



Title: Hypothalamic-pituitary-testicular axis response to sub-maximal aerobic exercise, in pre- and early- pubertal normal weight and obese boys

Authors:

George Paltoglou^{1,2}, Alexandra Avloniti³, Athanasios Chatzinikolaou³, Aimilia Mantzou², Charikleia Stefanaki¹, Maria Papagianni⁴, Ioannis G. Fatouros⁵, George Mastorakos¹.

Affiliations:

1. Endocrine Unit, "Aretaieion" Hospital, National and Kapodistrian University of Athens - Faculty of Medicine, Athens, Greece.
2. First Department of Pediatrics, "Aghia Sophia" Children's Hospital, National and Kapodistrian University of Athens - Faculty of Medicine, Athens, Greece.
3. Department of Physical Education and Sports Sciences, Democritus University of Thrace, Komotini, Greece.
4. Pediatric Endocrine Unit, Third Department of Pediatrics, Aristotle University of Thessaloniki, School of Medicine, "Hippokrateion" General Hospital of Thessaloniki, Thessaloniki, Greece.
5. Department of Physical Education and Sports Sciences, University of Thessaly, Trikala, Greece.

Introduction:

Puberty is a maturation period characterized by changes of the dynamically regulated HPG axis. Obesity in childhood and especially after the onset of puberty is a relatively hypogonadal state. Oxidative stress is a state of imbalance between pro- and anti-oxidation within the cell. Pro-oxidation refers to mitochondrial and non-mitochondrial mechanisms, which generate reactive oxygen and nitrogen species (RONS). Anti-oxidation refers to the adaptive activation of enzymatic and non-enzymatic mechanisms, which scavenge pro-oxidants and their products. Obese individuals present with increased pro-oxidation and decreased anti-oxidation as compared to normal-weight, even in childhood and in the transition to early puberty. A short bout of aerobic exercise represents a potent stimulus of energy substrate utilisation that leads to the activation of pro- and the recruitment of anti-oxidation, while also interfering with HPG axis dynamic equilibrium.

Objective:

To investigate a putative association of gonadotrophins and testosterone concentrations with the increase of anti-oxidant capacity in early puberty, ninety-two pre- and early pubertal normal-weight and obese boys were studied at baseline and after an acute bout of sub-maximal (70% VO₂max) aerobic exercise. The exercise bout was employed as a potent stimulus of energy substrate utilisation and a putative stimulus of testosterone.

Patients and Methods:

In total 120 male pupils were initially selected for this study. Exclusion criteria:
a) exercise additional to that included in the school time-table,
b) dietetic intervention in the six months preceding this study
c) medical history of other known chronic pathology.
Following inclusion, BMI z-score was calculated and normal-weight and obese subjects were selected. Then pubertal status was assessed. By combining both characteristics (weight and pubertal status) four groups of subjects were formed. VO₂max of the selected subjects was measured.

In total 92 normal-weight and obese subjects were called for a second visit (Table 1). Baseline blood sampling was performed followed by an acute bout of aerobic exercise on a stationary cycle ergometer until exhaustion at an intensity corresponding to 70% of VO₂max. Post exercise blood sampling was performed at the end of the exercise bout.

Results:

Figure 1:

FSH, LH and testosterone concentrations (mean±SE) at baseline (white bar) and post-exercise (shaded bar) in pre-pubertal (panels A, C and E, respectively) and early pubertal (panels B, D and F, respectively) normal weight and obese subjects.
* denotes significant difference (P<0.05) of post-exercise from the respective baseline concentrations;
+ denotes significant difference (P<0.05) between obese and respective normal weight subjects;
denotes significant difference (P<0.05) between early pubertal and respective pre-pubertal subjects.

Multiple regression analyses:

Multiple regression analysis revealed statistically significant linear regression of ΔLH with ΔTBARS concentrations, respectively (P<0.05; r= -0.41).

Forward stepwise regression analysis:

Potential predictors of post exercise concentrations of pro- and the anti-oxidation markers (dependent variable) among baseline BMI z-score, waist to height ratio, waist to hip ratio, VO₂max, FSH, LH and testosterone (independent variables) Baseline LH concentrations were the best positive predictors (P<0.05, b= 0.41) for the post-exercise TAC concentrations.

