NEUROMUSCULAR CONSEQUENCES OF OBESITY

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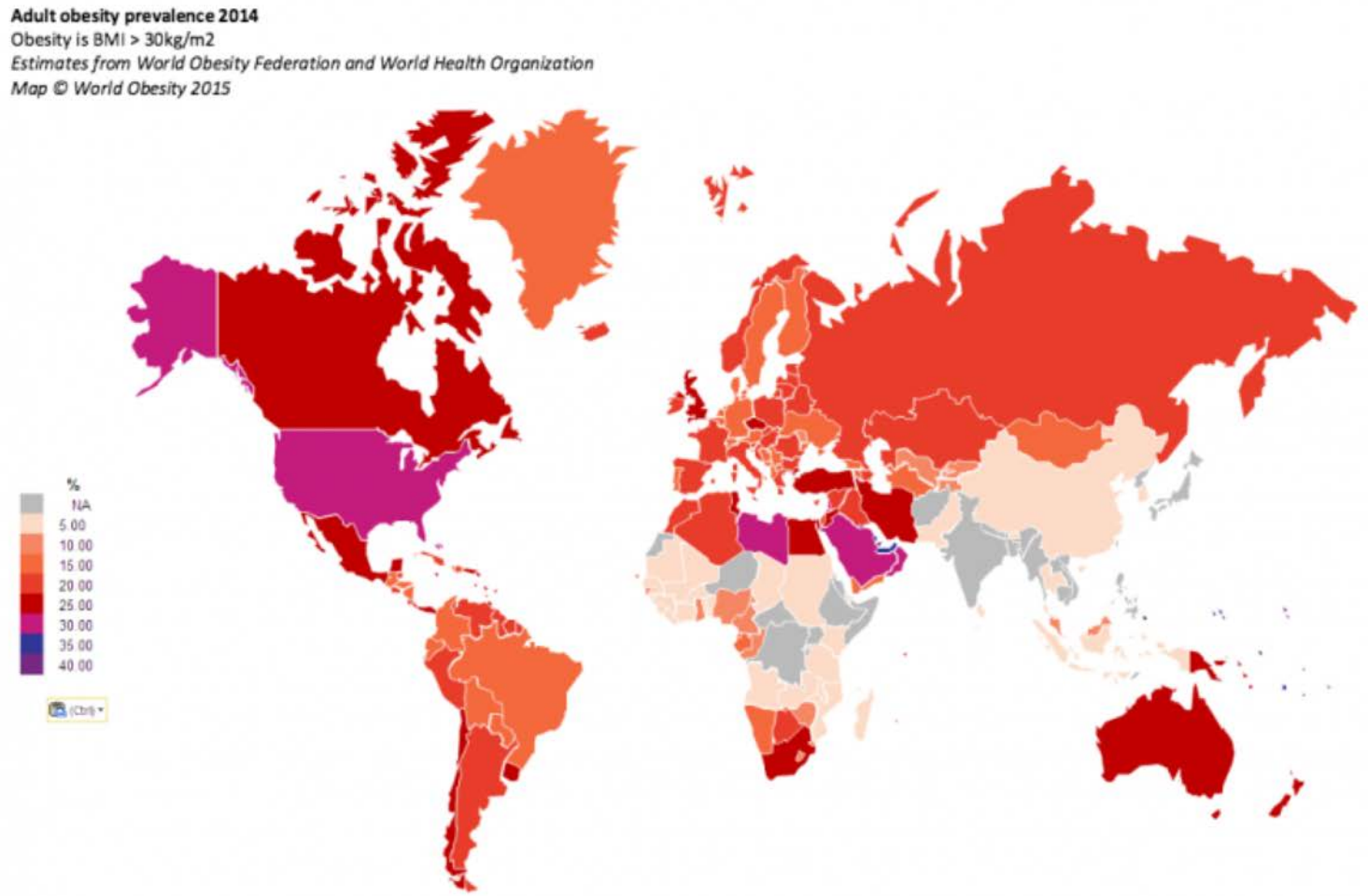
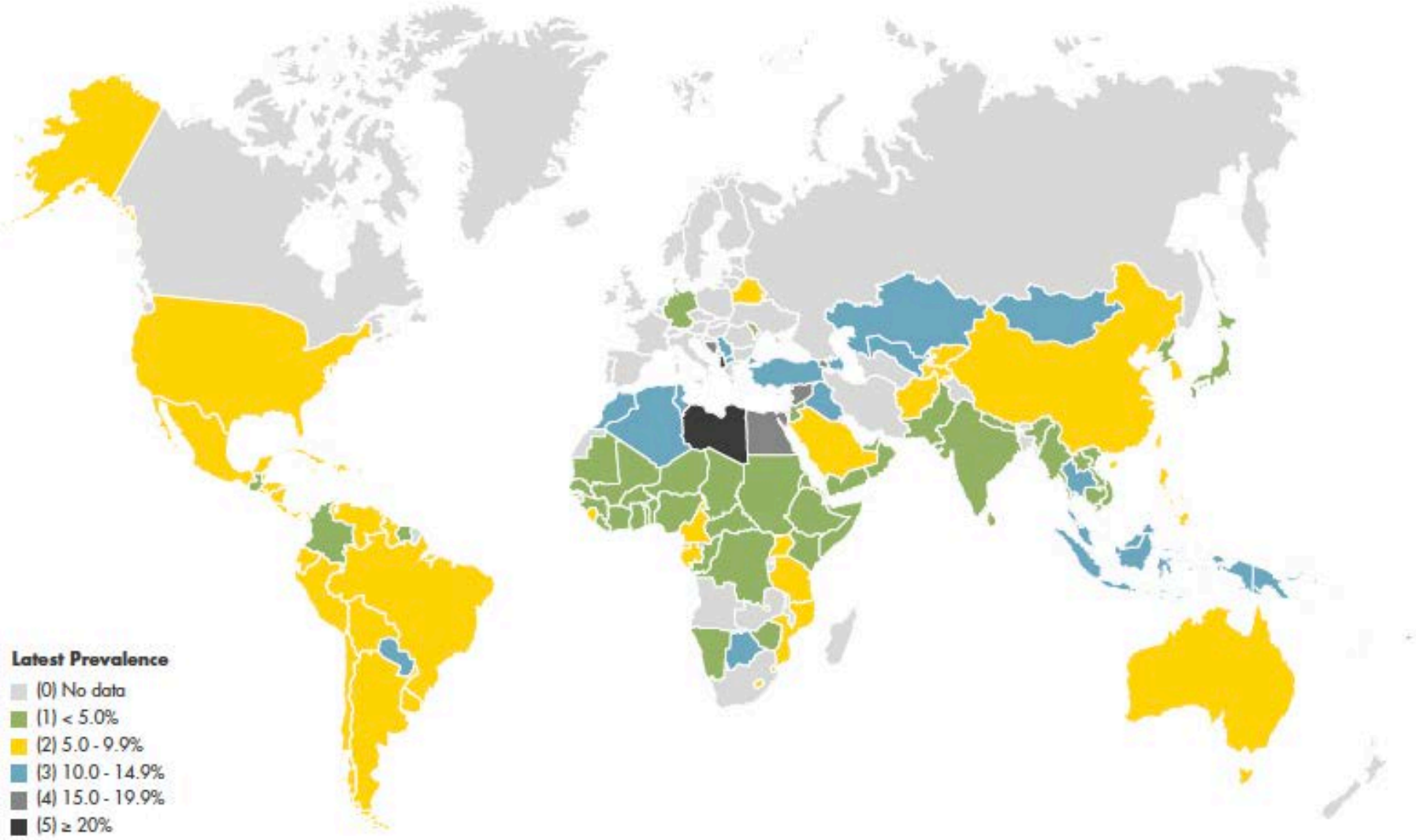
Laboratory of Metabolic Adaptations to Exercise in Physiological and Pathological Conditions

Obesity facts (WHO)



- ✓ Worldwide obesity has nearly tripled since 1975.
- ✓ In 2016, all over the world, 39% of adults aged 18 years and over were overweight in 2016, and 13% were obese.

AGE-STANDARDIZED PREVALENCE OF OVERWEIGHT IN CHILDREN UNDER 5 YEARS OF AGE, COMPARABLE ESTIMATES, 2014

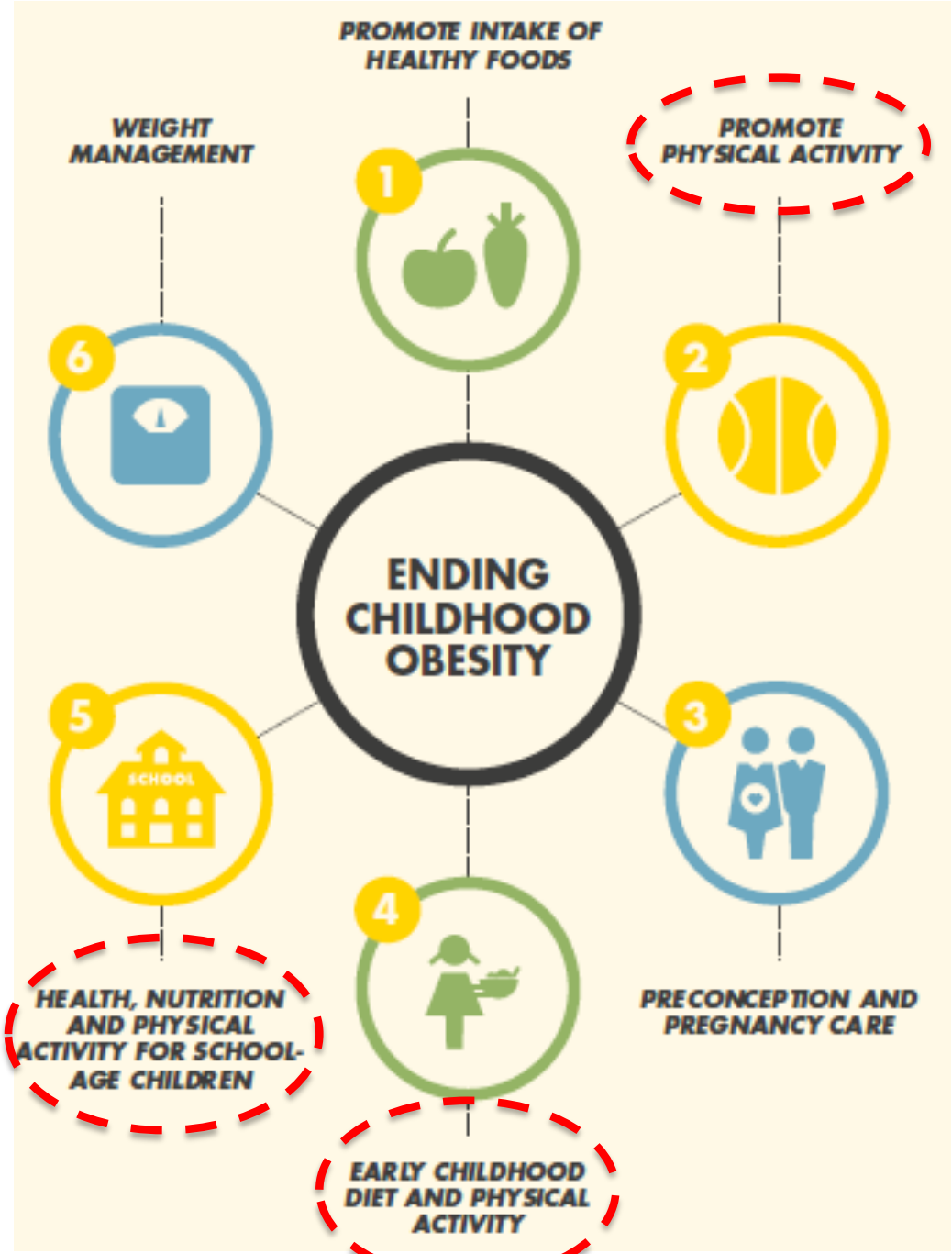


Source: Tracking tool (http://www.who.int/nutrition/trackingtool)

81%

of adolescents do not achieve the recommended 60 minutes of physical activity each day.

(Boys: 78%; Girls: 84%)



(WHO, 2016)

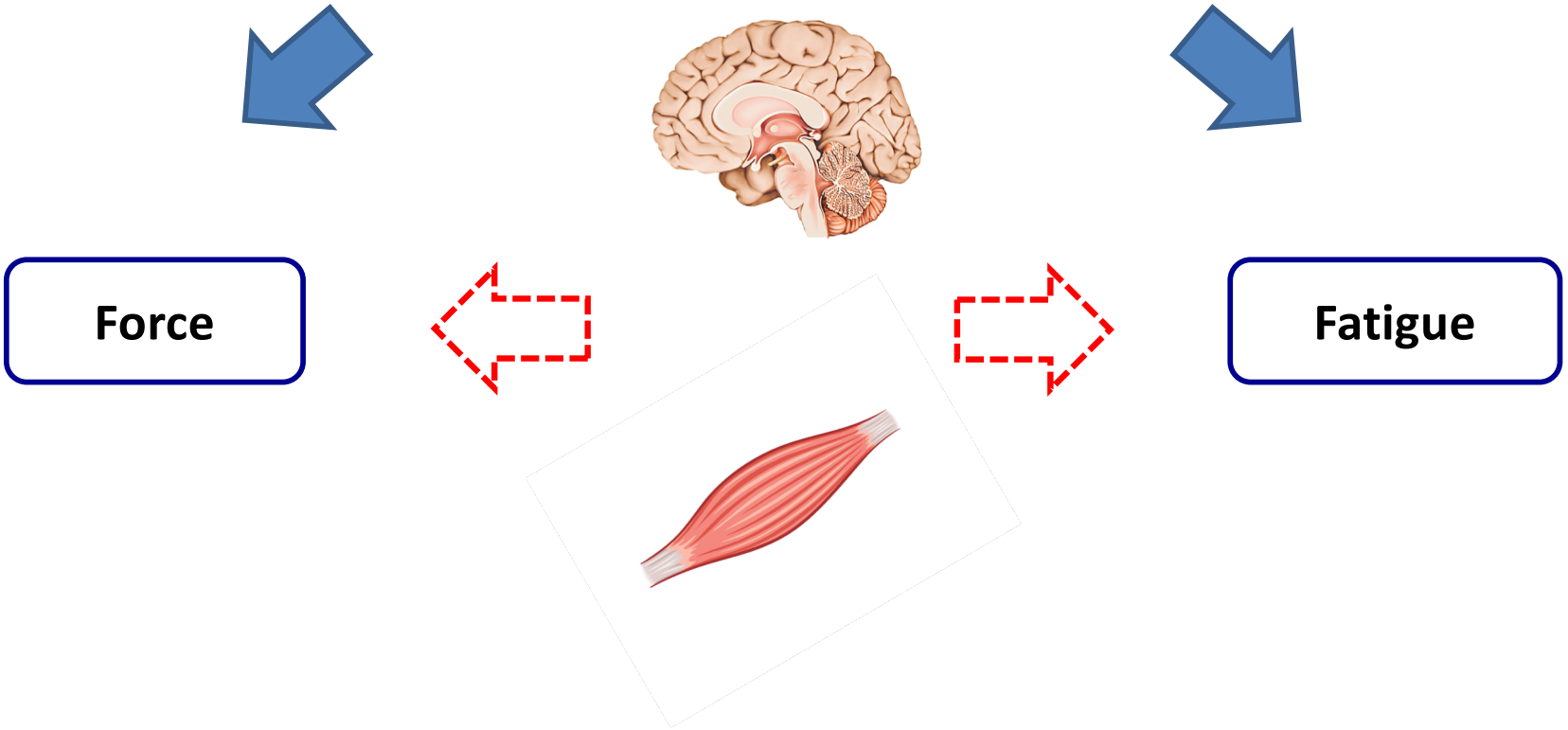
Effects of growth and obesity

Promotion of physical activity among children and adolescents

Need of physical activity programs suited to functional abilities

Context

Functional abilities



What are the effects of youth obesity on neuromuscular function ?

