

# Steroid hormones related to 11 $\beta$ -hydroxysteroid dehydrogenase in obese and non-obese adolescents



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## INTRODUCTION

- Glucocorticoids (GC) are involved in metabolic processes of the human body
- GC overproduction leads to metabolic disease such as obesity and metabolic syndrome
- The tissue specific enzyme 11 $\beta$ -hydroxysteroid dehydrogenase type 1 (11 $\beta$ -HSD 1) amplifies local GC levels by inter-conversion of inactive cortisone to biological active cortisol
- Cortisol production rates by 11 $\beta$ -HSD 1 are at least equivalent to that of the adrenal glands
- 11 $\beta$ -HSD 1 converts also 7-hydroxylated metabolites of dehydroepiandrosterone (DHEA) to 7-oxo-DHEA
- Substrates of the enzyme represent potent competitive inhibitors

## METHODS/ DESIGN

- 282 obese adolescents BMI (Body Mass Index) > 90<sup>th</sup> percentile related to gender and age:
  - 154 girls (median age 15.31, range 14.17-16.68 years)
  - 128 boys (median age 14.95, range 13.87-16.16 years)
- 100 normostenic controls BMI 25<sup>th</sup> to 75<sup>th</sup> percentile related to gender and age:
  - 50 girls (median age 15.29, range 14.32-16.79 years)
  - 50 boys (median age 15.29, range 14.47-16.77 years)
- Circulating levels of cortisol, cortisone, DHEA, 7-oxo-, 7 $\alpha$ -hydroxy-, 7 $\beta$ -hydroxy- and 16 $\alpha$ -hydroxy-DHEA
- Body composition: bioimpedance Tanita BC-418 MA
- Steroid hormones: API 3200 (AB Sciex, Concord, Canada) triple stage quadrupole – mass spectrometer with electrospray ionization (ESI) connected to the UPLC Eksigent ultraLC 110 system (Redwood City, CA, USA)
- Statistical analysis: repeated ANOVA followed by least significant multiple comparisons

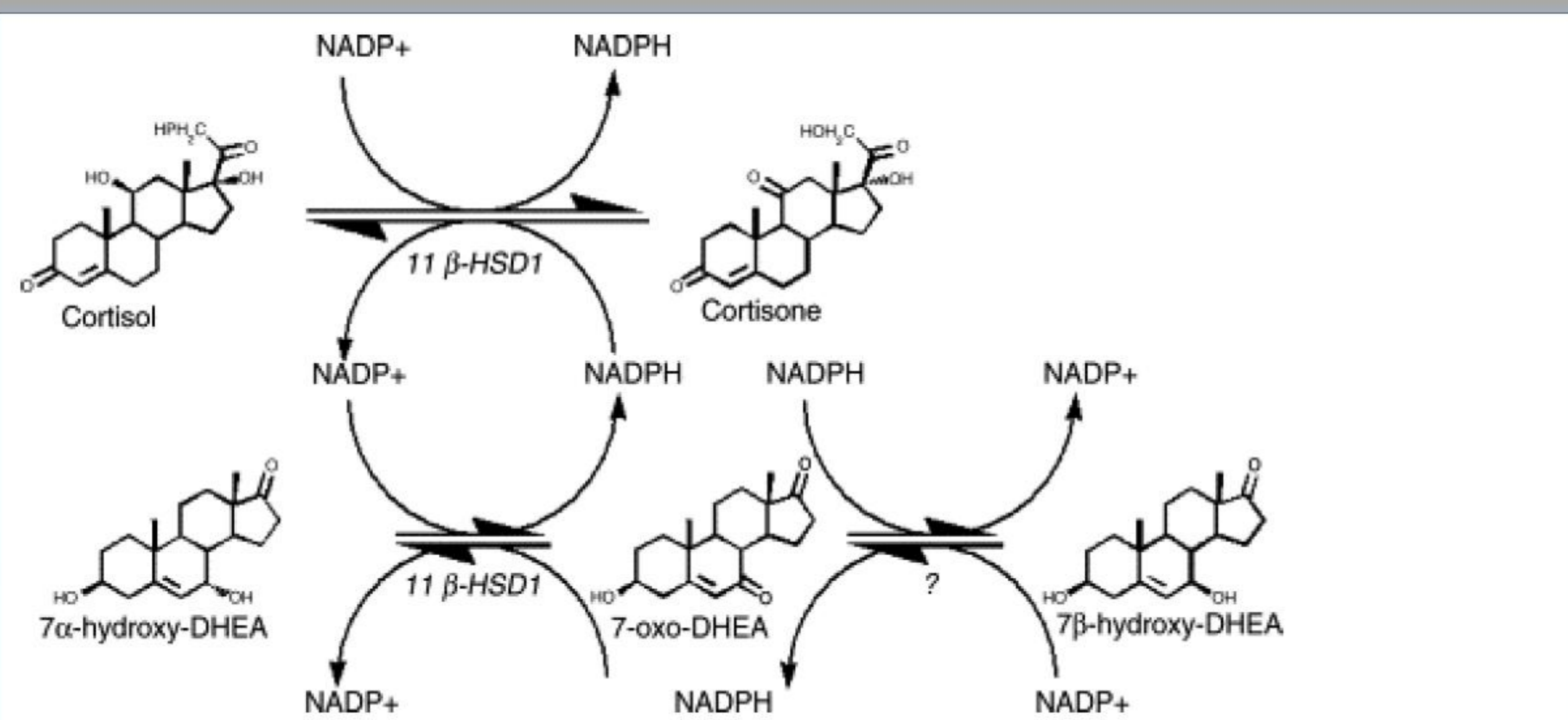


Fig.1 11 $\beta$ -HSD 1- mediated oxidoreduction of cortisol and 7 $\alpha$ -hydroxy-DHEA  
C.Muller et al./ The Journal of Steroid Biochemistry and Molecular Biology 99 (2006) 215-222

