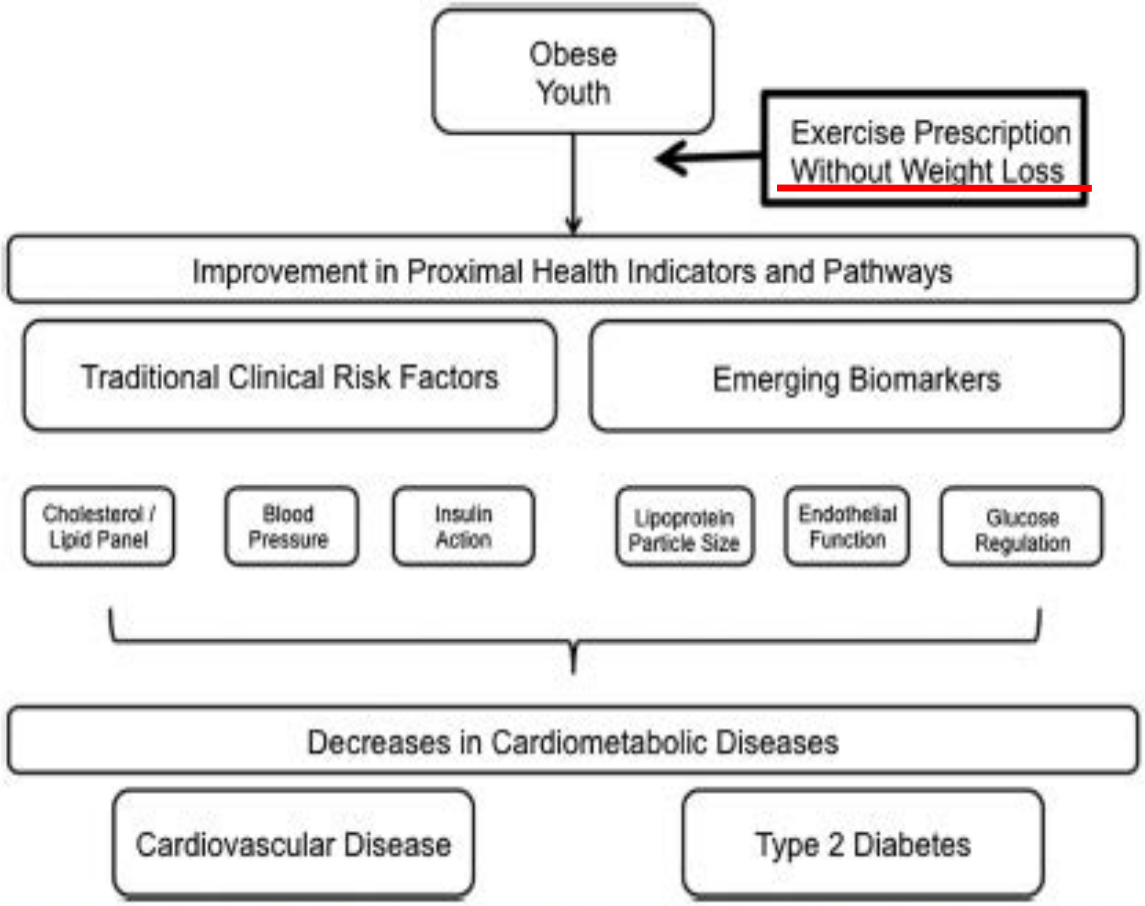


Figure 1. Conceptual framework for exercise to improve cardiometabolic health in obese youth independent of weight loss.

Shaibi G Q et al. Exercise and Sport Sciences Reviews
Volume 43 & Number 1 & January 2015

Ai concetti di quantità, intensità e qualità dell'esercizio fisico è legata anche un altro fattore che influisce sul metabolismo basale e quindi sul dispendio energetico…

EPOC

EPOC, acronimo di **Excess Postexercise Oxygen onsumption** (volgarmente detto "afterburn"), traducibile in italiano come *Consumo di ossigeno in eccesso post-allenamento*, è l'indice di misurazione dell'aumento del consumo di ossigeno a seguito della intensa attività, destinato a soddisfare il "debito di ossigeno" del corpo. L'EPOC rappresenta in altri termini l'incremento del metabolismo totale e del dispendio energetico per diverse ore a seguito dell'allenamento fisico

Gli studi hanno riscontrato che la portata (l'elevazione del consumo di ossigeno) e la durata (il tempo in cui il consumo di ossigeno rimane elevato) del EPOC **dipendono dall'intensità e dalla durata dell'esercizio**

EPOC

Di solito, occorrono al corpo tempi largamente variabili che vanno **da 15 minuti a 48 ore,** per recuperare completamente i valori allo stato di riposo. Altri fattori che influenzano l'EPOC includono lo stato dell'allenamento e il sesso

A seguito dell'aerobica a **bassa intensità e basso volume (<65% FCmax per meno di un'ora)**, approssimativamente **5 kcal** totali in eccesso sono impiegate dopo l'esercizio. A seguito dell'aerobica a **moderata intensità e maggiore volume (>65% FCmax per più di un'ora)** l'EPOC può consistere in un dispendio approssimativo di **35 kcal totali**. A seguito **dell'esercizio intenso (attorno al 85% FCmax, quindi esercizio anaerobico**), il dispendio calorico post-esercizio può arrivare a **180 kcal**.

Gran parte degli individui non è capace di sostenere intensità di esercizio abbastanza elevate da generare un grande EPOC con l'esercizio aerobico. Tranne alcune eccezioni (**atleti d'élite o allenamenti a volumi molto alti**), l'EPOC dell'esercizio aerobico difficilmente risulta significativo in maniera tale da incidere sul bilancio calorico complessivo

Zelasko CJ. J Am Diet Assoc. 1995 Dec;95(12):1414-7.
Bahr R. Acta Physiol Scand 1992

il Dispendio Energetico
è una questione di quantità ma anche di qualità del movimento:

-Volume di allenamento
-Intensità di allenamento
-Tipo di allenamento (aerobico e/o anaerobico)

Ma anche di…

Quantità e Qualità di massa magra (metabolicamente attiva)

Quantità e Qualità di massa magra (metabolicamente attiva)

HELENA study; EYHS study

(Sogg. Attivi e Sogg. Meno Attivi)

More Physically Active and Leaner Adolescents Have Higher Energy Intake

The Journal of Pediatrics 2014; 164: 159-166

Study design The study subjects were adolescents who participated in 1 of 2 cross-sectional studies, the Healthy Lifestyle in Europe by Nutrition in Adolescence **(HELENA) study (n = 1450; mean age, 14.6 years**) or the European Youth Heart Study **(EYHS; n = 321; mean age, 15.6 years**). **Physical activity** was measured by **accelerometry,** and **energy intake** was measured by **24-hour recall**. In the HELENA study, **body composition** was assessed by 2 or more of the following methods: **skinfold thickness, bioelectrical impedance analysis, plus dual-energy X-ray absorptiometry or air-displacement plethysmography in a subsample**. In the EYHS, body composition was assessed by skinfold thickness.