(Maffiuletti et al., 2013)

What are the effects of youth obesity on the force production capacity ?

Effects of youth obesity on force production

Absolute force obese > non obese

- **Relative force (/body mass)**
  Obese < Non obese
- **Relative force (/lean mass)**
  Obese = Non obese
- **Relative force (/muscle mass)**
  Obese > Non obese

Importance of normalization

Table 2. Strength measurements.

	Obese (n = 12)	P value	Controls (n = 10)
MVC torque (N·m)	232.1±65.2	<0.05	176.0±55.1
MVC torque/BM (N·m·kg^{-1})	2.46±0.59	<0.05	3.27±0.78
MVC torque/FFM (N·m·kg^{-1})	4.31±0.70	NS	3.94±0.82
MVC torque/LM$_{thigh}$ (N·m·kg^{-1})	40.2±9.3	<0.05	33.0±5.9
MVC torque/MM$_{thigh}$ (N·m·kg^{-1})	57.3±12.8	<0.05	46.9±8.7

(Abdelmoula et al., 2012)

Effects of youth obesity on force production

Force obese > non obese

=

?

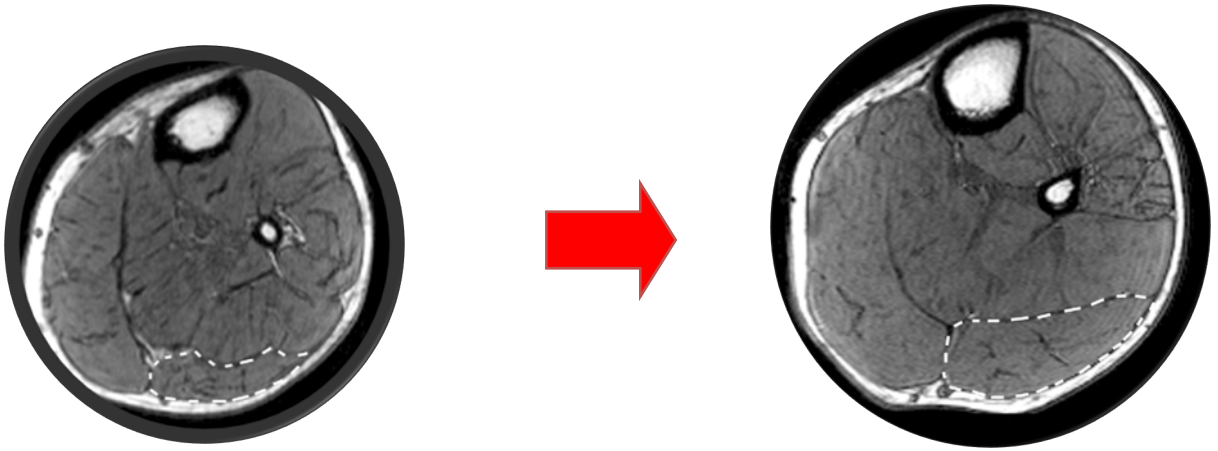
(Forbes, 1964; Duché et al., 2002; Abdelmoula et al., 2012)

Hypothesis: Overweight could act as a training stimulus.

Effects of youth obesity on force production

Force obese > non obese

Muscle hypertrophy ?



Negative impact of obesity on muscle hypertrophy ?

(Blimkie et al., 1990; Sitnick et al., 2009)

Effects of youth obesity on force production

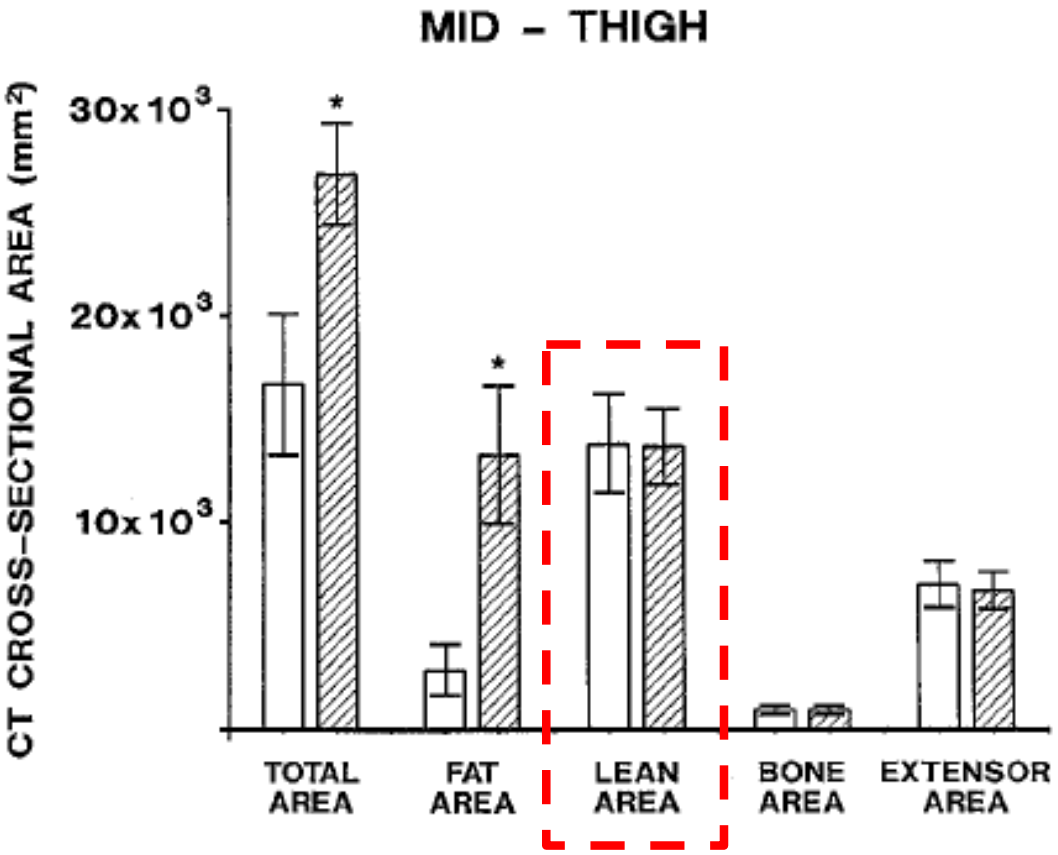


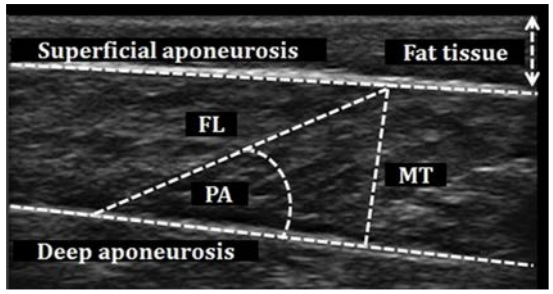
Fig. 3. Morphological characteristics of the right mid-thigh of obese (▨) and non-obese (▭) adolescent males determined from CT scans. Values are means (mm^2) and SD. * Significant difference ($P<0.05$) between groups

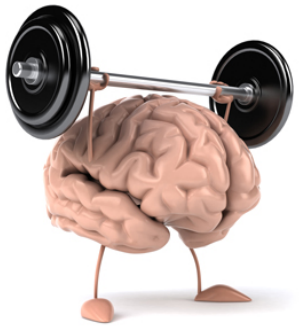
(Blimkie et al., 1990)

Hypothesis: No/limited muscle hypertrophy in obese adolescent girls.

Effects of youth obesity on force production

Relative force obese > non obese





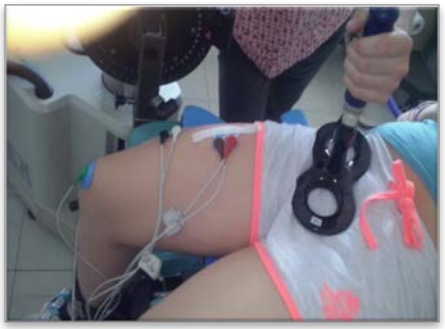
Muscle architecture ?

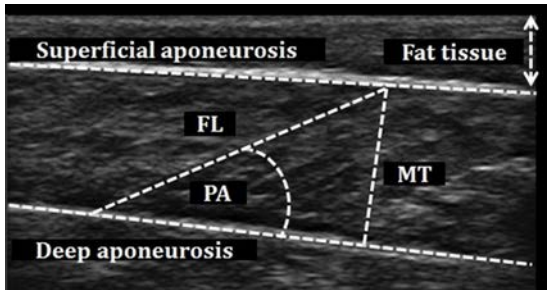
Activation level ?

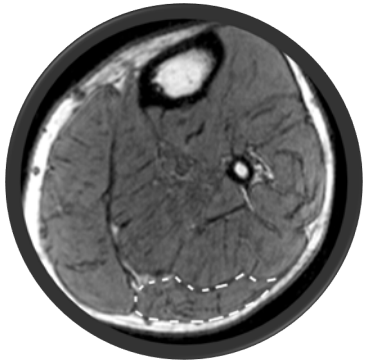
Hypothesis: **Overweight could trigger positive adaptations of the muscle architecture and neural drive in the muscles involved in weight bearing.**

Effects of youth obesity on force production

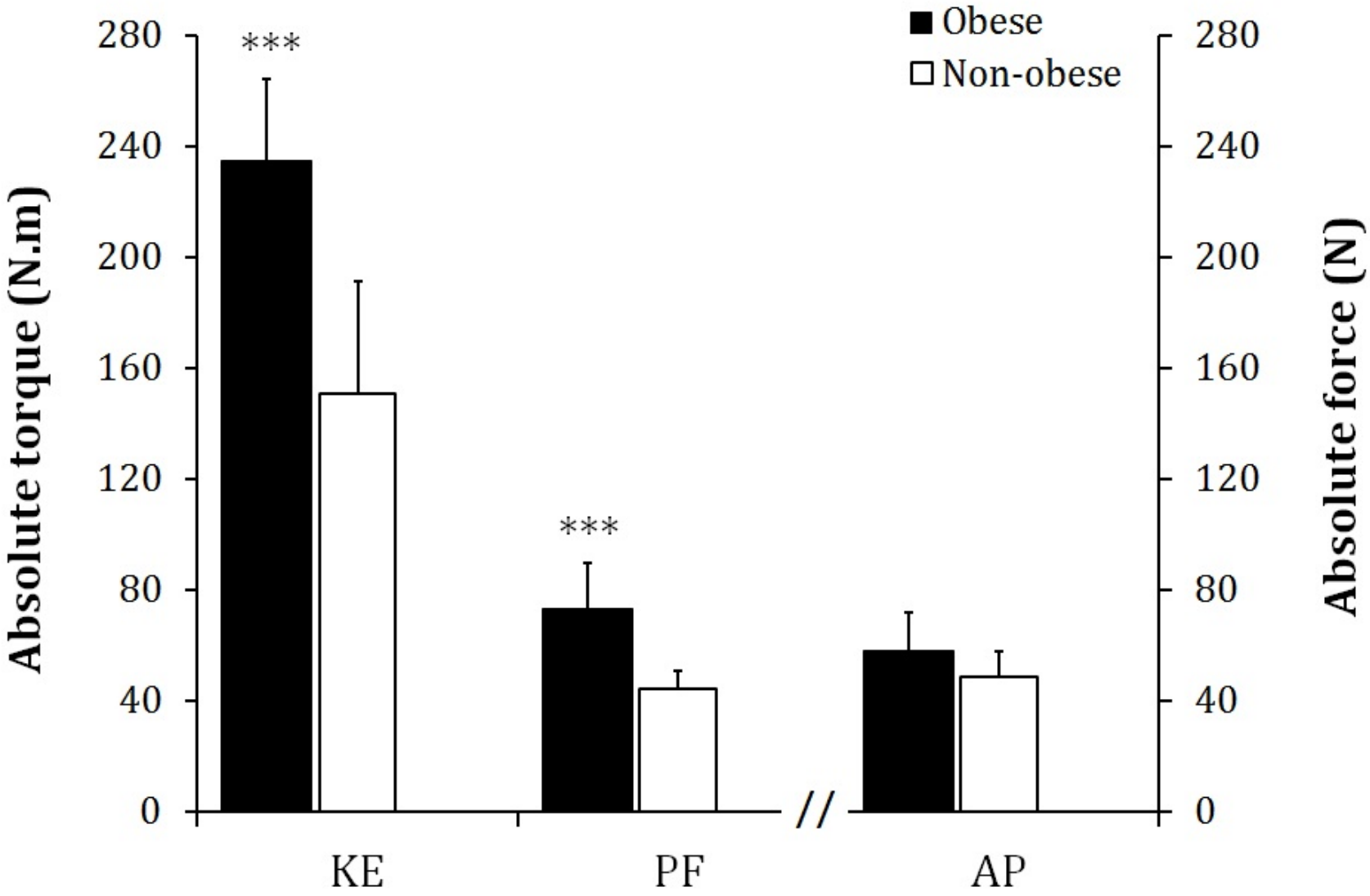
- ✓ **Participants:** Obese vs. non obese adolescent girls, comparable PA & maturation levels
- ✓ **Muscles:** involved (KE & PF) vs. non-involved (AP) in weight bearing
- ✓ **Main outcomes:** maximal voluntary force (MVC), maximal voluntary activation level (AL), pennation angle & CSA.