Conclusions:

1. An acute bout of aerobic exercise at 70% VO₂max resulted in specific HPG axis changes in pre- and early pubertal boys.
2. In pre-pubertal boys baseline LH correlated positively with anti-oxidation, while in early pubertal normal-weight boys baseline testosterone correlated with anti-oxidation, suggesting a direct and/or indirect role of HPG maturation during puberty in anti-oxidation.
3. It appears that the maturation of the HPG axis during puberty in boys is positively associated with accentuation of anti-oxidation.
4. This association is stronger with the LH and testosterone components of the HPG axis in this cohort of pre- and early pubertal boys.
5. Further studies could investigate the potential beneficial clinical effect of these hormones in the development of anti-oxidative defensive mechanisms in specific pathologic entities.

Table 1: Anthropometric data of subjects. Measurements were compared among groups by employing factors ANOVA. Significant main effects were revealed by the Unequal N HSD post-hoc test. Statistical significance was set at (P<0.05). + denotes significant difference between obese and respective normal weight subjects. # denotes significant difference between early pubertal and respective pre-pubertal subjects.

	Pre-pubertal (n=47)		Early pubertal (n=45)	
	Normal weight (n=34)	Obese (n=13)	Normal weight (n=31)	Obese (n=14)
Age (yrs)	10.32±0.24	10.43±0.38	11.53±0.22#	11.71±0.33#
Height (m)	1.43±0.03	1.38±0.04	1.48±0.02	1.43±0.05
Weight (kg)	37.24±2.24	55.74±3.86 +	45.57±2.23	61.91±2.63 +
BMI z-score	0.16±0.15	2.62±0.34 +	0.22±0.18	2.91±0.18 +
VO ₂ max (l/min.)	1.88±0.02	1.85±0.03	1.92±0.02	1.72±0.02 +