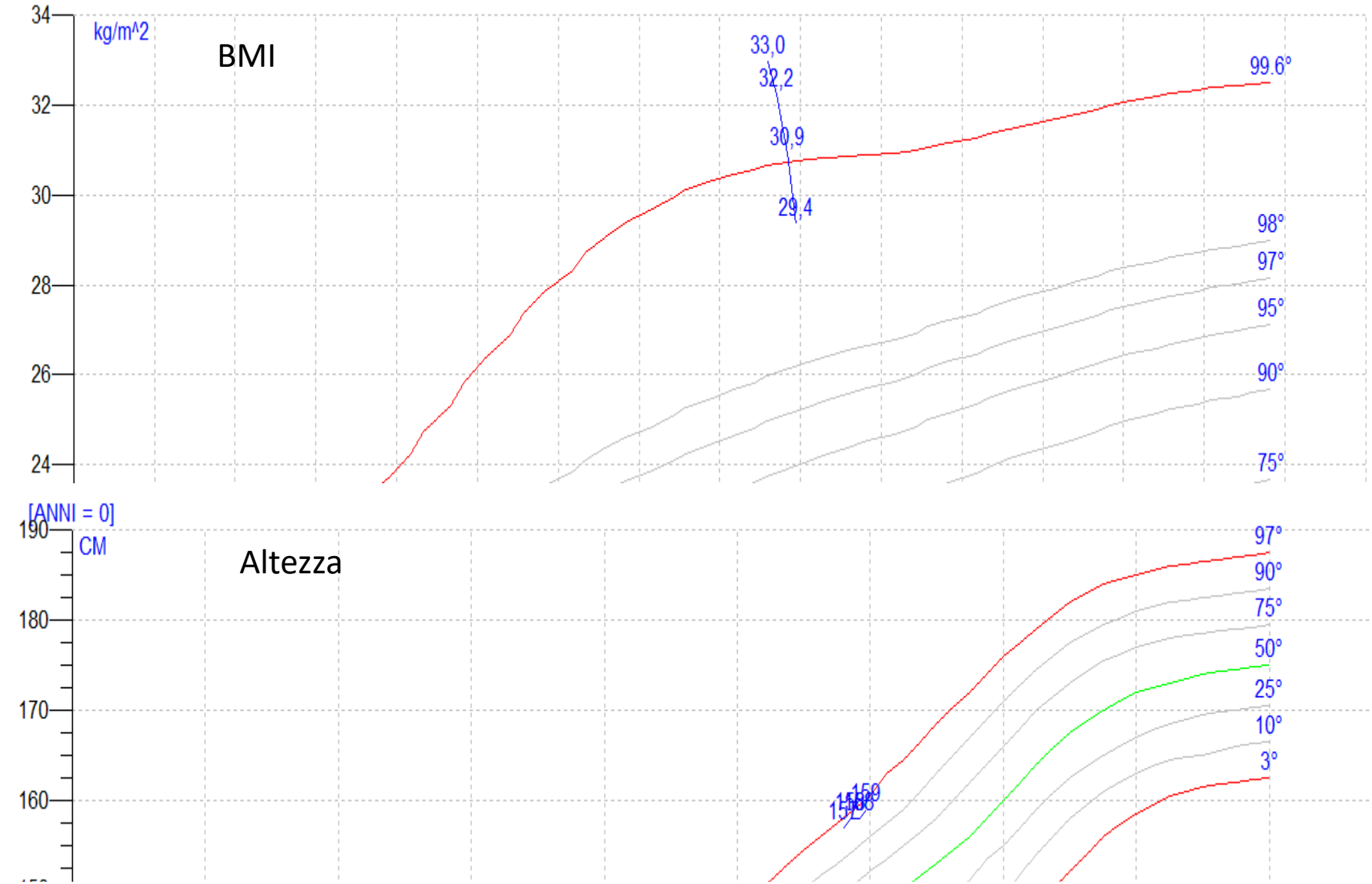
HELENA study; EYHS study
(Sogg. Attivi e Sogg. Meno Attivi)

Conclusion: Our data are consistent with the hypothesis that more physically active and leaner adolescents have higher energy intake than less active adolescents with larger amounts of fat mass.

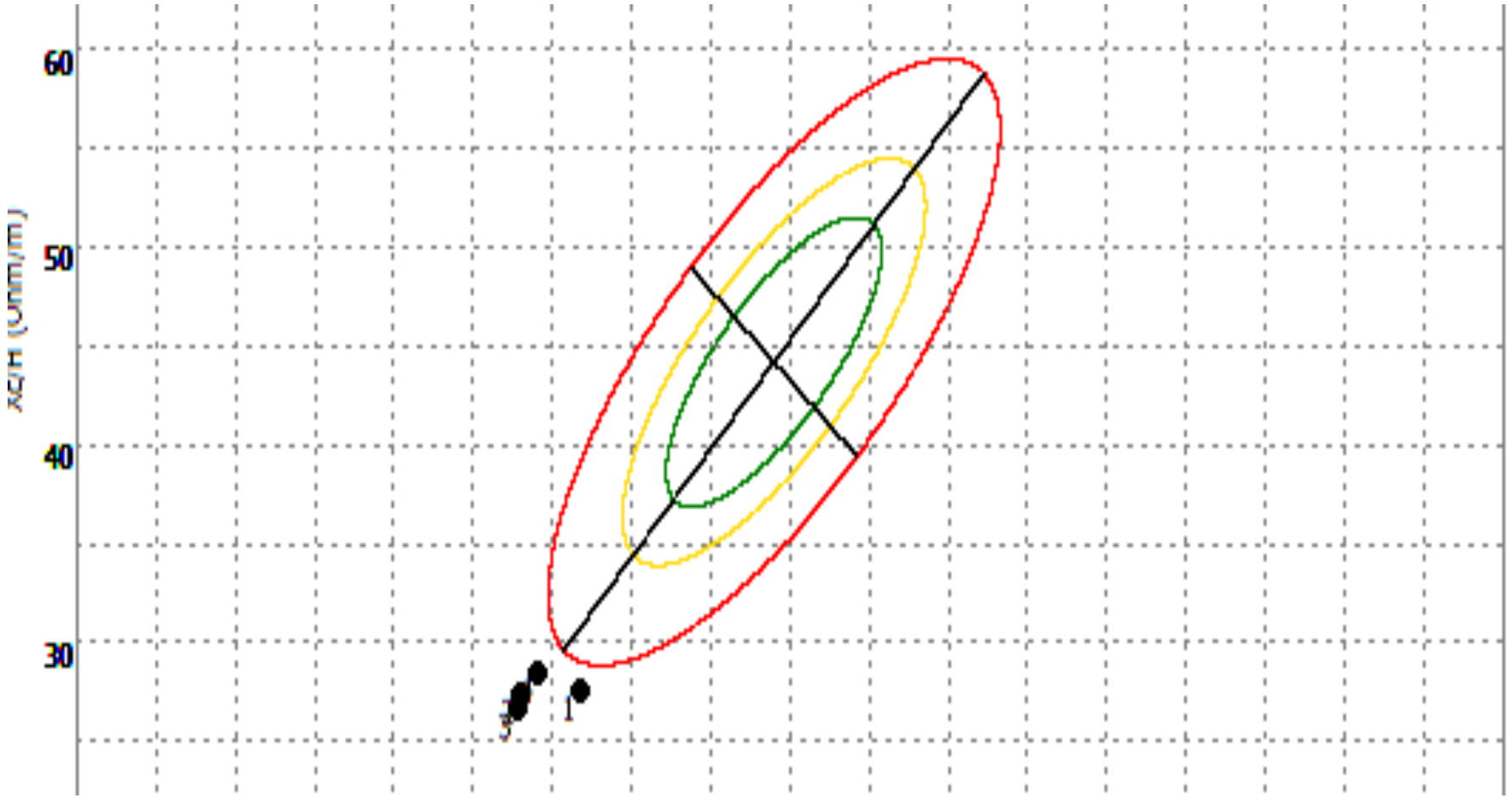
↑ Attività Fisica → ↑ Assunzione di Energia (quantità di cibo)

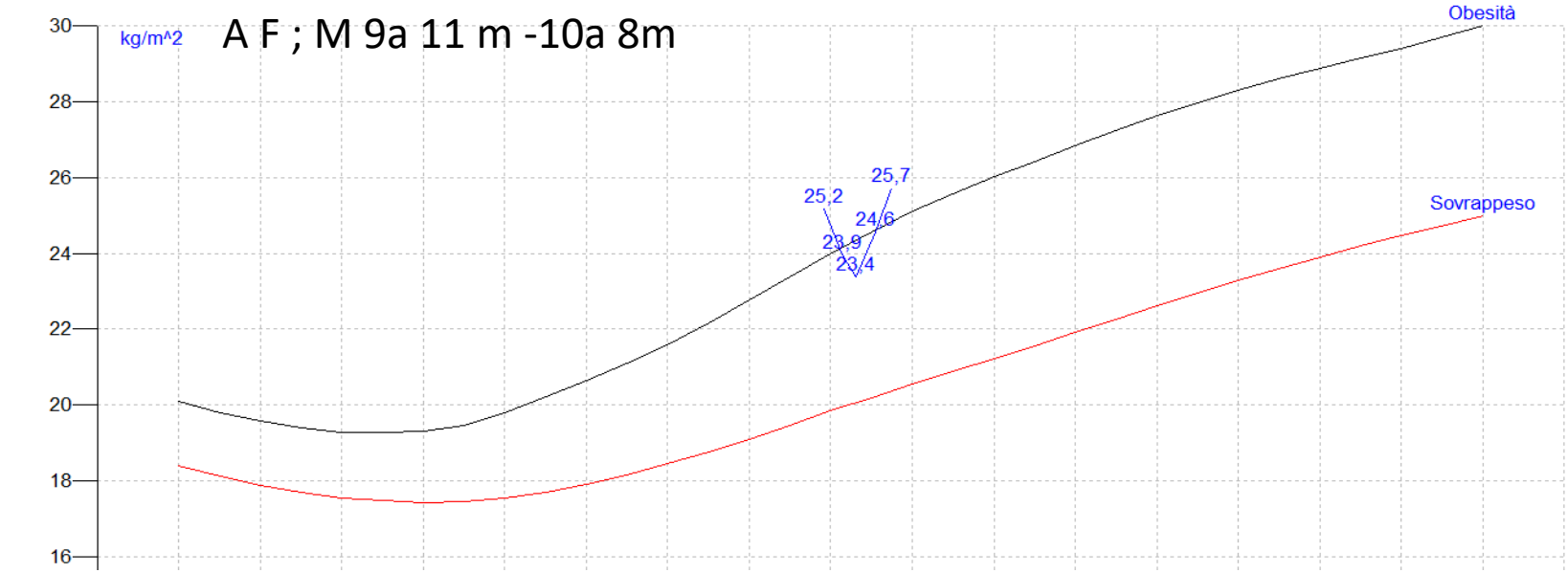
↑ Adiposità (Massa Grassa) → ↓ Assunzione di Energia (quantità di cibo)