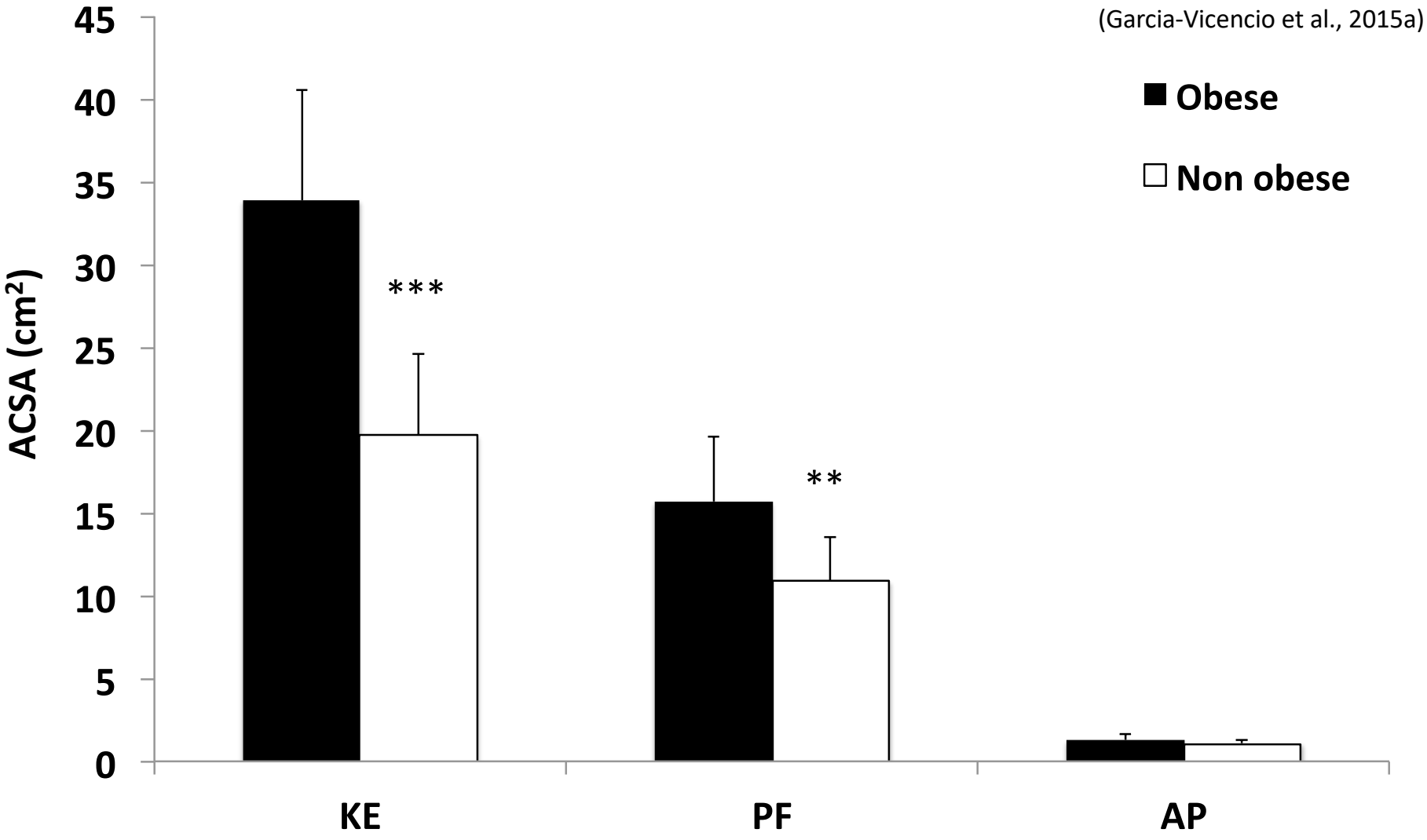


Effects of youth obesity on force production



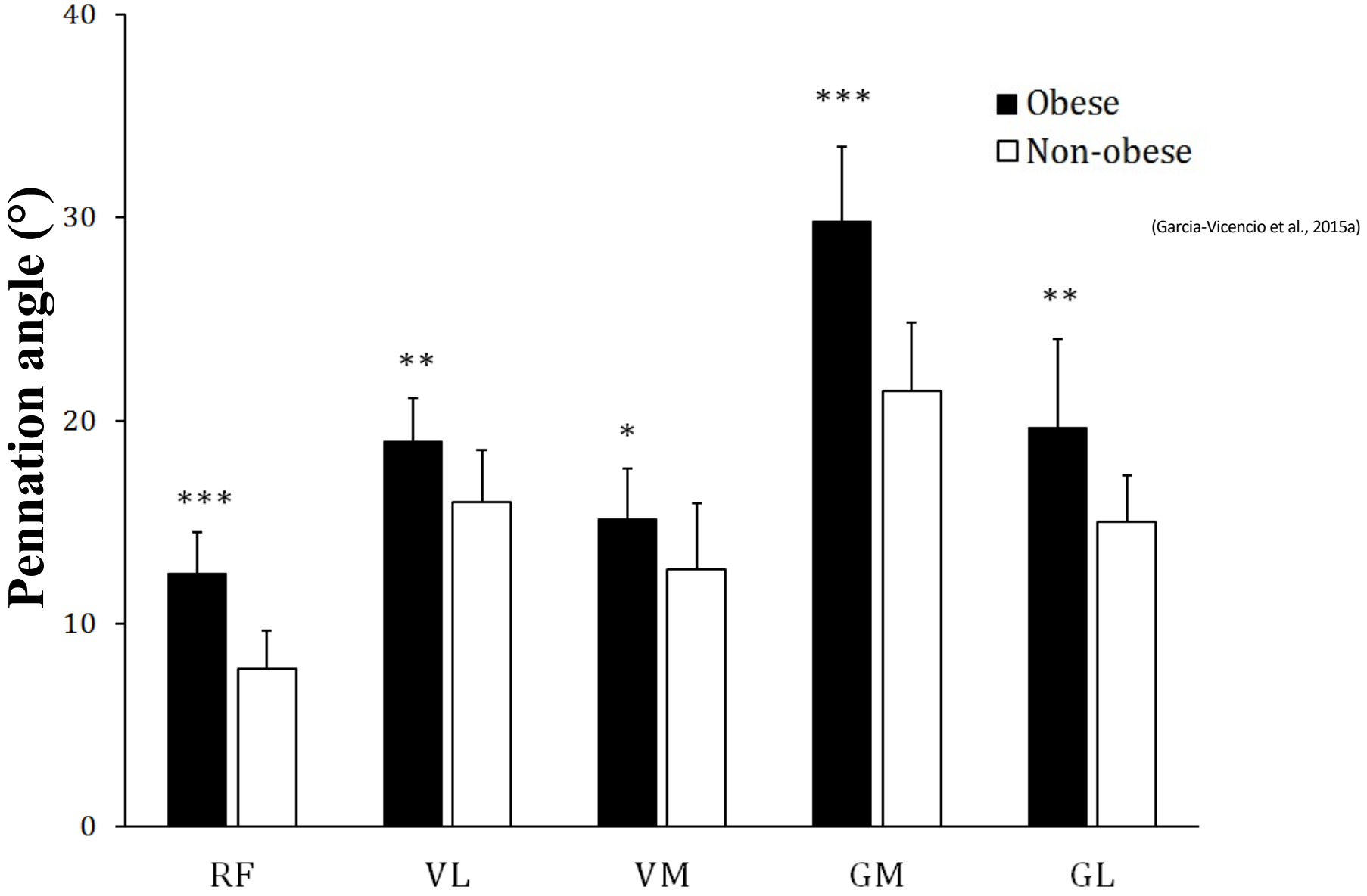
Increased force in obese adolescents (Garcia-Vicencio et al., 2015a)

Effects of youth obesity on force production



Muscle hypertrophy in the weight bearing muscles in obese girls

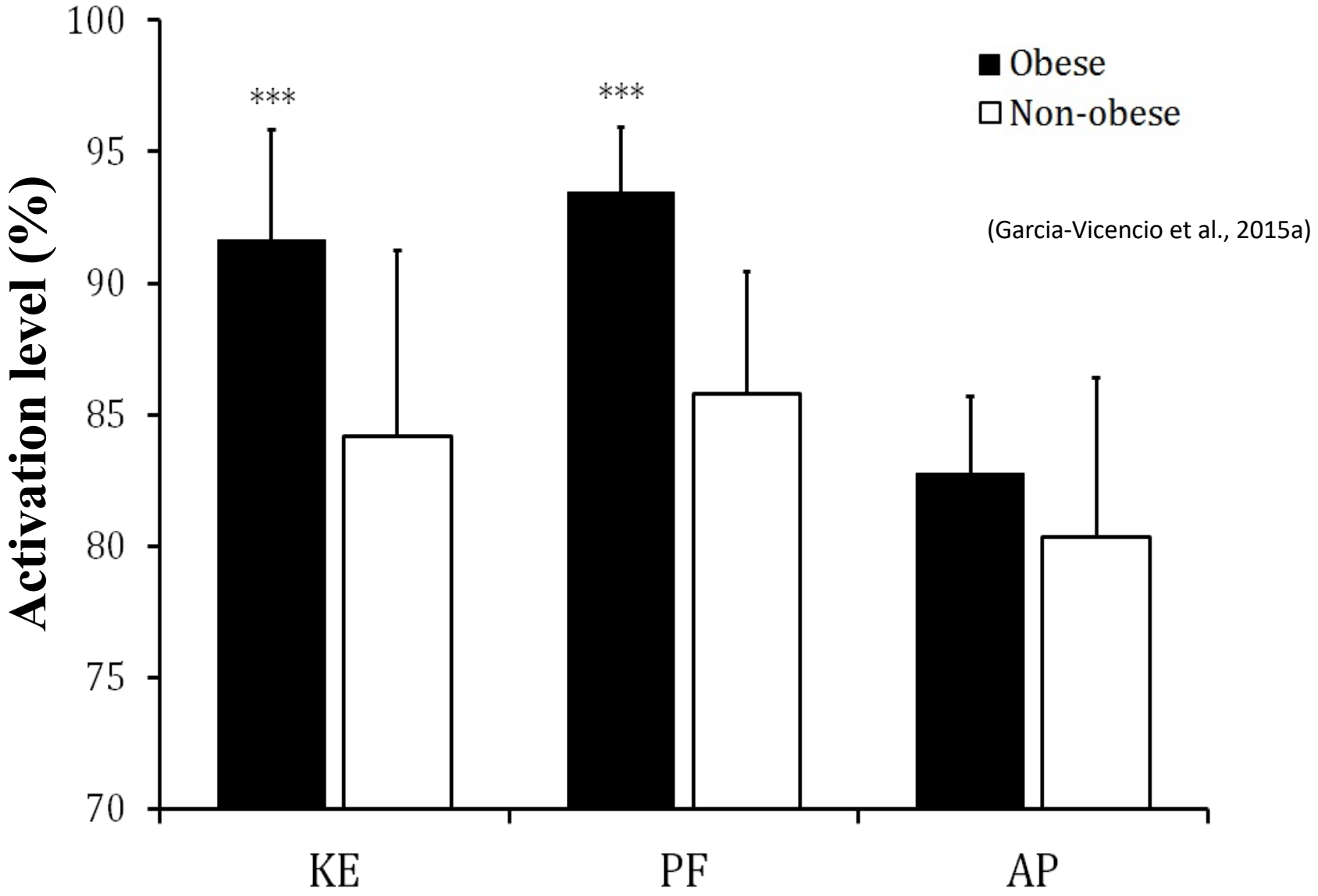
Effects of youth obesity on force production



(Garcia-Vicencio et al., 2015a)

Increased pennation angle in obese girls

Effects of youth obesity on force production



(Garcia-Vicencio et al., 2015a)

Increased activation level in obese girls

Effects of youth obesity on force production

In obese adolescent girls:

- ✓ **Hypertrophy**
- ✓ **Increased pennation angle**
- ✓ **Increased activation level**
- ✓ **Adaptation restricted to muscles involved in weight bearing**

=

!!

Overweight = training stimulus. Neuromuscular consequence of weight loss ?

Effects of youth obesity on force production

Weight loss strategies

Lean mass preservation

Preservation of neuromuscular adaptations ?

+

Energy expenditure

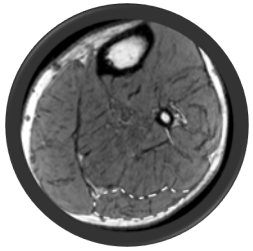
vs.

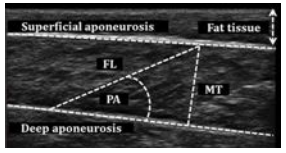
Energy expenditure

Hypothesis: Strength training (= artificial overload) could help preserving the neuromuscular adaptations to obesity.

Effects of youth obesity on force production

- ✓ **MVC force**
- ✓ **Activation level**
- ✓ **CSA**
- ✓ **Pennation angle**



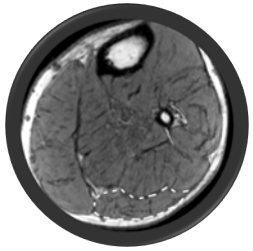


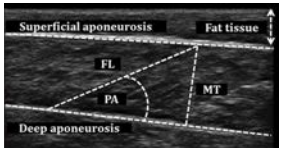
(n=12 obese girls)
2 sessions/week
Endurance

9-month physical activity program + controled energy intake

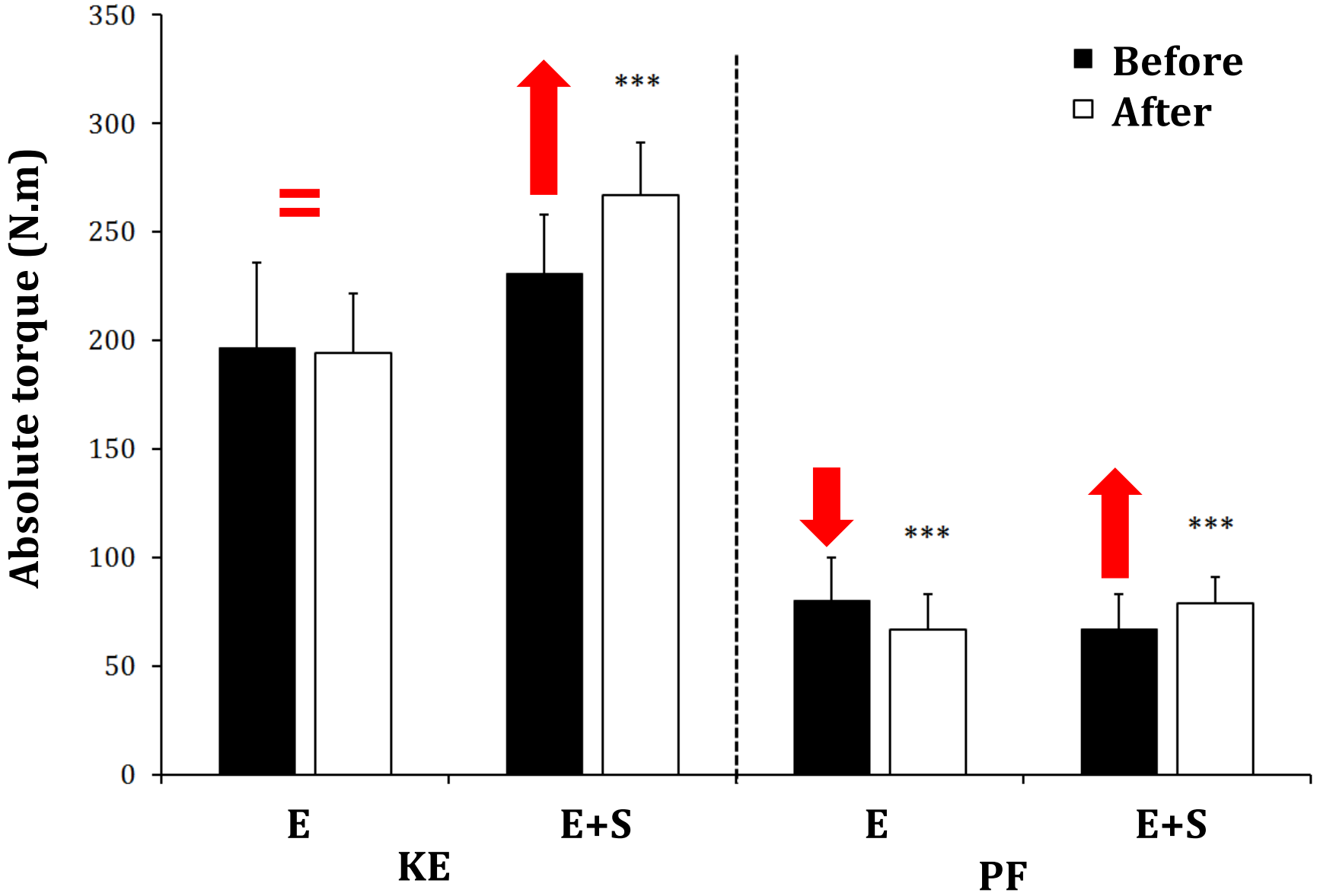
Endurance + Strength
(n=12 obese girls)
2 sessions/week