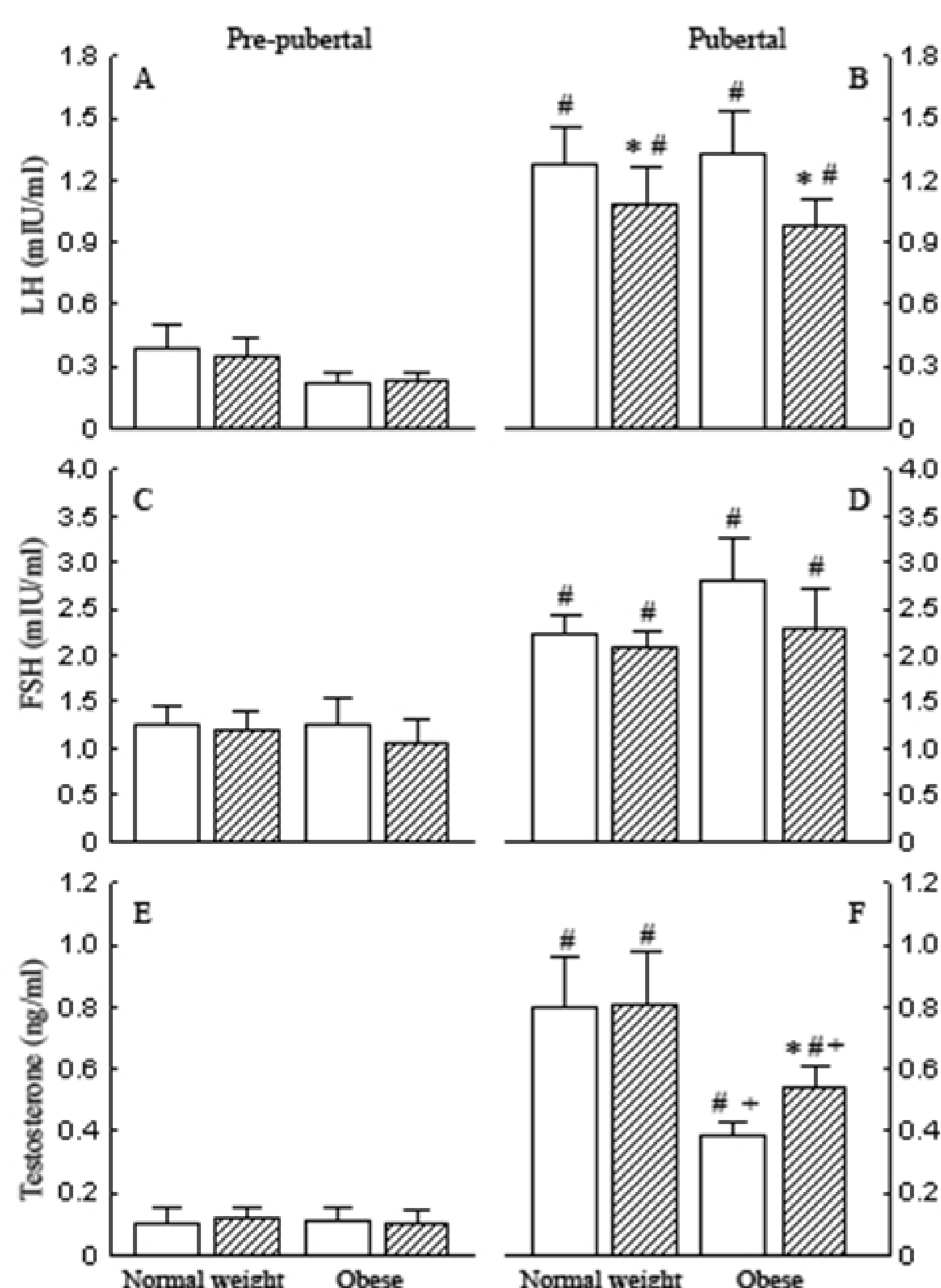


Table 2: Significant correlations between baseline LH, FSH and testosterone concentrations and baseline and changes (Δ) of concentrations of pro- and anti-oxidation markers. Correlations were evaluated by Pearson's correlation test. The level of significance was set at (P<0.05).

Pre-pubertal normal-weight		
Testosterone	Catalase	r=0.80
LH	ΔTAC	r=0.63
Pre-pubertal obese		
LH	GSH	r=0.92
LH	GSSG	r= -0.85
FSH	GSH	r=0.90
LH	ΔTAC	r=0.82
LH	ΔGSH	r= -0.82
LH	ΔGSH/GSSG	r= -0.93
Early pubertal normal-weight		
Testosterone	ΔTAC	r=0.86
Testosterone	ΔGSH/GSSG	r=0.73

References

1. Vandewalle S, et al. Sex steroids in relation to sexual and skeletal maturation in obese male adolescents. *JCEM*. 2014.
2. Finkel T, Holbrook NJ. Oxidants, oxidative stress and the biology of ageing. *Nature*. 2000.
3. Alleman RJ, et al. The "Goldilocks Zone" from a redox perspective-Adaptive vs. deleterious responses to oxidative stress in striated muscle. *Front Physiol*. 2014.
4. Paltoglou G, et al. Anti-oxidation improves in puberty in normal weight and obese boys, in positive association with exercise-stimulated growth hormone secretion. *Pediatr Res*. 2015.
5. Mastorakos G, et al. Exercise and the stress system. *Hormones (Athens)*. 2005.
6. Fisher-Wellman K, Bloomer RJ. Acute exercise and oxidative stress: a 30 year history. *Dyn Med*. 2009.
7. Veldhuis JD, et al. Developmentally delimited emergence of more orderly luteinizing hormone and testosterone secretion during late prepuberty in boys. *JCEM*. 2001.
8. Paltoglou G, et al. Interrelations among the adipocytokines leptin and adiponectin, oxidative stress and aseptic inflammation markers in pre- and early-pubertal normal-weight and obese boys. *Endocrine*. 2017.
9. Veldhuis JD, et al. Role of endogenous opiates in the expression of negative feedback actions of androgen and estrogen on pulsatile properties of luteinizing hormone secretion in man. *JCI*. 1984.
10. Cumming DC, et al. Reproductive hormone increases in response to acute exercise in men. *Med Sci Sports Exerc*. 1986.