LN; M 11a 8m – 12 a 0m



LN; M 11a 8m – 12 a 0m




A F ; M 9a 11 m -10a 8m
kg/m^2
30
28
26
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16
Obesità
Sovrappeso
25,2
25,7
24,6
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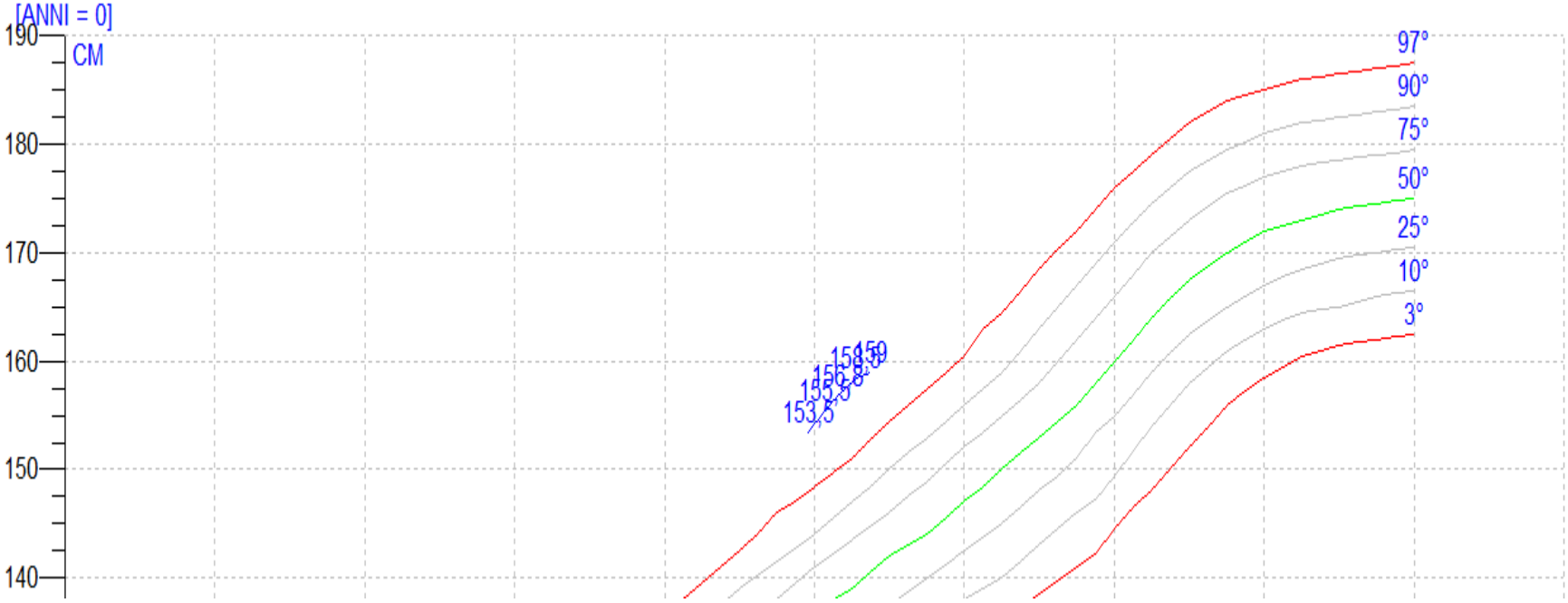
23,4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CM
190
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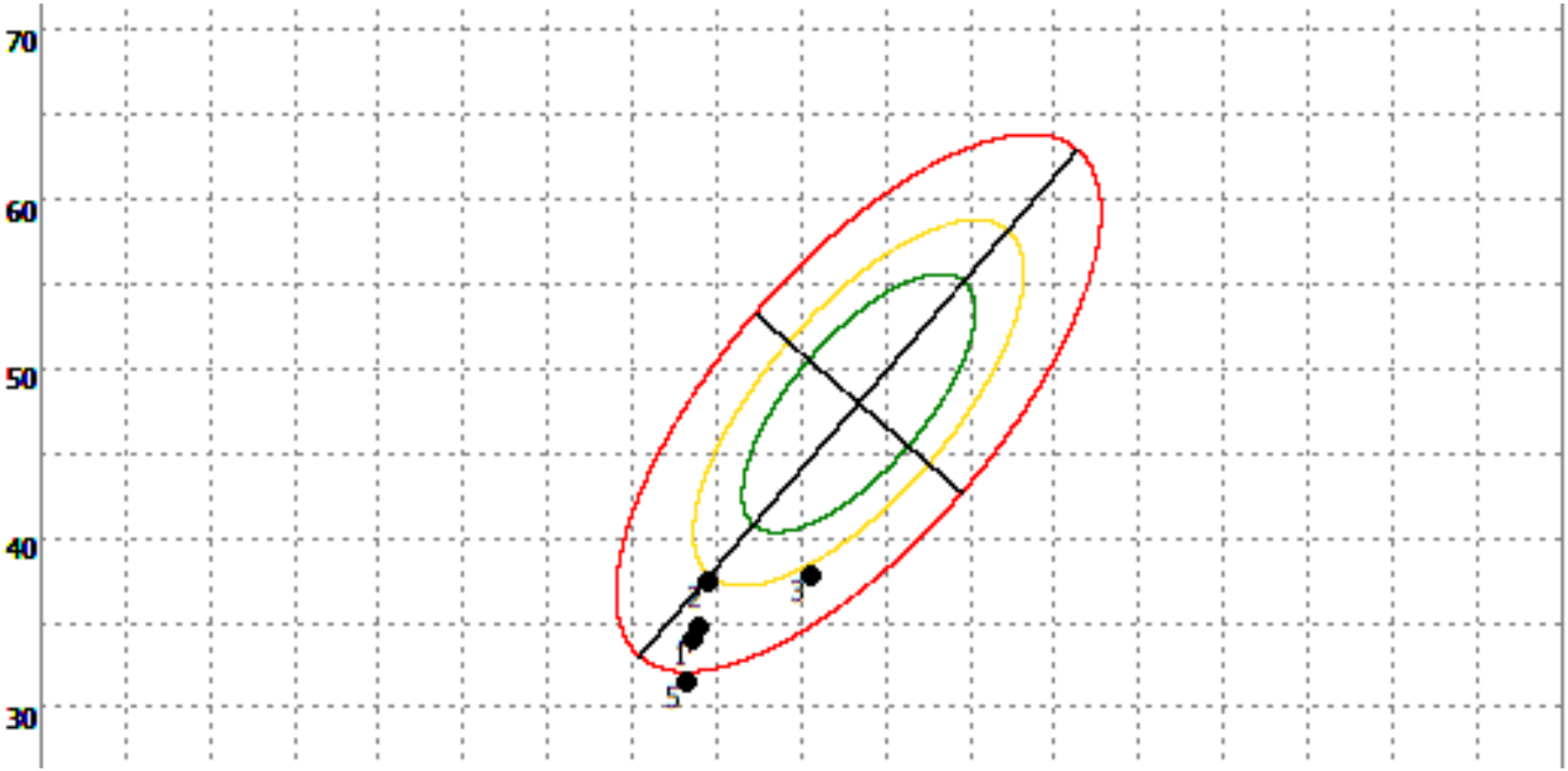
A F ; M 9a 11 m -10a 8m



Quantità e **Qualità** di massa magra (metabolicamente attiva)

I ragazzi obesi hanno in assoluto un **minor volume** di attività fisica **Low Intensity** e più lunghi periodi di riposo

Mc Manus 2011
Maffeis 1993
Yu CW et al 2002

I ragazzi obesi hanno **minori abilità motorie**

Hills P et al. 2011

I ragazzi obesi hanno minor volume di P.A. ma uguale EEE se proporzionato alla **FFM**

Ekelund 2002

I ragazzi obesi sono meno attivi, hanno generalmente **(*)** minore **FFM** e minore introito energetico

Jimenez-Pavon 2013 (HELENA e EHYS)

(*)

(1) sarcopenic obesity (high FMI and low FFMI)
(2) proportional obesity (high FMI and normal FFMI)
(3) muscular obesity (high FMI and high FFMI)

CIRCOLO VIZIOSO

Bilancio energetico positivo
Alterazioni endocrine
Alterazioni metaboliche in vari tessuti

Impaccio fisico meccanico
Alterazioni metaboliche muscolari
Alterazioni funz. Cardiovasc.
Motivazioni psicologiche
Determinanti socio-economici

PERCHE' L'ATTIVITA' FISICA COME CURA E' DIFFICILE ?