- ✓ **MVC force**
- ✓ **Activation level**
- ✓ **CSA**
- ✓ **Pennation angle**



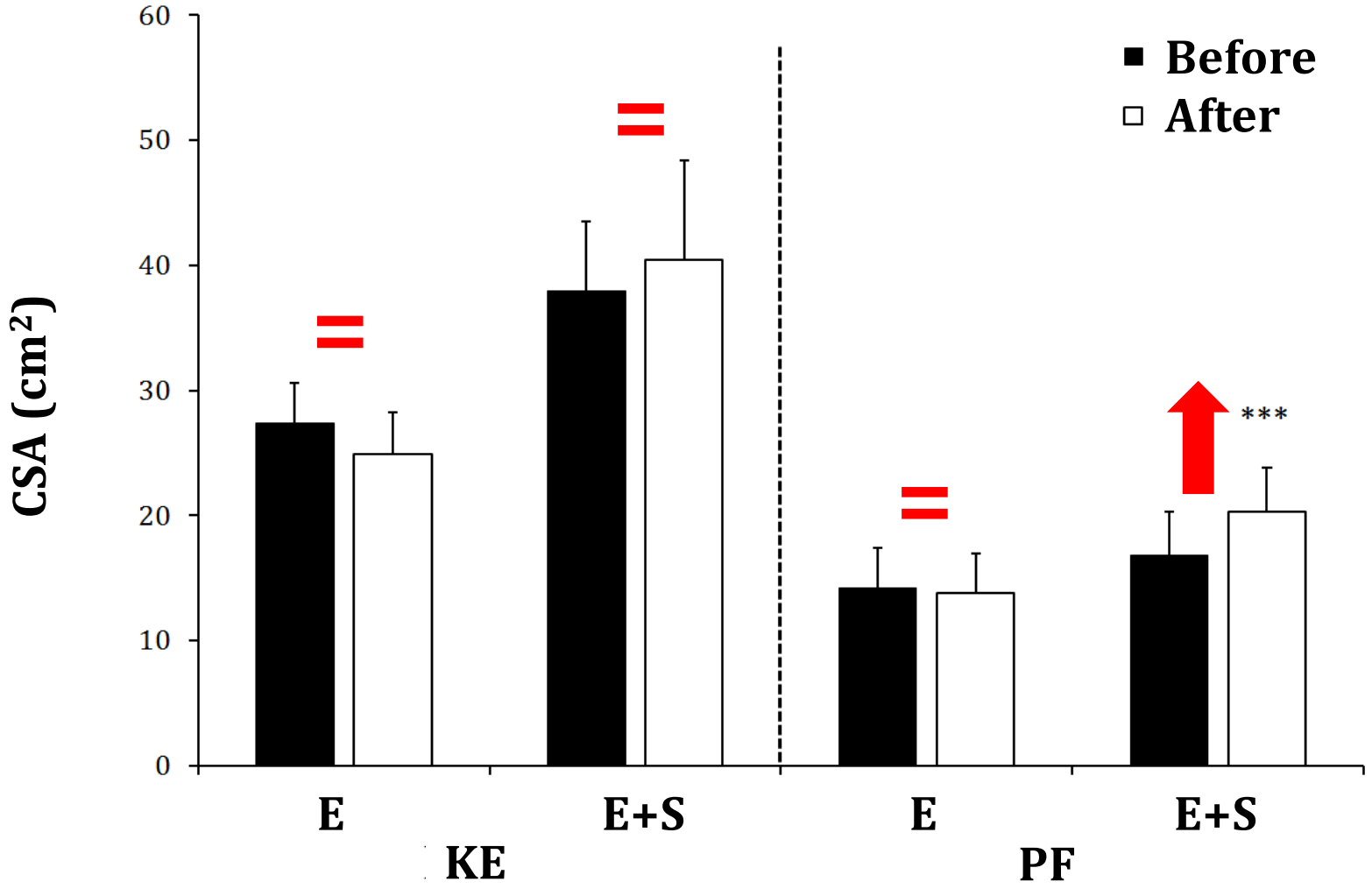


Effects of youth obesity on force production



(Garcia-Vicencio et al., unpublished data)

Effects of youth obesity on force production



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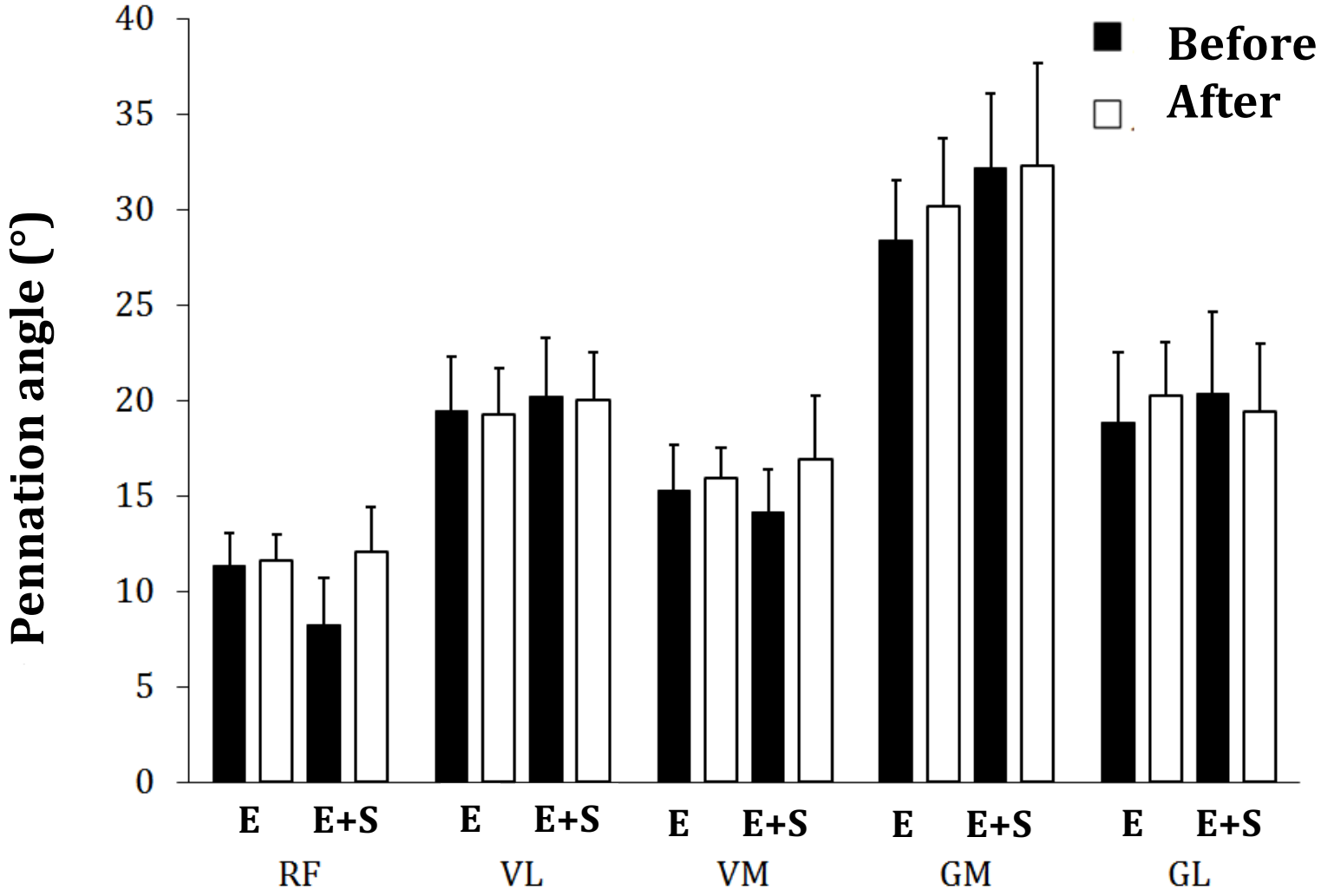

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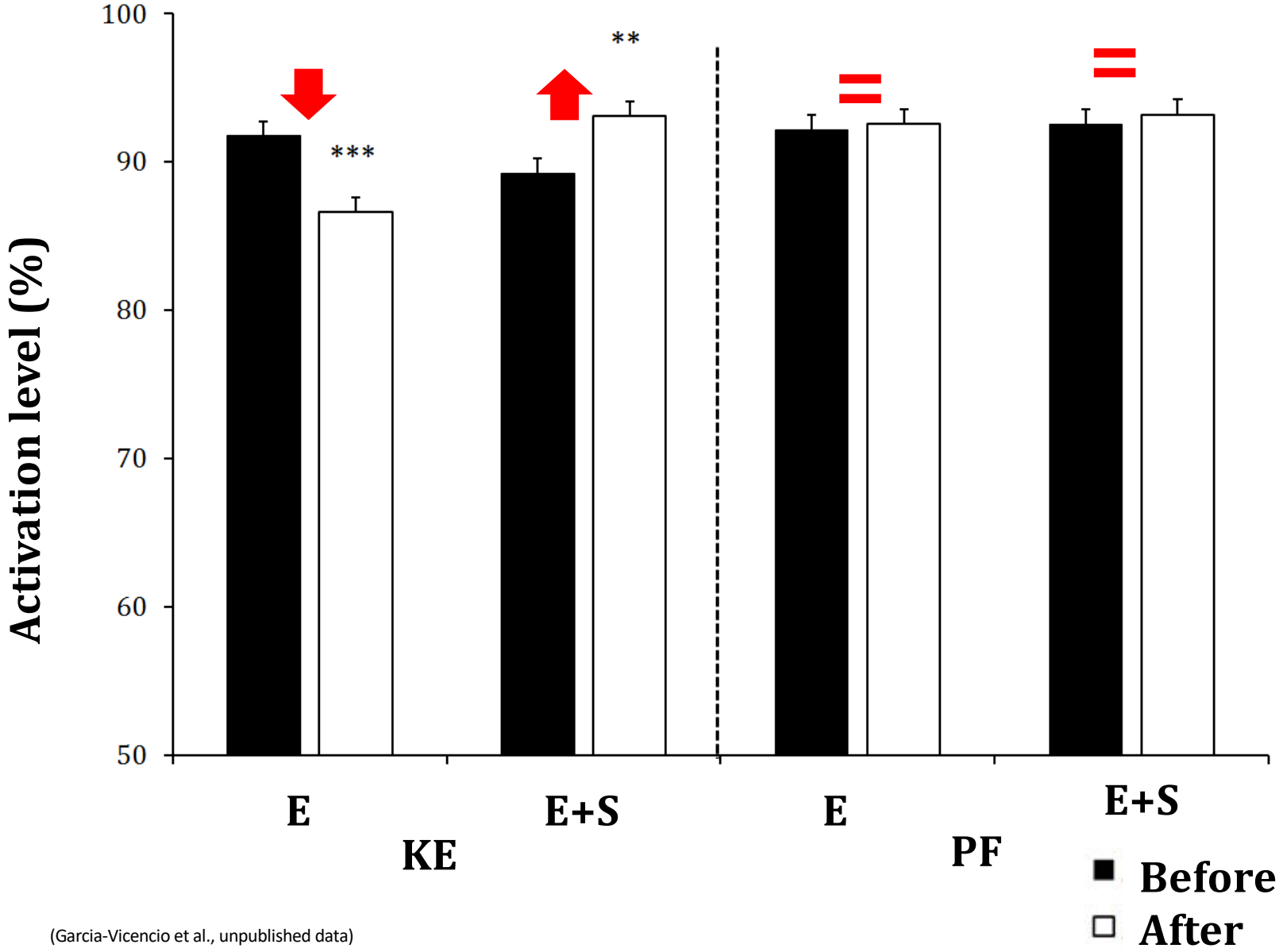
Effects of youth obesity on force production



(Garcia-Vicencio et al., unpublished data)

Effects of youth obesity on force production

Differential effects of PA programs on neuromuscular function:

- ✓ Maintenance/improvement of neuromuscular properties with endurance + strength training

- ✓ Maintenance/decrease of neuromuscular properties with endurance training

Artificial loading as a compensation for weight loss.

Bariatric surgery

Bariatric surgery as an acute unloading model

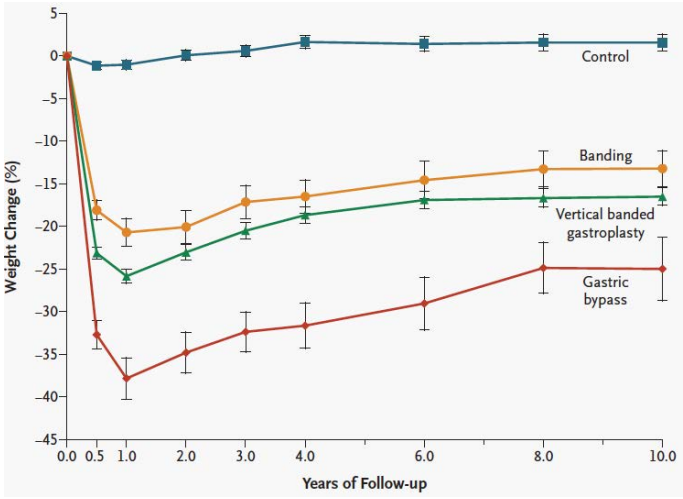
- **Force loss etiology ?**

→ **mass *vs.* nervous factors & architecture**

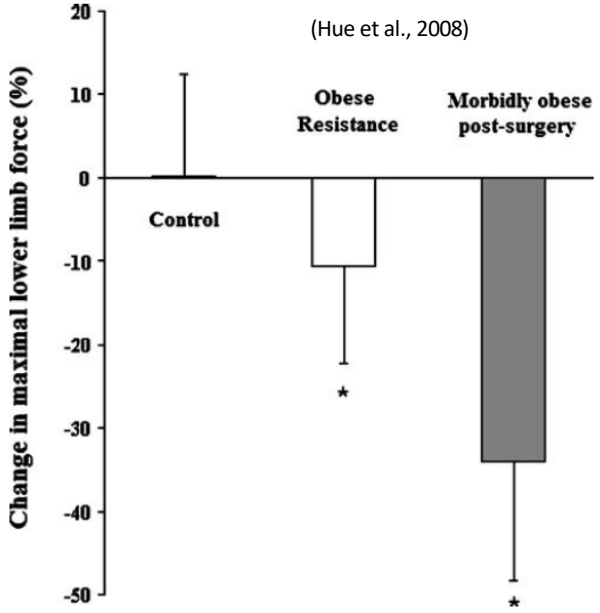
- **Counter-measures ?**

→ **Physical activity modality ?**

(Sjöström et al., 2004)



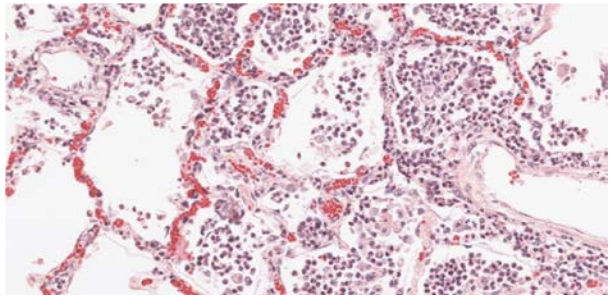
(Hue et al., 2008)



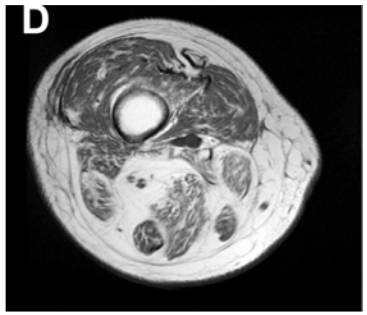
Influence of obesity-related diseases ?