## CONCLUSIONS

- Identical levels of cortisol but increased levels of cortisone indicate an altered activity of 11 $\beta$ -HSD 1 in obese patients
- This assumption is also supported by significantly higher levels of 7-oxo-DHEA
- We do not expect that measured changes in steroid levels caused other enzyme able to metabolize cortisol/cortisone - 11 $\beta$ -HSD type 2
- Firstly, 11 $\beta$ -HSD 2 does not metabolize derivatives of DHEA and secondly, its activity remains unchanged with development of obesity
- Increased local cortisol production in adipose tissue induces likely a compensatory mechanism to maintain whole-body levels balanced
- The mechanism involves the reduction of hepatic 11 $\beta$ -HSD 1 and the activation of 5 $\alpha$ -reductase which metabolizes cortisol towards waste products, both observed in obesity
- Considering the prevailing contribution of hepatic 11 $\beta$ -HSD 1 to extra-adrenal cortisol production, we suppose that the presented changes in circulating (neuro)steroid levels were due to altered activity of hepatic 11 $\beta$ -HSD 1

## AIM OF THE STUDY

- Examine the circulating levels of steroids related to 11 $\beta$ -HSD 1 in obese patients and compare them with that of healthy controls
- Try to estimate the role of the 11 $\beta$ -HSD 1 in obesity

## RESULTS

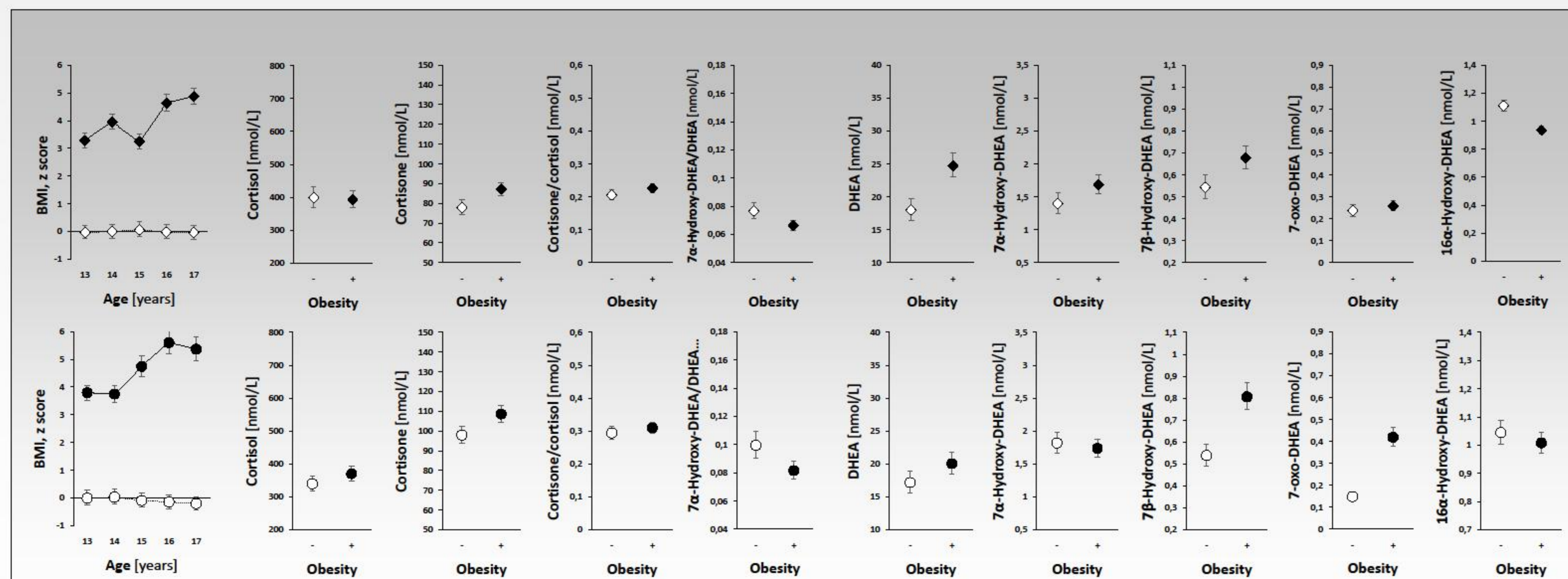


Fig. 2 Compared circulating steroids in obese and non-obese adolescents. Girls shown as a square symbol, boys with the round

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