PROBLEMI PSICOLOGICI
DETERMINANTI SOCIO-ECONOMICI
PROBLEMI METABOLICI

PROBLEMI PSICOLOGICI

…**lifestyle** interventions are generally **not very effective for severely** affected children .

…the **promotion of patient compliance** with commonly accepted paediatric recommendations for health should remain the **main focus** of metabolic syndrome clinical management.

Mameli et al 2017

Gli interventi di dieta e esercizio comprendono generalmente l'adozione **di tecniche di terapia comportamentale** (**autoapprendimento, tecniche di controllo degli impulsi, ristrutturazione cognitiva, sviluppo di strategie di problem solving, sistemi di amplificazione, contratti comportamentali, apprendimento modellistico tramite genitori, curve di auto-riflessione**) che mirano a **sviluppare nuove abitudini alimentari e di esercizio, modificando così l'ambiente individuale**.

T. Reinehr, Lifestyle intervention in childhood obesity: changes andchallenges, Nat. Rev. Endocrinol. 9 (2013) 607–614.

DETERMINANTI SOCIO-ECONOMICI

Children (n = 324) aged 9–13 years and their parents were surveyed on personal, interpersonal and environmental correlates of physical activity.

Consistent predictors across multiple physical activity measures were: **parent support** for physical activity, having **appropriate clothing** for sport, **enjoyment of physical activity** and **perceived availability of sporting clubs**.

Keren Best et al. In Search of Consistent Predictors of Children's Physical Activity
Int. J. Environ. Res. Public Health **2017, 14, 1258;**

Socio-economic determinants of physical activity across the life course: A "Determinants of DIet and Physical ACtivity" (DEDIPAC) umbrella literature review
PLOS ONE | https://doi.org/10.1371/journal.pone.0190737 January 19, 2018

Results

Nineteen reviews were included

Conclusions

Available evidence on the socioeconomic determinants of PA behaviour across the life course is probable (shows fairly consistent associations) at best. While some evidence is available for adults, less was available for youth. This is mainly due to a limited quantity of primary studies, weak research designs and lack of accuracy in the PA and SES assessment methods employed**. Further PA domain specific studies** using longitudinal design and clear measures of SES and PA **assessment are required**.

PROBLEMI METABOLICI

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Motivazioni psicologiche
Determinanti socio-economici

ALTERAZIONI METABOLICHE MUSCOLARI

Studi basati anche su **biopsie muscolari** hanno confermato che negli **adulti obesi** c'è una maggiore percentuale di **fibre muscolari di tipo II** (metabolismo anaerobico) e una diminuzione dei **mitocondri** (metabolismo aerobico).

Tanner CJ et al. Am J Physiol Endocrinol Metab 2002;282:E1191e6.
Hickey MS et al. Am J Physiol 1995;268(3 Pt 1):E453e7.

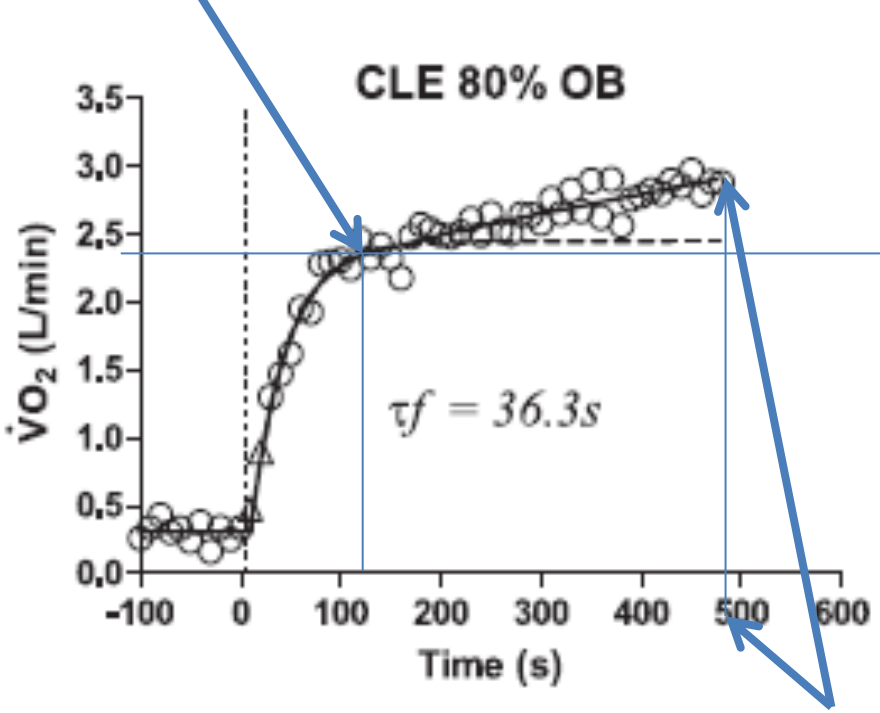
Nei bambini e adolescenti è un metodo poco praticabile quindi ci sono pochi studi. Sappiamo che i bambini hanno un maggior metabolismo aerobico. Per sapere se nei bambini obesi peggiora, è meglio usare lo **studio della VO2.**

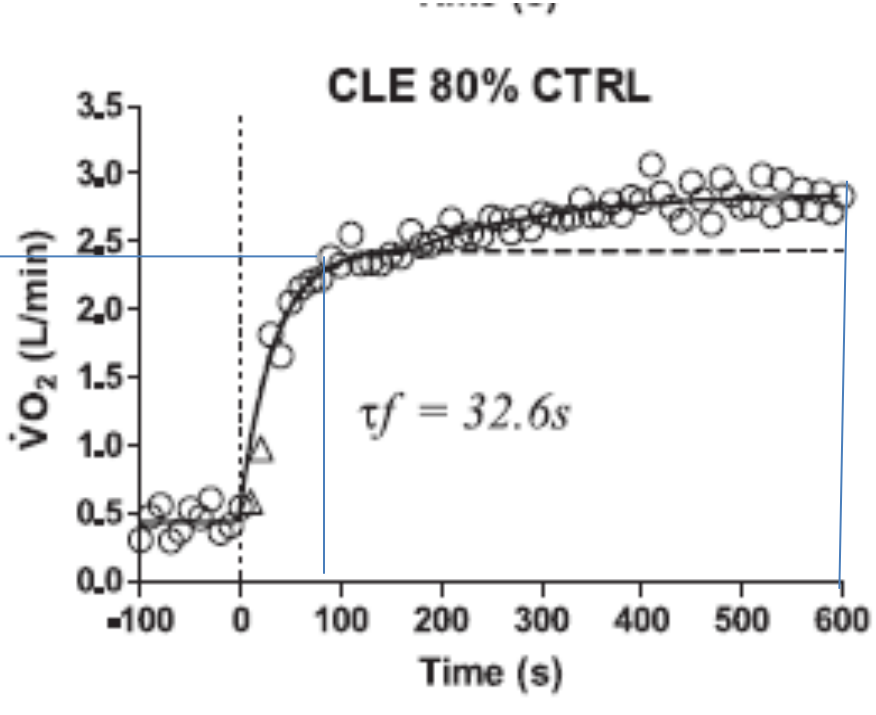
Zunquin G et al. Br J Sports Med 2009;43:869e70.