Healthy *vs.* non-healthy obese ?

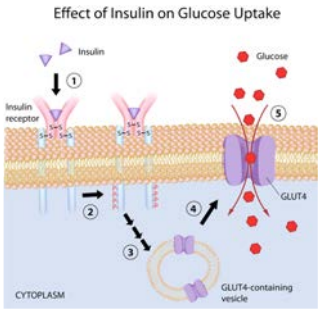
Obesity-related disorders



Low-grade inflammation



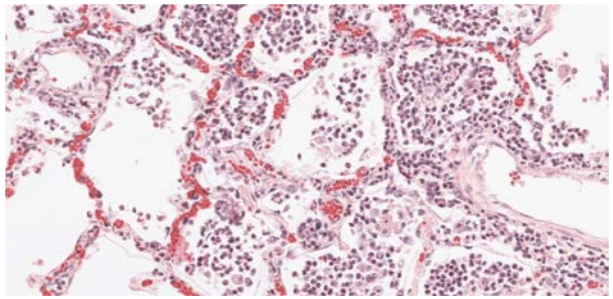
Fat infiltration

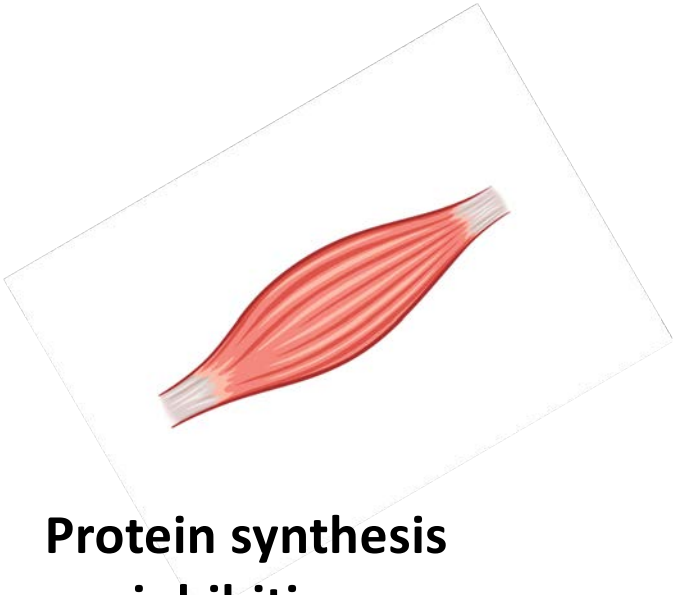


Type II diabetes

Influence of obesity-related diseases ?

Low-grade inflammation



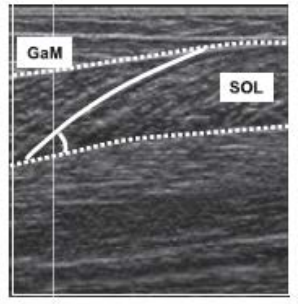


Protein synthesis inhibition

(Guillet et al., 2012)

Nervous inhibition ?

(Dousset et al., 2007)

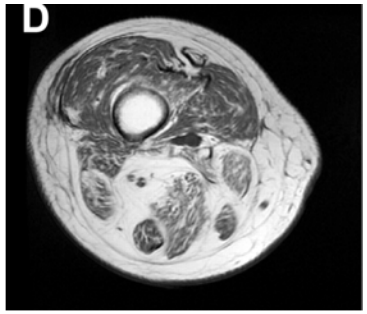


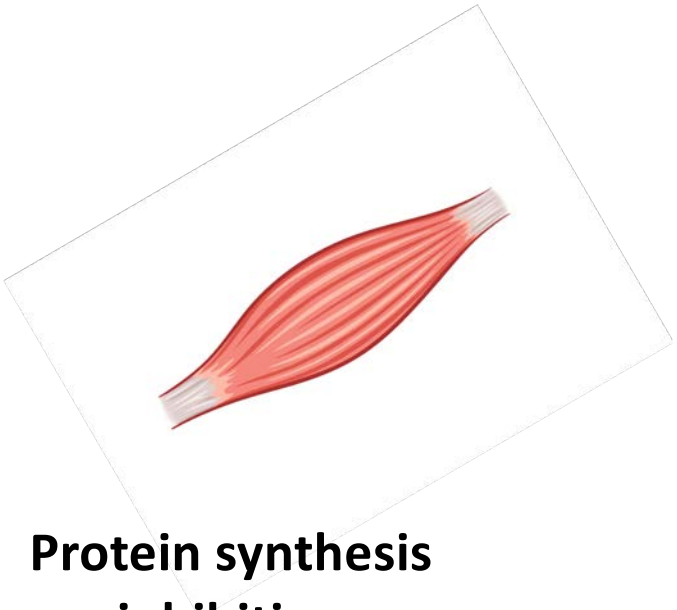
Architecture modification ?

(Ishikawa et al., 2006)

Influence of obesity-related diseases ?

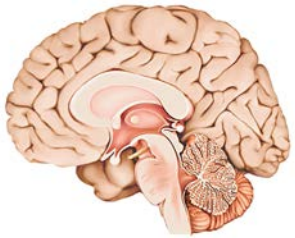
Fat infiltration





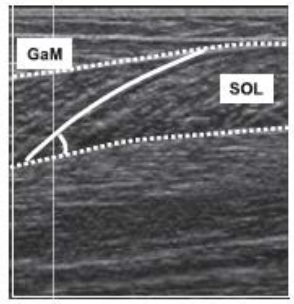
Protein synthesis inhibition

(Guillet et al., 2012)



Nervous inhibition ?

(Yoshida et al., 2012)



Architecture modification ?

(Rahemi et al., 2015)

Influence of obesity-related diseases ?

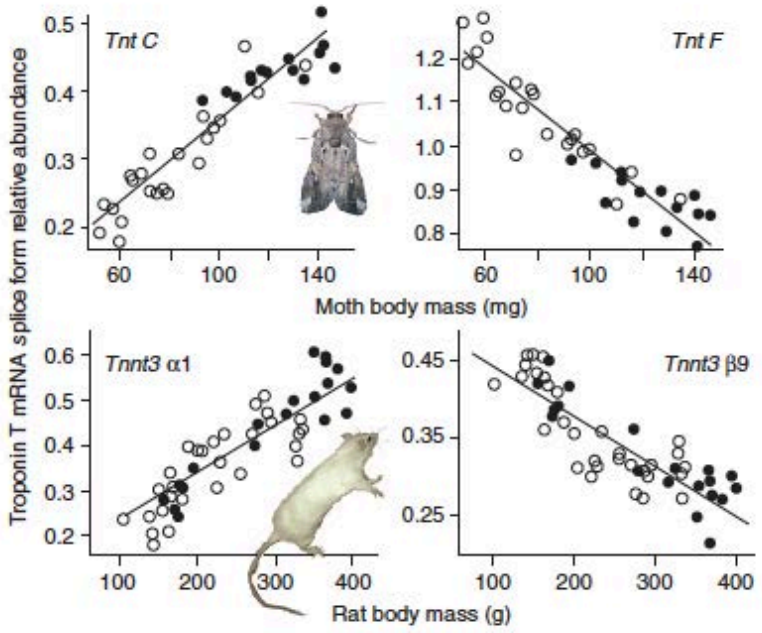
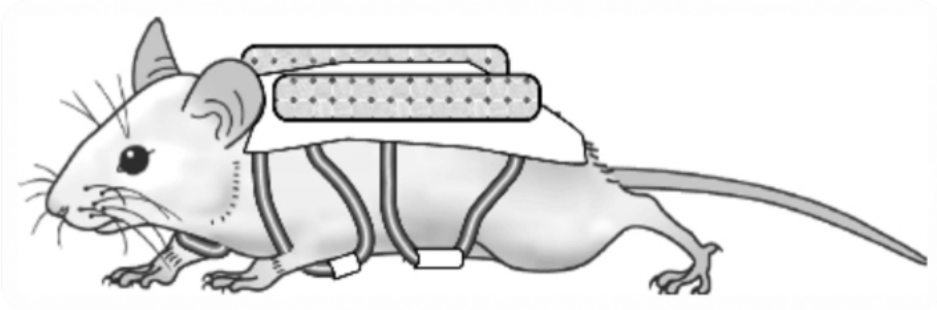


Fig. 7. Comparison of body weight-dependent *troponin T* alternative splicing in insects and mammals. Insects [upper panels; graphs are modified from data originally published in Marden et al. (Marden et al., 2008)] and mammals (lower panels; data from this study) show very similar body weight-dependent reaction norms for the troponin T mRNA splice form profile. In both taxa the response is identical for growth-related changes in body mass (open circles) and experimental weight loading (filled circles). There is not a direct homology of the exon structure of the alternative troponin T mRNA transcripts for which relative abundance is shown here; precisely how these molecular variations affect function in either taxa remains to be determined.

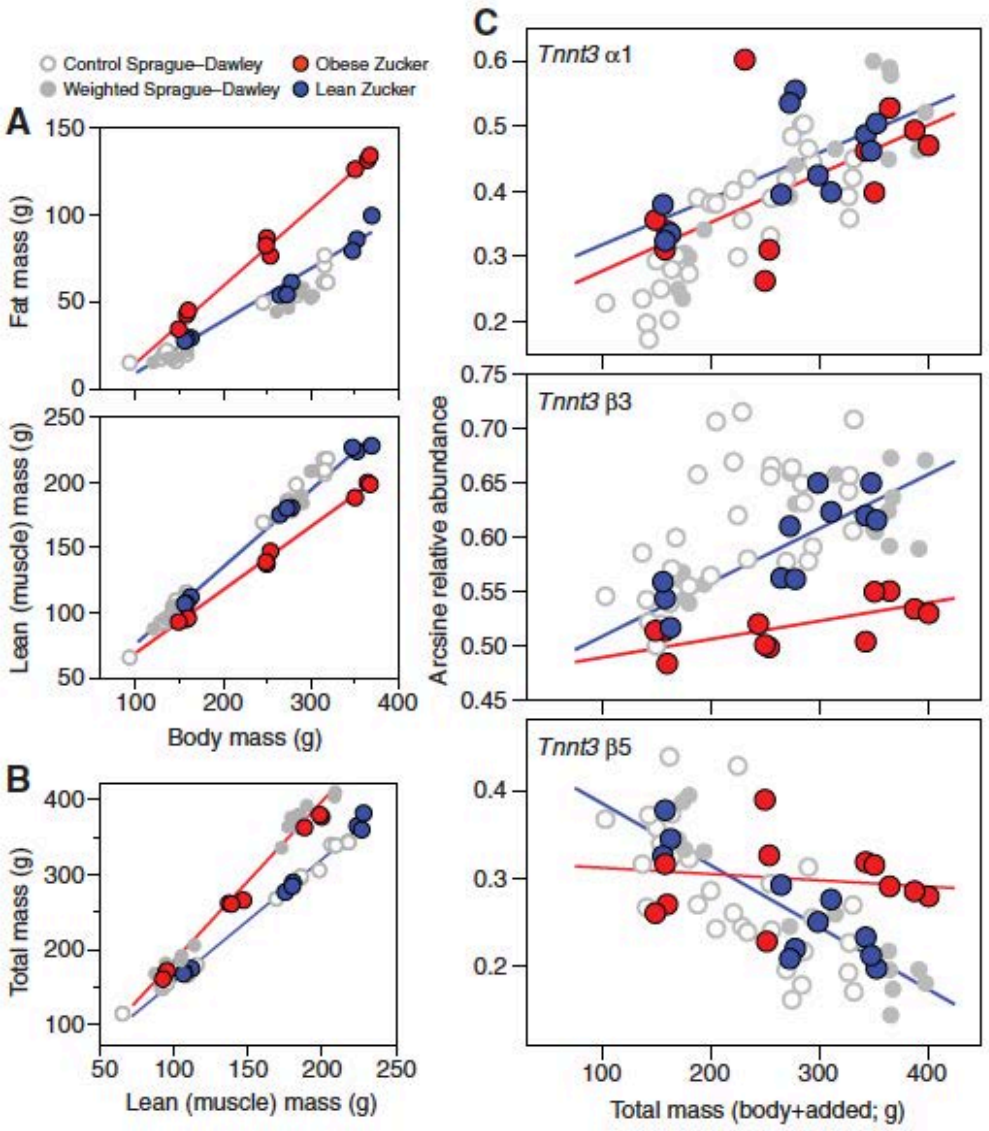
(Schilder et al., 2011)



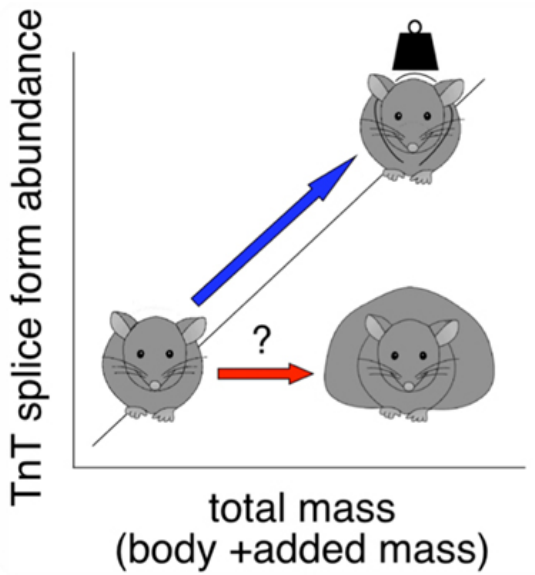
Artificial loading paradigms

Body-weight « sensing » mechanisms

Influence of obesity-related diseases ?