Lower primary component :

Chi ha maggior oxygen deficit utilizza di più il **metab. Anaerobico** e arriva **dopo al plateau**

→ minore tolleranza all'esercizio a tutte le intensità → dimin. Activity Bouts e aum. Rest periods (Zunquin G et al 2009)





Slow Component più «ripida» e breve:

Hanno **maggiore sensazione di fatica durante l'attività fisica intensa** perché arrivano **prima** al **VO2 max** (più basso/Kg), all'accumulo di **H+** e all'**esaurimento**) (Hughes AR et al 2006; Page A et al 2005)

Stessa età-stessa intensità di esercizio ma in soggetto obeso

Table 3. *Estimated $\dot{V}O_{2max}$ and gas exchange threshold (GET)*

	OB	Control
$\dot{V}O_{2max}$, l/min	3.27 ± 0.51 [1.98–4.06]	3.21 ± 0.61 [2.30–4.18]
$\dot{V}O_{2max}$, ml·min^{-1}·kg^{-1}	31.8 ± 4.9 [20.8–38.5]*	49.0 ± 9.6 [34.4–65.7]
$\dot{V}O_{2max}$, ml·min^{-1}·kg^{-1} FFM	51.6 ± 8.0 [34.4–60.1]	58.6 ± 11.1 [42.0–75.6]
GET, l/min	1.80 ± 0.28 [1.42–2.48]*	2.08 ± 0.37 [1.45–2.61]
GET, %$\dot{V}O_{2max}$	55.7 ± 6.7 [46.8–71.9]*	65.1 ± 5.2 [59.5–74.5]

Gas exchange threshold (GET) is the noninvasive equivalent of **lactate threshold (LT)**

Salvadego D et al. 2010 (40%, 60%, and 80% of estimated peak VO2)

PRESCRIZIONE INDIVIDUALIZZATA

Nella prescrizione dell'Attività Fisica (PA) bisogna tener conto che gli obesi consumano più energia ma … provano più fatica e arrivano prima all'esaurimento

Quindi bisogna tenere conto della **GET** e non solo delle % di VO2 max (generiche) come si fa di solito

Salvadego D et al. 2010

OBESITA' - ATTIVITA' FISICA E ORMONI

25 obese children and healthy controls were studied. We observed that, much like in adults, the **obese** group displayed significantly lower circulating **GH, epinephrine, norepinephrine, and dopamine**. Other components of the GH-IGF-1 (IGF-1, IGF-, and GH-binding proteins) axis were not significantly different .

Interestingly, **the more obese the children, the more blunted the GH** response to exercise; this effect was also maintained both in early- and late-pubertal subjects.

the combined effect of **lipid ingestion and obesity** almost completely **suppressed the GH response to exercise,** that is, reduced it to a much greater extent than could be expected by adding the separate effect of obesity and of fat ingestion alone, suggesting the presence of a synergistic effect of the two conditions [32].

Brian Tran et al. Exp Diabetes Res. 2012; 2012:683-680

OBESITA' - ATTIVITA' FISICA E ORMONI

…maximal epinephrine concentration was significantly (P < 0.05) higher in lean vs obese and was negatively correlated to body fat percentage (r = -0.60, P < 0.05).

JABBOUR G et al. Med Sci Sports Exerc. 2011 Mar;43(3):408-15.

…to a **low-level chronic inflammatory state**, …have been **associated with a decrease in plasma catecholamine .**

McMurray RG, Hackney AC. Sports Med. 2005;35(5):393–412

…**in vivo lipolysis**, … shows a **decreased sensitivity to epinephrine in childhood onset obesity**.

Bougnères P et al. J Clin Invest. 1997;99(11):2568–73.

…after **30min of intermittent (2min on, 1min off) cycling at ~80% VO2max**. **Basal** insulin (pmol/L) was significantly higher in Ob vs. other groups**; postexercise**, **insulin** increased in NW (+7 +/- 3) and OW (+5 +/- 8) but decreased in Ob (–15 +/- 5 p < .0167 vs NW). This insulin drop in Ob was disproportionately more pronounced in the half of Ob children with higher basal insulin (Ob-H)

Brian D. Tran et al. Pediatric Exercise Science, 2014, 26, 434-443

Ma come si creano queste alterazioni metaboliche ?

OBESITA'-INSULINO RESISTENZA-SINDROME METABOLICA
fisiopatologia

GENETICA

To date, there are more than:

50 established loci for various measures of **obesity**,
157 loci associated with **lipid and lipoprotein levels**,
120 loci associated with **type 2 diabetes** and fasting or 2-h glucose levels
90 loci associated with **hypertension** .

A. Stancakova, M. Laakso, Genetics of metabolic syndrome, Rev. Endocr.Metab. Disord. 15 (2014) 243–252.

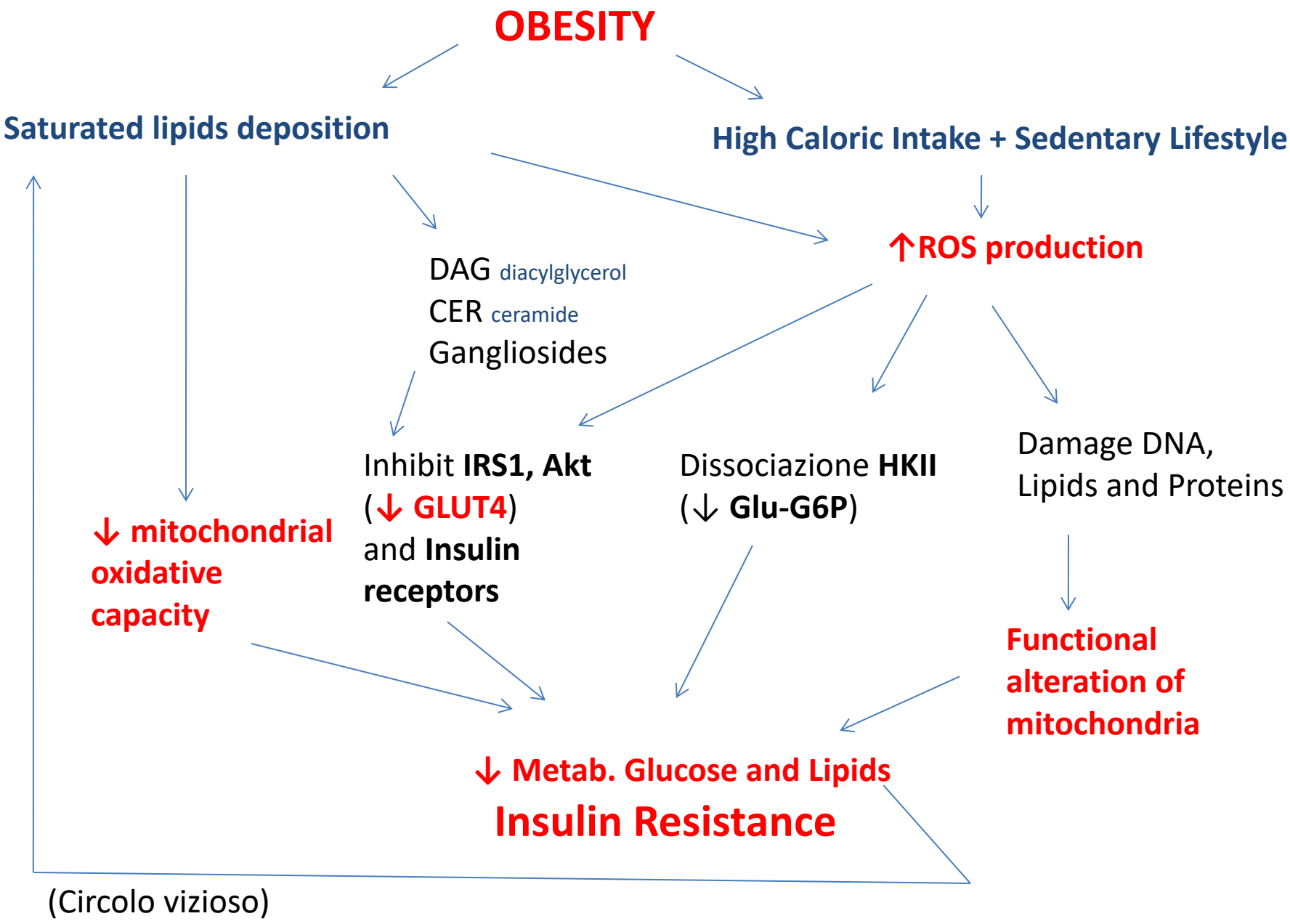
EPIGENETICA

…Our findings, to date, **demonstrate a cross talk relationship between inflammation, extracellular remodeling, cytoskeletal interactions, mitochondrial function, and insulin resistance in human skeletal muscle** .

Based on our previous findings in skeletal muscle, we hypothesize that there will **be alterations in the methylation of genes** involved in **mitochondrial function, inflammation, and extracellular matrix remodeling**

We identified **12 genes (encompassing 22 methylation sites)** that demonstrated a **negative relationship between gene expression and DNA methylation**. Of these, sorbin and SH3 domain containing 3 (**SORBS3**) had increased methylation (**9 DMCs)** and was associated with a decrease in gene expression. The 11 remaining genes had an increase in gene expression that correlated with a decrease in methylation

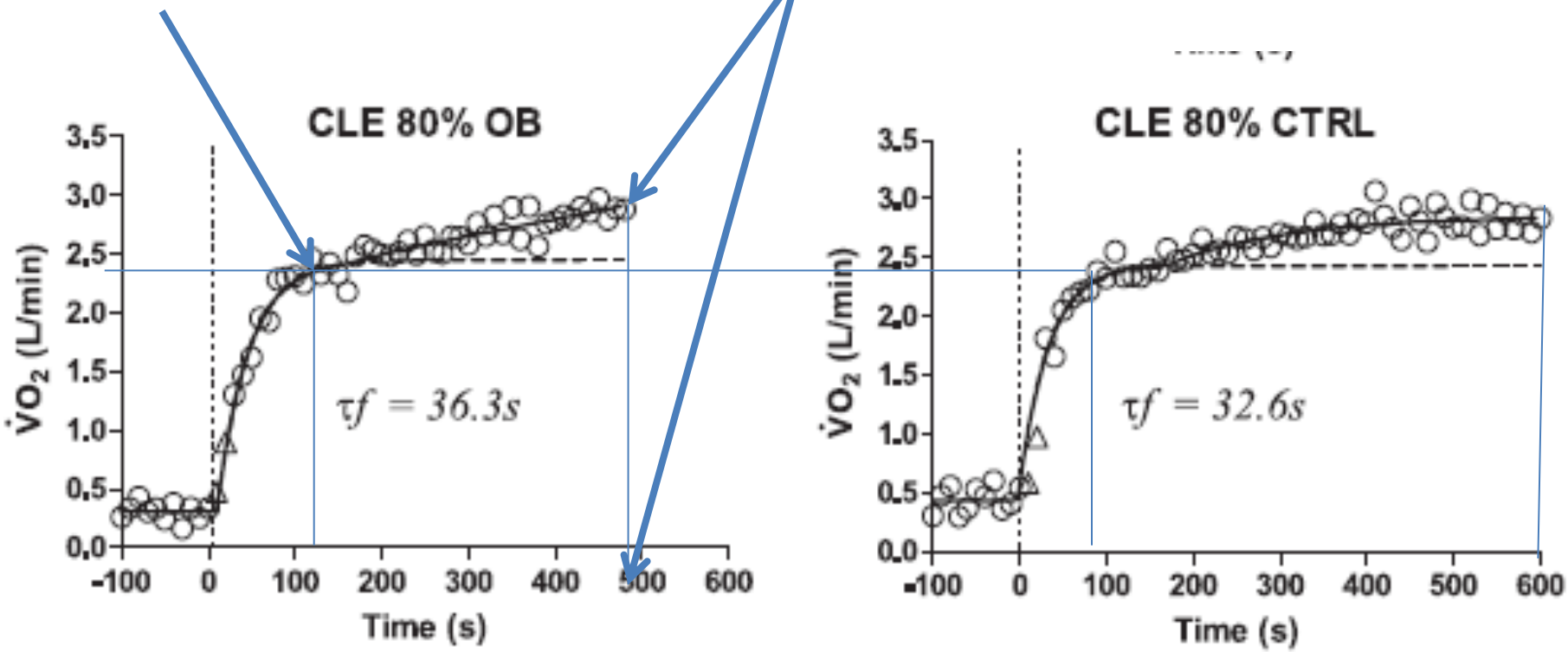
Day SE et al. **Next-generation sequencing methylation profiling of subjects with obesity identifies novel gene changes.** Clin Epigenetics. **2016** Jul 18;8:77


OBESITY
Saturated lipids deposition
High Caloric Intake + Sedentary Lifestyle
↑ROS production
DAG diacylglycerol
CER ceramide
Gangliosides
Inhibit IRS1, Akt
(↓ GLUT4)
and Insulin
receptors
Dissociazione HKII
(↓ Glu-G6P)
Damage DNA,
Lipids and Proteins
↓ mitochondrial
oxidative
capacity
Functional
alteration of
mitochondria
↓ Metab. Glucose and Lipids
Insulin Resistance
(Circolo vizioso)

↓ mitochondrial oxidative capacity

utilizza di più il **metab. Anaerobico** e arriva **dopo al plateau**

arrivano **prima** al **VO2 max** (più asso/Kg), all'accumulo di **H+** e all'**esaurimento**



→ **minore tolleranza all'esercizio** a tutte le intensità → dimin. Activity Bouts e aum. Rest periods (Zunquin G et al 2009)

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Bilancio energetico positivo
Alterazioni endocrine
Alterazioni metaboliche in vari tessuti

Impaccio fisico meccanico
Alterazioni metaboliche muscolari
Alterazioni funz. Cardiovasc.
Motivazioni psicologiche

SPEZZARE IL CIRCOLO VIZIOSO E' POSSIBILE !

La contrazione muscolare (P.A.) porta a risposte adattative che migliorano l'efficienza metabolica, la capacità ossidativa e l'attività contrattile attraverso una modifica dei profili di espressione genica e formazione di mitocondri e nuove proteine contrattili

Coffey VG, Hawley JA . The molecular bases of training adaption Sports Med 2007; 37 (9): 737-63

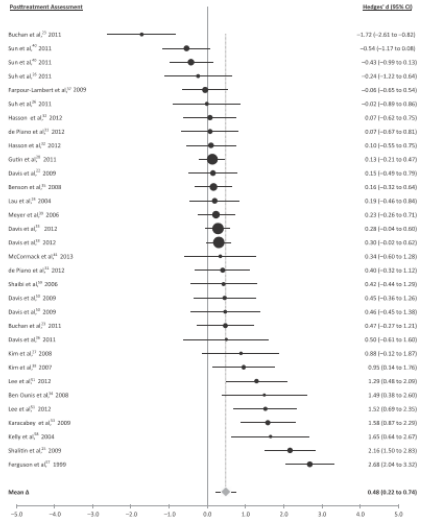
Evidence is available that indicates deficits in fat oxidation can be reversed through targeted PA intervention, which may also augment positive alterations in body composition.

Ben Ounis O et al. Ann Nutr Metab 2010;56:260e6.
Ben Ounis O et al. Ann Endocrinol (Paris) 2011;72:34e41.

TABLE 1 Studies Examining the Effect of Exercise Training on Fasting Insulin and IR in Children and Adolescents