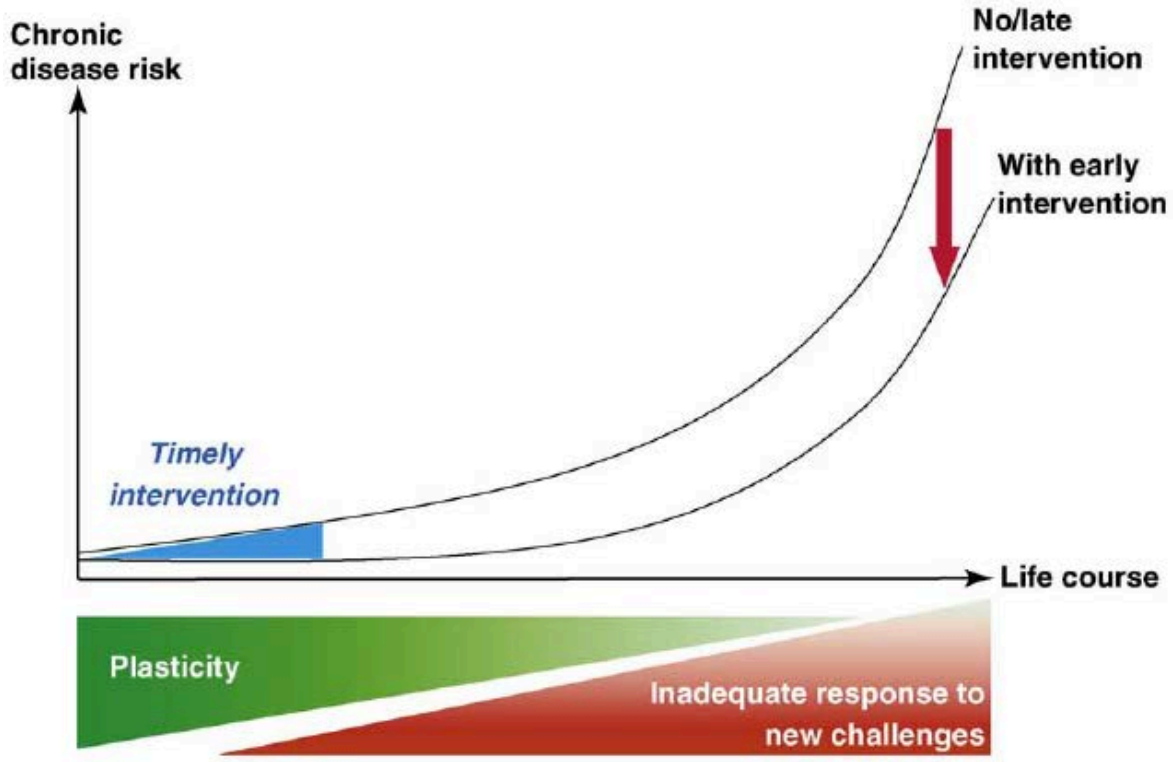
(Schilder et al., 2011)



Inability to adjust the molecular composition of muscles to the increased body weight.

Influence of age ?

Youth *vs.* adult *vs.* old obese ?

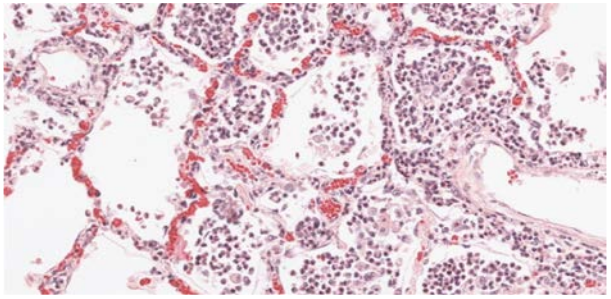


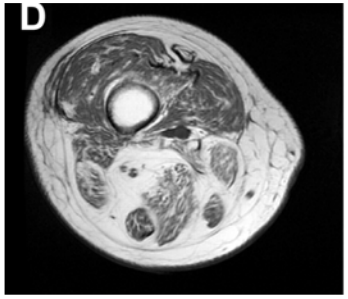
(Godfrey et al., 2010)

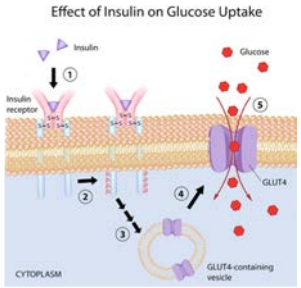
Healthy *vs.* non-healthy obese ?

Young *vs.* old obese ?

Neuromuscular function – human and animal models







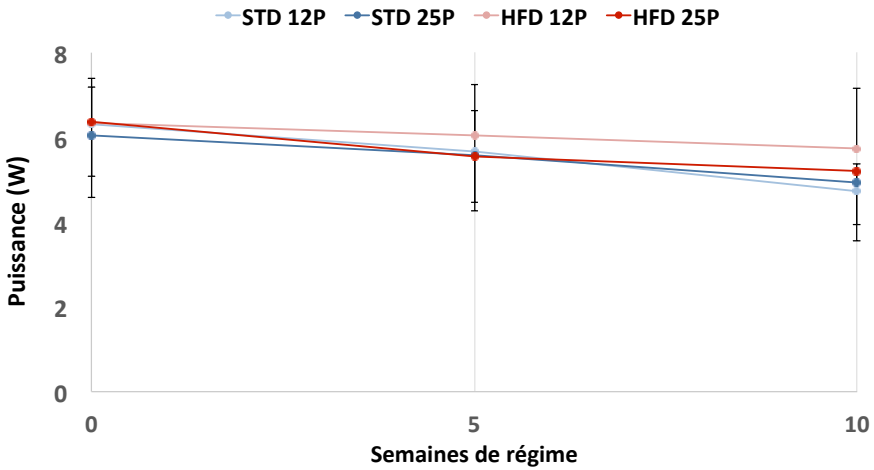
Effect of age

Ageing & obesity

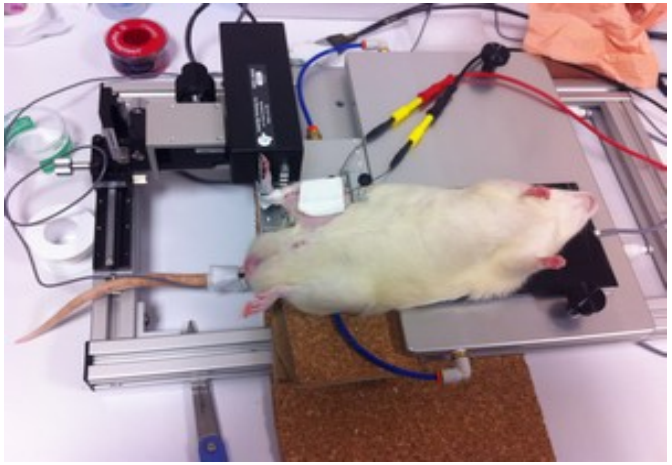
No adaptation to obesity during ageing ?

After 10 weeks of high-fat diet, with conventional or increased protein intake:

- ✓ **Increased body mass**
- ✓ **Unchanged muscle power**
- ✓ **Unchanged muscle force**



(Carayon et al., pilot data)



What are the effects of youth obesity on neuromuscular fatigue ?

Effects of youth obesity on fatigability

Initial force level

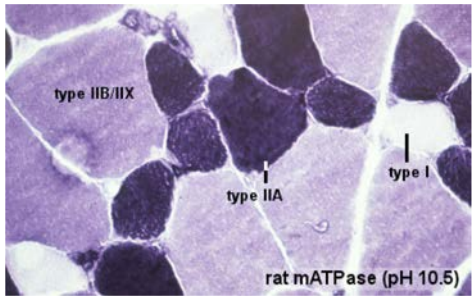
Myotypology

Men/Women
Young/Old
Children/adults

(Hicks et al., 2001; Hunter et al., 2004, Ratel et al., 2015, Piponnier et al. 2018)

Greater proportion of type II fibers

(Wade et al., 1990; Kriketos et al., 1997)



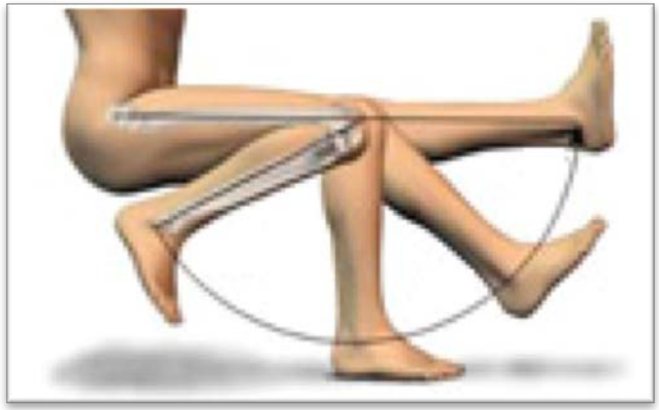
Influence of the initial force level on the obese/non obese fatigue difference ?

Hypothesis: Increased peripheral fatigue and reduced central fatigue in obese youth. Smaller difference when initial force level taken into account.

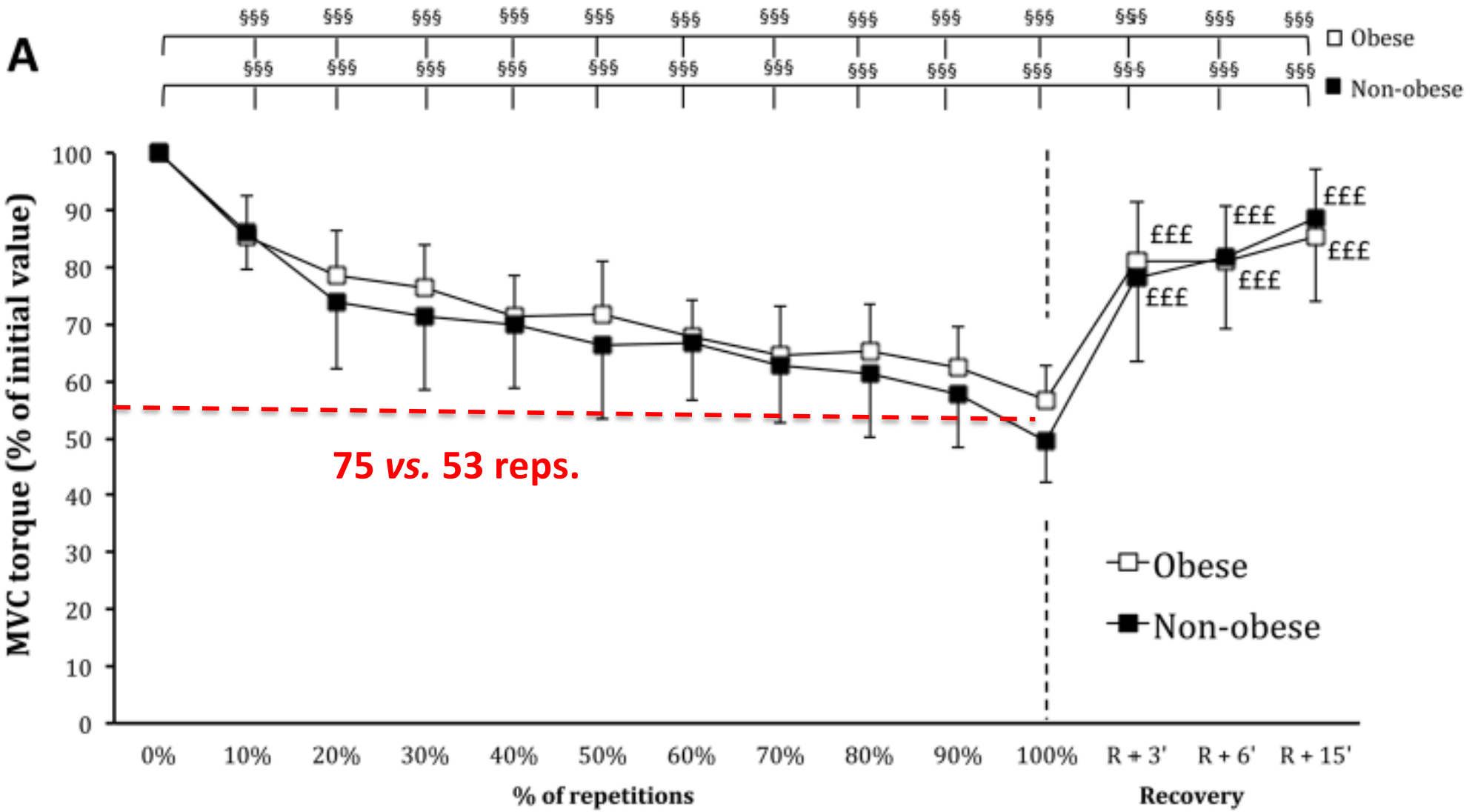
Effects of youth obesity on fatigability

Hypothesis: Increased peripheral fatigue and reduced central fatigue in obese youth. Smaller difference when initial force level taken into account.

- ✓ **Participants: Obese vs. non obese adolescent girls, comparable PA & maturation levels**
- ✓ **Exercise: 5-s MVCs (R = 10 s) repeated until MVC reduction = 45%**
- ✓ **Main outcomes: number of repetitions, KE maximal voluntary force (MVC) & maximal voluntary activation level (AL), twitch amplitude.**



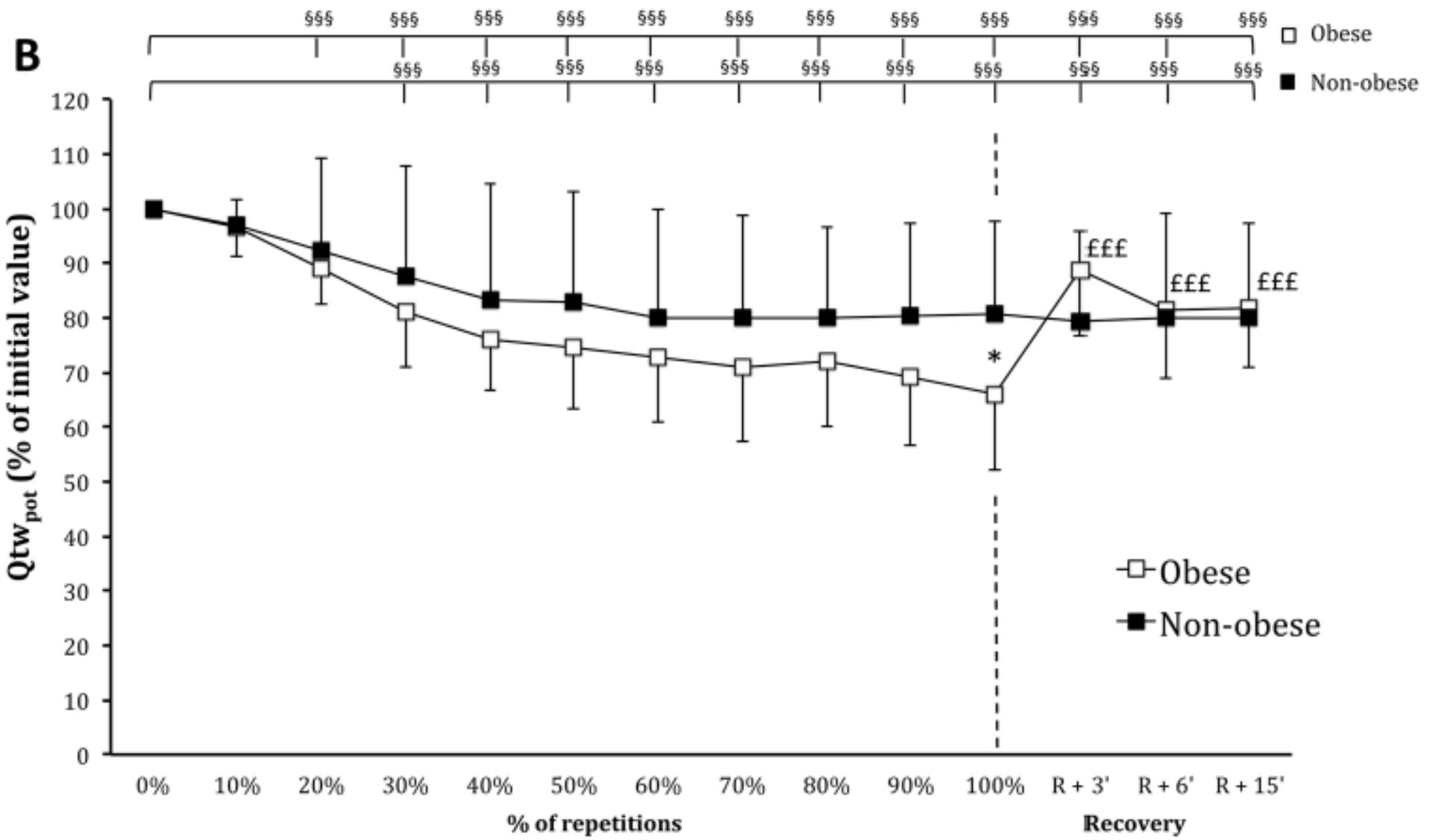
Effects of youth obesity on fatigability