Source	*N*	Gender (M/F)	Age (y)	Intervention Groups	Duration (min/d)	Frequency (d/wk)	Study Length (wk)
Benson et al,[35] 2008	78	46/32	12.3 ± 1.3	RT or CON	—	2	8
Ben Ounis et al,[34] 2008	24	24/0	12–14	AT, AT + diet, or diet	90	4	8
Buchan et al,[23] 2011	57	10/47	16.4 ± 0.7	Moderate-intensity AT, high-intensity AT, or CON	3–20	3	7
Davis et al,[33] 2012	222	94/128	9.4 ± 1.1	High-dose AT, low-dose AT, or CON	20–40	5	13
Davis et al,[50] 2009	41	0/41	15.2 ± 1.1	RT + diet, RT + AT + diet, or CON	60	2	16
Davis et al,[22] 2009	54	28/26	15.5 ± 1.0	RT + diet, diet, or CON	60	2	16
Davis et al,[36] 2011	38	0/38	15.8 ± 1.1	RT + diet, RT + AT + diet, diet, or CON	60–90	2	16
de Piano et al,[31] 2012	58	27/31	16.5 ± 1.4	RT + diet, RT + AT + diet, or diet	60	3	52
Farpour-Lambert et al,[37] 2009	44	16/28	8.9 ± 1.5	RT + AT or CON	60	3	12
Ferguson et al,[57] 1999	79	26/53	9.5 ± 1.0	AT or CON	40	5	16
Gutin et al,[28] 2011	242	0/242	8–11	RT + AT + games or CON	80	5	10
Hasson et al,[32] 2012	100	39/61	15.4 ± 1.1	RT + diet or diet	—	2	16
Karacabey,[53] 2009	40	40/0	11.8 ± 0.5	AT or CON	30–60	3	12
Kelly et al,[58] 2004	20	9/11	10.9 ± 2.0	AT or CON	30–50	4	8
Kim et al,[38] 2007	26	26/0	17.0 ± 0.1	AT or CON	40	5	6
Kim et al,[27] 2008	17	17/0	11.0 ± 0.0	RT + AT or CON	50	2	12
Lau et al,[24] 2004	36	24/12	10–17	AT + diet or diet	60	3	6
Lee et al,[51] 2012	45	45/0	12–18	RT, AT, or CON	60	3	12
McCormack et al,[41] 2013	18	5/13	13.0 ± 1.9	RT + AT or CON	60	3	8
Meyer et al,[39] 2006	67	34/33	14.7 ± 2.2	AT or CON	60–90	3	24
Shaibi et al,[59] 2006	21	21/0	15.4 ± 1.6	RT or CON	60	2	16
Shalitin et al,[25] 2009	162	81/81	6–11	RT + AT, RT + AT + diet, or diet	90	3	
Suh et al,[26] 2011	30	15/15	13.1 ± 0.5	RT + diet, AT + diet, or diet	40–60	3	
Sun et al,[40] 2011	93	46/47	13.6 ± 0.7	AT, diet, AT + diet, or CON	40	4	

Age is reported as mean 6 SD when available or the age range of participants included in the study. Empty cells are present when a component of the training protocol wa
author. AT, aerobic training; CON, control group; F, female; M, male; RT, resistance training.



Fedewa MV et al 2014

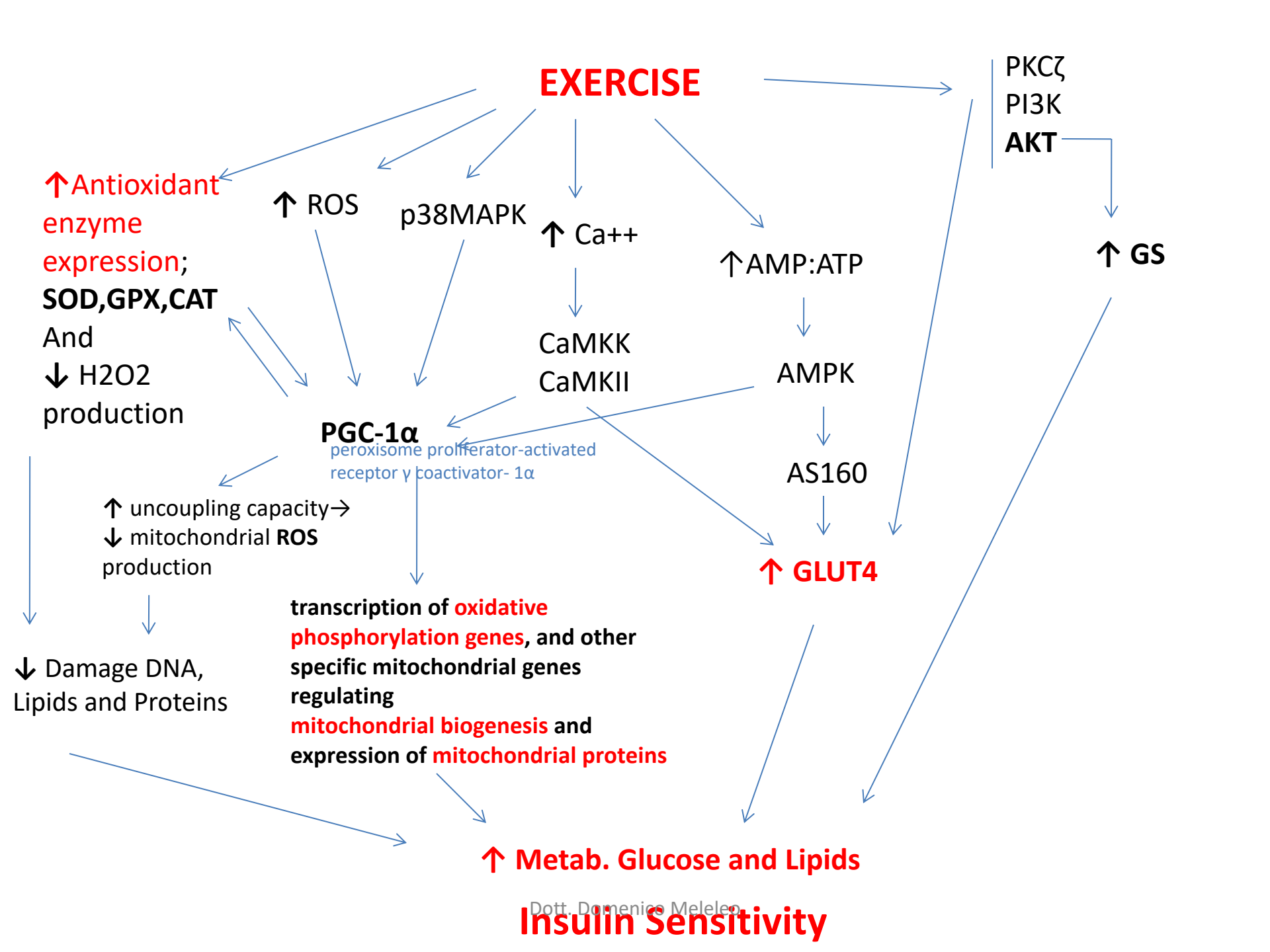
J Endocrinol. **2017** Sep;234(3):R159-R181. doi: 10.1530/JOE-17-0186.

Improvement of obesity-linked skeletal muscle insulin resistance by strength and endurance training.

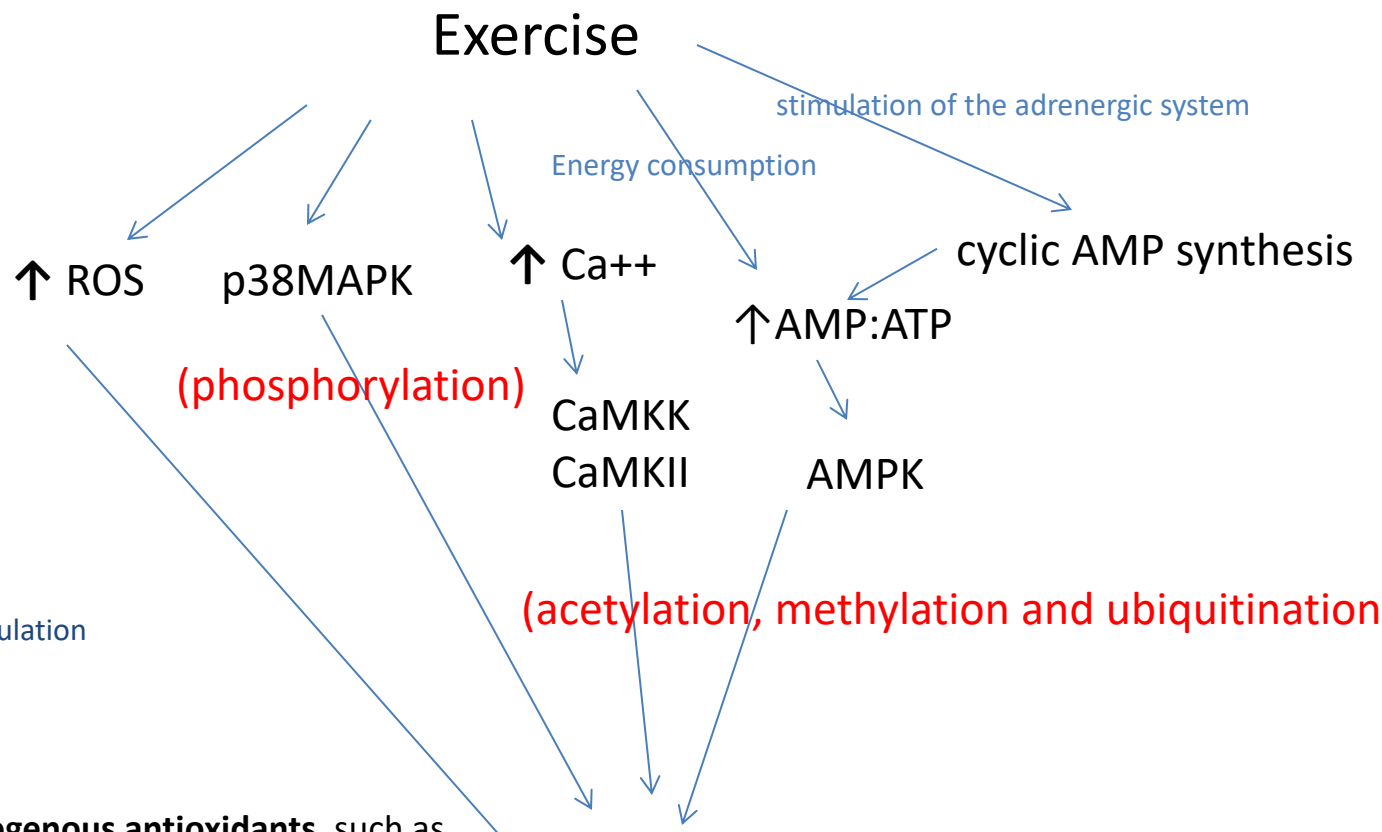
Di Meo S[1], Iossa S[2], Venditti P[2].

Abstract

Obesity-linked insulin resistance is mainly due to fatty acid overload in non-adipose tissues, particularly skeletal muscle and liver, where it results in high production of reactive oxygen species and mitochondrial dysfunction. Accumulating evidence indicates that resistance and endurance training alone and in combination can counteract the harmful effects of obesity increasing insulin sensitivity, thus preventing diabetes. This review focuses the mechanisms underlying the **exercise role** in opposing skeletal muscle insulin resistance-linked metabolic dysfunction. It is apparent that exercise acts through two mechanisms: **(1) it stimulates glucose transport** by activating an insulin-independent pathway and **(2)** it protects against mitochondrial dysfunction-induced insulin resistance by **increasing muscle antioxidant defenses and (3) mitochondrial biogenesis**. However, antioxidant supplementation combined with endurance training increases glucose transport in insulin-resistant skeletal muscle in an additive fashion only when antioxidants that are able to increase the expression of antioxidant enzymes and/or the activity of components of the insulin signaling pathway are used.



Dott. Domenico Meleleo



regulate expression of endogenous antioxidants, such as Cu/ZnSod, MnSod and Gpx, in skeletal muscle

TRASCRIZIONE

Then, the activated **PGC-1α** moves into the nucleus and **coactivates the transcription** factors that regulate expression of **mitochondrial proteins.**

transcription factors NRF-1 and NRF-2

NRF-1 and NRF-2 promote the **transcription of oxidative phosphorylation genes, and other specific mitochondrial genes**,

Dott. Domenico Medeleo

TRASLAZIONE

Participants were recruited into two distinct age groups: young (**18–30 years**) or older (**65–80 years**) with a goal of an equal number of men and women

Here we report that **12 weeks** of high-intensity aerobic interval **(HIIT**), resistance **(RT),** and combined **exercise training** **enhanced insulin sensitivity and lean mass**, but only HIIT and combined training **improved aerobic capacity** and skeletal muscle mitochondrial respiration. Both RT and HIIT enhanced proteins involved in translational machinery irrespective of age. Only small **changes of methylation of DNA promoter regions** were observed. We provide evidence for predominant **exercise regulation** at the translational level, **enhancing translational capacity and proteome abundance** to explain phenotypic gains in muscle mitochondrial function and hypertrophy in all ages.

Matthew M. Robinson ; Enhanced Protein Translation Underlies Improved Metabolic and Physical Adaptations to Different Exercise Training Modes in Young and Old Humans . **Cell Metab. 2017** March 07; 25(3): 581–592

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Ormesi dei ROS

Thus, a moderate, intermittent ROS production during short time periods in a program of graduate aerobic training can activate signaling pathways leading to cellular adaptation and protection against future stresses. **Conversely**, moderate levels of ROS production over long time periods (e.g. hours) **or** high levels produced during brief strenuous exercise can lead to structural and functional tissue damage inactivating important cellular molecules.

…Because ROS seem to be involved in exercise-induced stimulation of PGC-1α expression**, the question** arises whether **antioxidant integration can block** the adaptive responses to endurance training mediated by PGC-1 in insulin-resistant muscle

Il nostro ruolo:

World Health Organization

WHO Discussion Paper (December 2017)

Physical activity for health

More active people for a healthier world: draft global action plan on physical activity 2018–2030

BACKGROUND

1. Regular physical activity is a well-established risk factor for the prevention and treatment of the leading noncommunicable diseases (NCD), namely heart disease, stroke, diabetes and breast and colon cancer[1]. It also contributes to the prevention of other important NCD risk factors such as hypertension, overweight and obesity, and is associated with improved mental health, delay in the onset of dementia[2] and improved quality of life and well-being[3].

PARTNERSHIPS FOR ACTION

World Health Organization
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32. Implementation of this global action plan demands partnership as the agenda is beyond scope of any single agency. By working together to achieve the vision of this global actio plan and improve health for all, partners can also accelerate progress to achieve their ov respective goals.

33. These partners include, but are not limited to:

- **Member States** – ministries of health, transport, education, sports, youth, urban planning, environment, tourism, finance, and labour
- **Development Agencies** - international financial institutions such as the World Bank, regional development banks, subregional intergovernmental organizations and development aid agencies
- **Intergovernmental Organizations** - UN agencies, UN Interagency Taskforce on NCDs (UNIATF) and others
- **International Organizations** – global health initiatives and agencies
- **Non-governmental Organizations** - civil society, community-based organizations, human

- **Professional Associations** - in medical and allied health areas such as sports medicine, physical therapy, general practice, nursing, exercise and sports science, physical activity and public health and other relevant disciplines such as transport, sport, education
- **Philanthropic Foundations** - that are committed to promoting global health and achievement of the SDGs
- **Academic and Research Institutions** - across multiple disciplines including implementation science and the network of WHO collaborating centres
- **Industry Leaders and Private Sector -** committed to improving the health of employees, their families and communities
- **Media** - journalists and media outlets, including both traditional and new
- **City Leaders and Local Government** – mayors, governors and local officials
- **Community -** representatives of faith-based, social and cultural groups
- **WHO -** at all levels, headquarters, regional and country offices

Dott. Dal Monte Michele

World Health Organization

WHO Discussion Paper (December 2017)

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6. Medical and other health professional societies and other stakeholders should support the development and dissemination of resources and best practice guidance on the promotion of physical activity through primary and secondary health care and social services, adapted to different contexts and cultures and health care providers

7. Stakeholders in the government and private recreation, sports and leisure sector should assess potential, and where appropriate, develop partnerships with health care providers to support the provision of appropriate physical activity opportunities and programmes for different patient populations

8. Medical and other health professional societies and interested stakeholders should support the development and delivery of appropriate in-service training programmes on how to assess and counsel patients on physical activity, particularly focusing on LMIC and the least active patients

P.A. COME CURA

ADEGUATO VOLUME:

Stile di vita attivo

Attività Fisica Organizzata : effettiva e più volte alla settimana (volumi anche inferiori a 60 minuti al giorno si sono dimostrati efficaci a migliorare la salute degli obesi)

PROGRAMMA MISTO AEROBICO/CONTRORESISTENZA

Anche in **circuiti**

PERSONALIZZATO, GRADUALE , DURATURO:

Eventuali patologie

Caratteristiche e problematiche fisiologiche

COLLABORAZIONE CON ESPERTI :

Scienze Motorie

Medici specialisti (Cardiologo, endocrinologo ecc.)

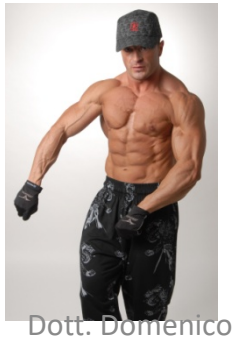
Dietista, Biologo Nutrizionista

Psicologo

***prima fase di trasferimento* e di applicazione** delle principali evidenze scientifiche e metodologiche

Paziente Obeso

Esperti dell'attività fisica



fasi successive, cioè la **programmazione,** *la conduzione e la* **valutazione** *dell'esercizio, la scelta delle attività, le metodologie e gli* **adattamenti** alle caratteristiche organiche e psicologiche del soggetto obeso

GRAZIE E… ATTENZIONE !

Dott. Domenico Meleleo

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