(Garcia-Vicencio et al., 2015b)

Effects of youth obesity on fatigability

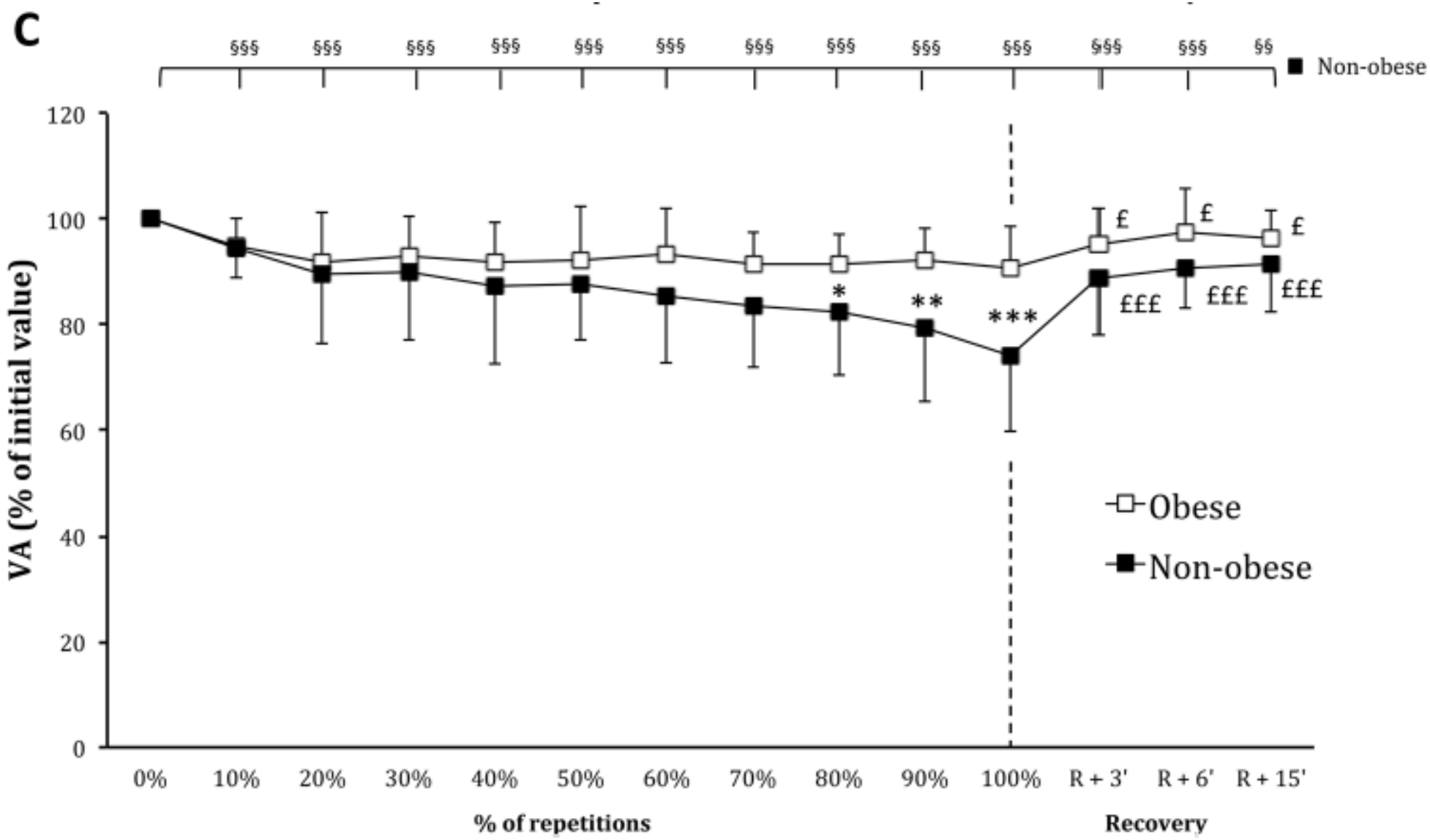
(Garcia-Vicencio et al., 2015b)



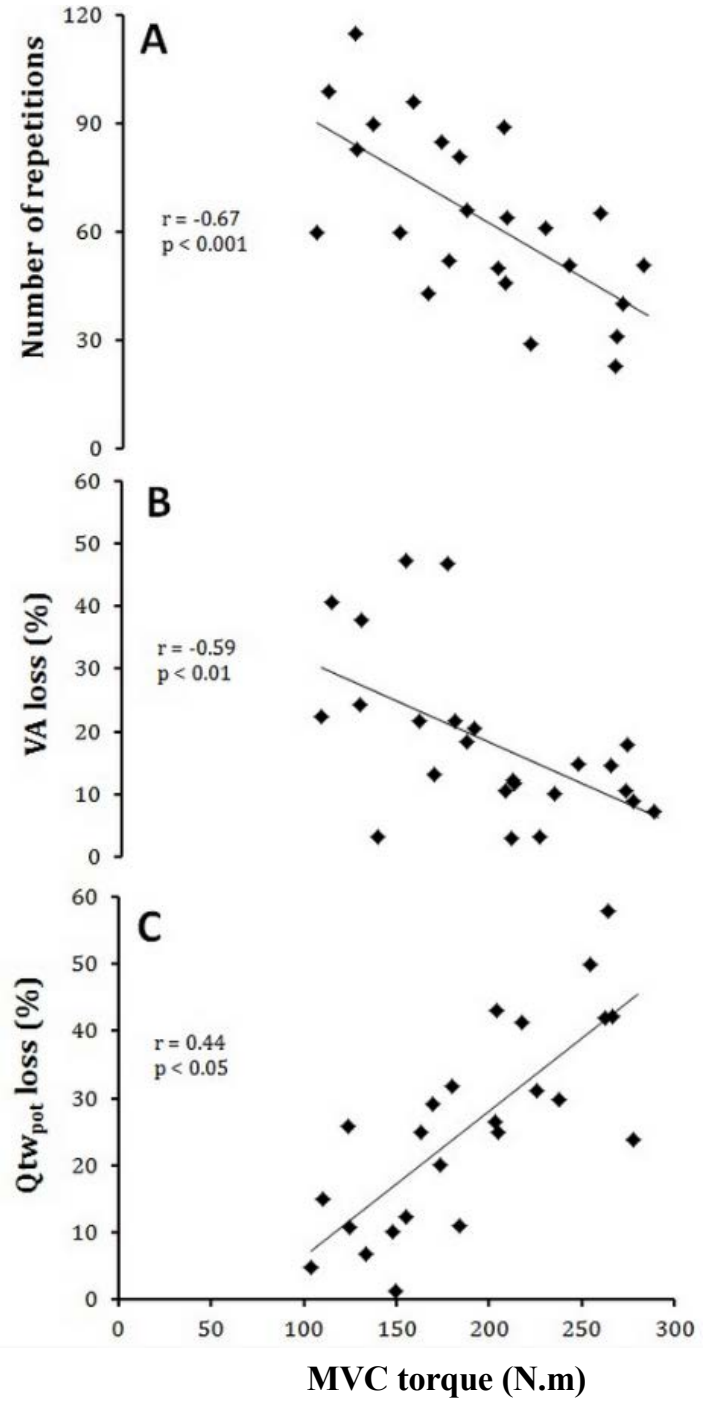
Increased peripheral fatigue in obese girls

Effects of youth obesity on fatigability

(Garcia-Vicencio et al., 2015b)



Lower central fatigue in obese girls

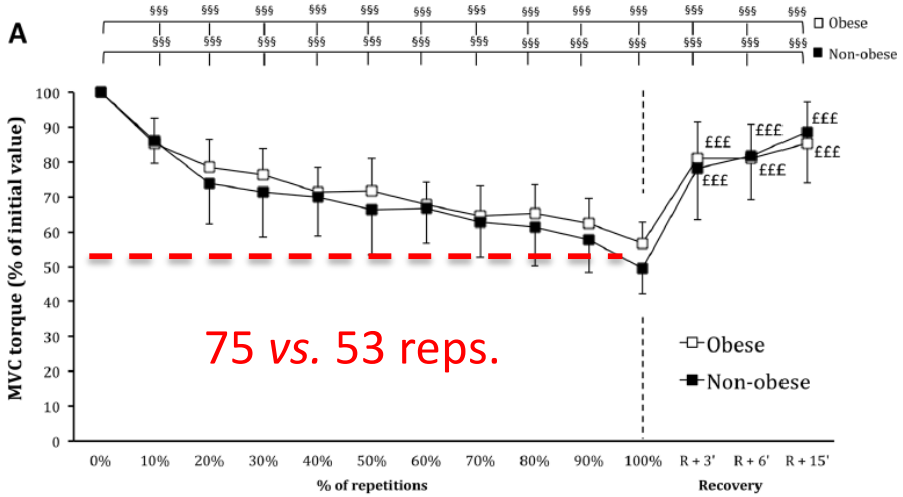


(Garcia-Vicencio et al., 2015b)

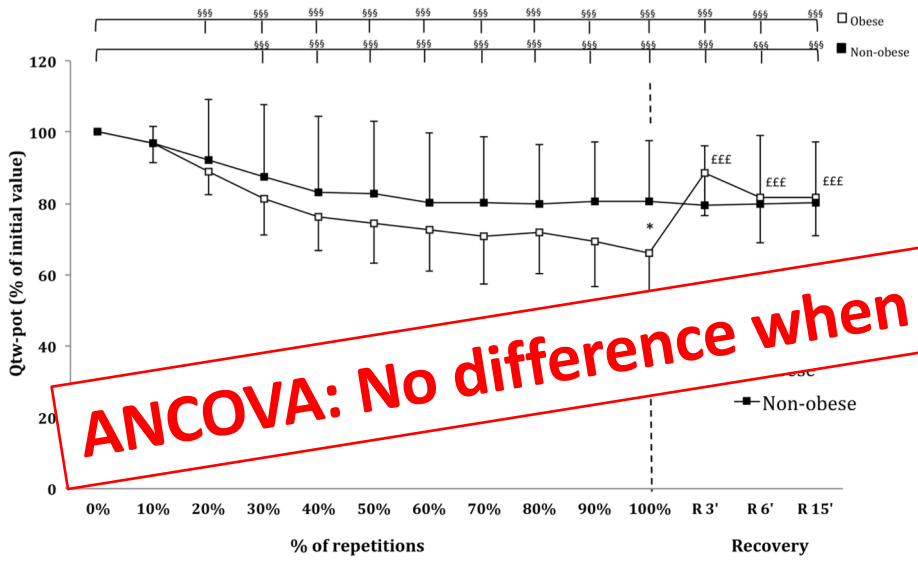
Effects of youth obesity on fatigability

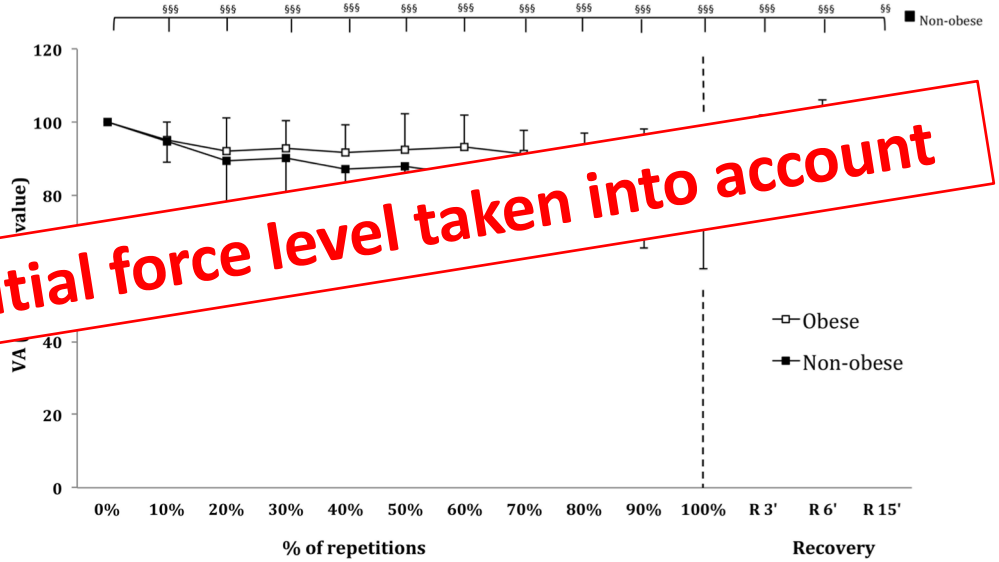
At comparable exhaustion level, in obese adolescent girls:

- ✓ **No central fatigue**
- ✓ **Increased peripheral fatigue**



(Garcia-Vicencio et al., 2015b)





ANCOVA: No difference when initial force level taken into account

Effects of youth obesity on force production

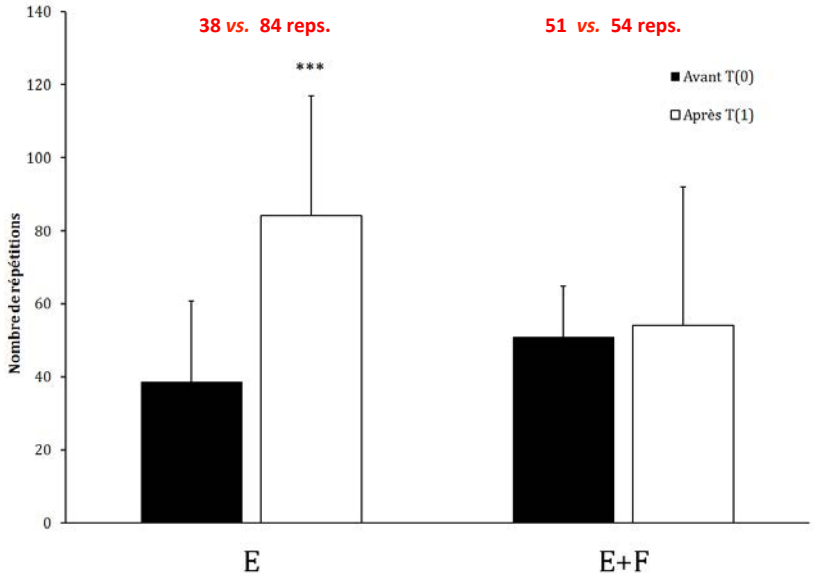
Differential effects of PA programs on neuromuscular fatigue ?

- ✓ **Improved fatigue resistance with endurance training ?**
- ✓ **Altered fatigue resistance with endurance + resistance training ?**

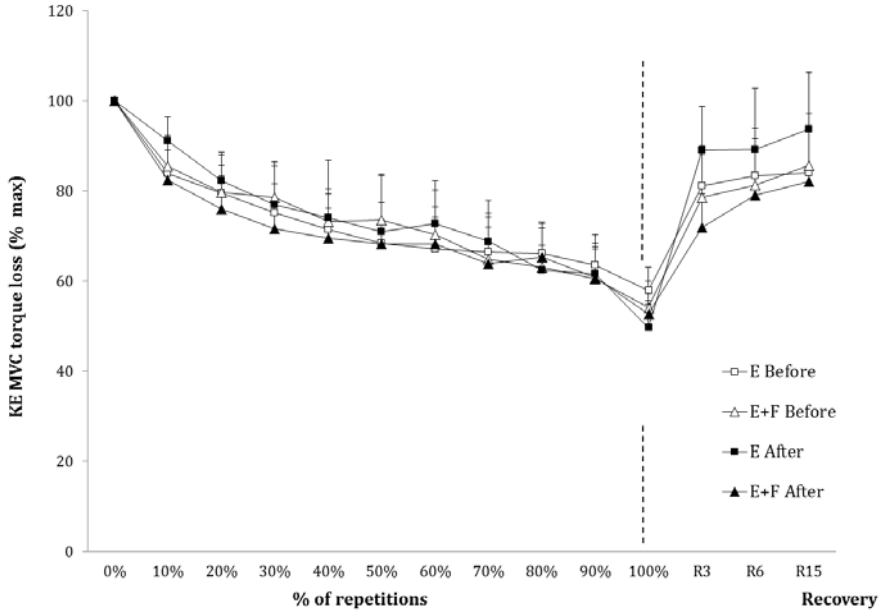
Effects of youth obesity

Differential effects of PA programs:

- ✓ Increased fatigue resistance after endurance training
- ✓ Unchanged fatigability after E + S but higher force level → relative improvement



(Garcia-Vicencio et al., unpublished data)

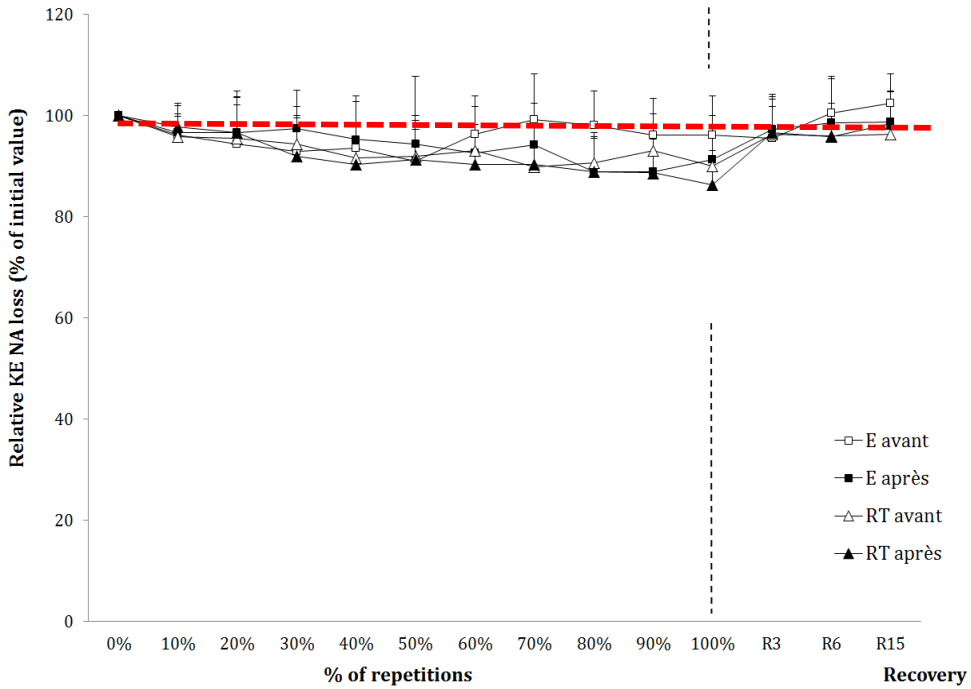


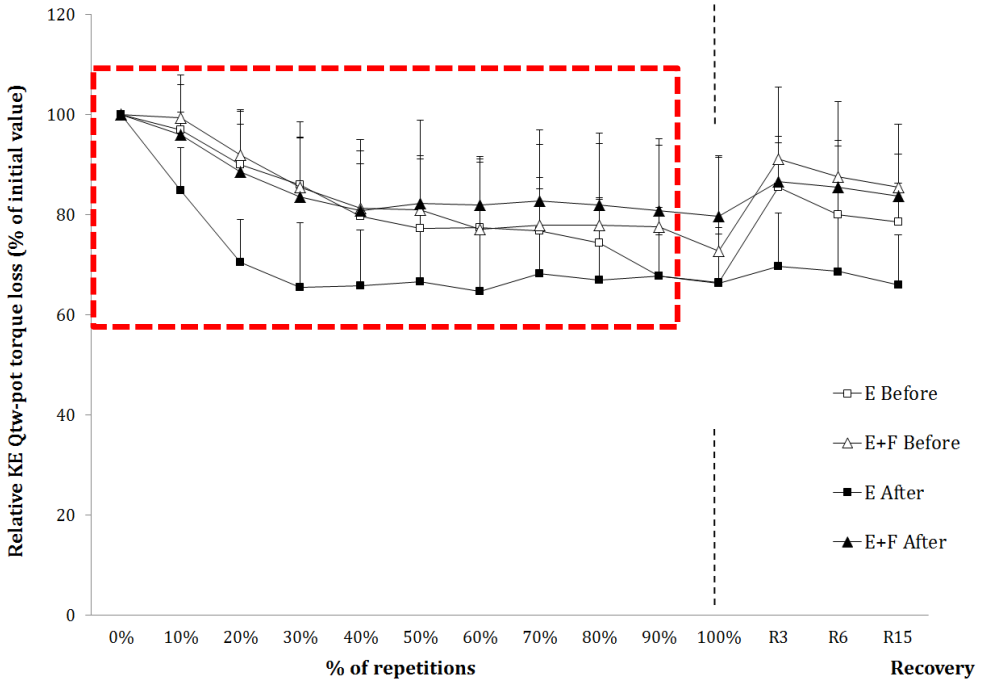
Differential effects of PA programs:

- ✓ No change in central fatigue
- ✓ Increased peripheral fatigue after E

Increased tolerance to peripheral fatigue ?

(Zghal et al., 2015)

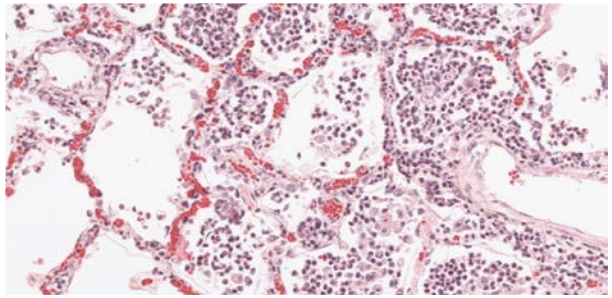




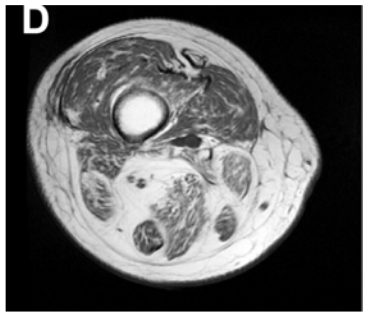
Influence of obesity-related diseases ?

Healthy *vs.* non-healthy obese ?

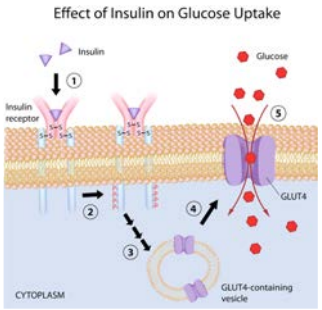
Obesity-related disorders



Low-grade inflammation



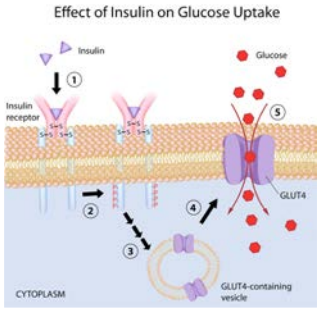
Fat infiltration

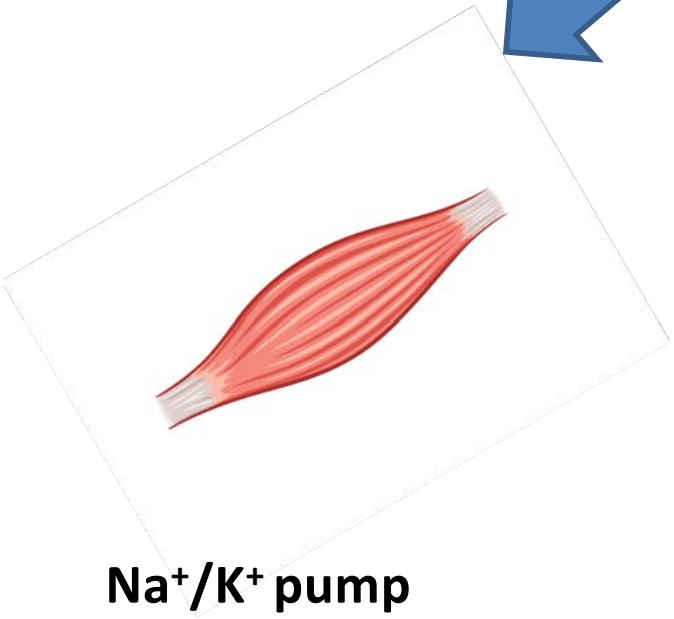


Type II diabetes

Influence of obesity-related diseases ?

Insulin resistance



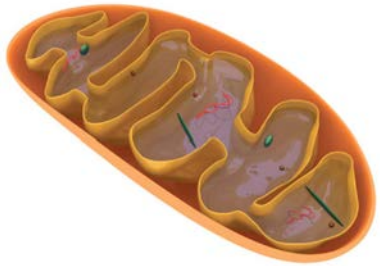


Na^+/K^+ pump
E-C coupling
Muscle typology

(Orlando et al., 2015)
(Houmard et al., 1999)

Blood perfusion

(Petrosky et al., 1999)



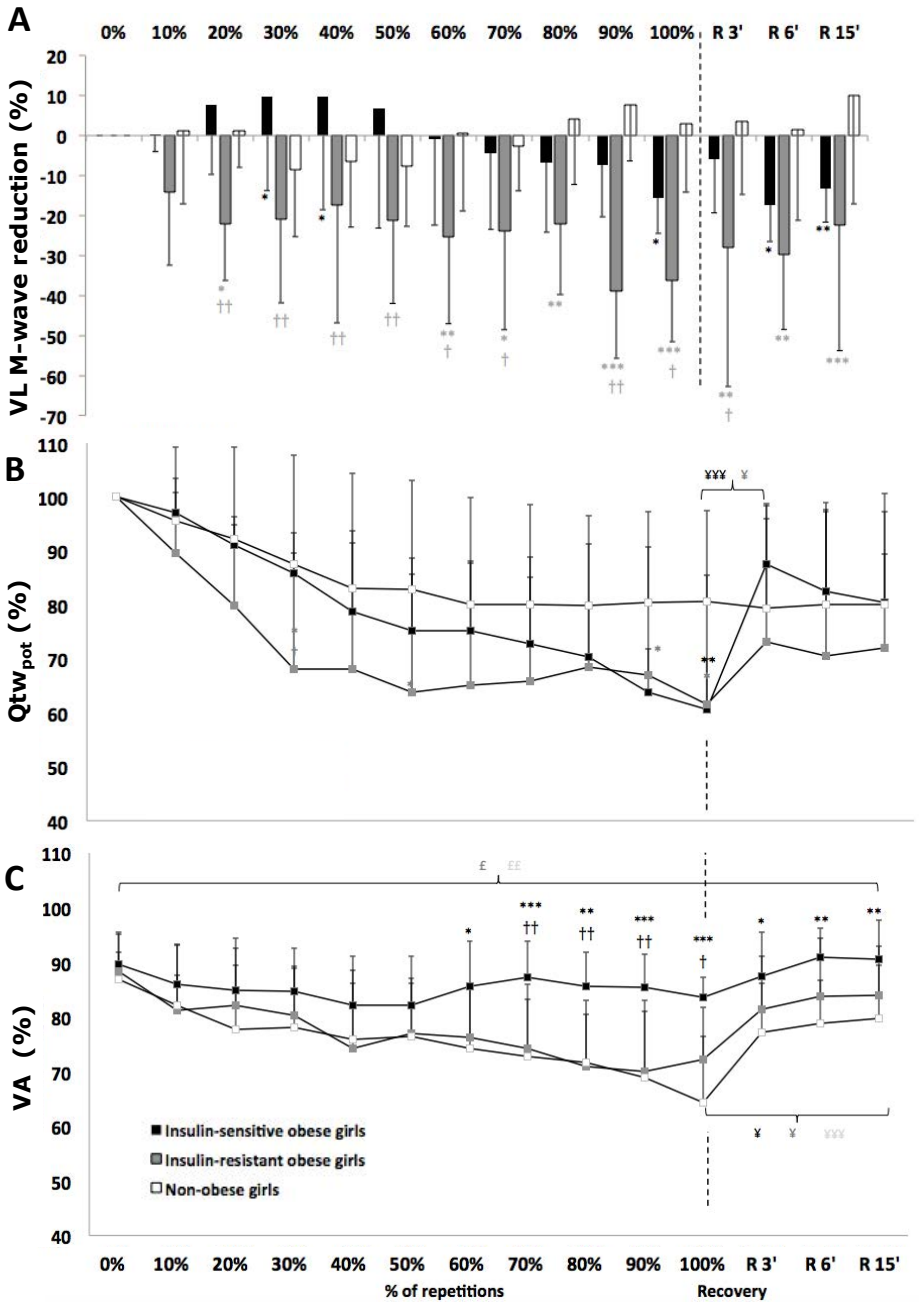
Mitochondrial function

(Slattery et al., 2014)

Influence of insulin resistance

For a comparable exhaustion level, in insulin-resistant obese girls:

- ✓ **Early peripheral fatigue (M-wave alteration)**
- ✓ **Increased central fatigue**
- ✓ **Altered recovery**



(Faure et al., unpublished data)