Sex Steroid Hormones Affect Carnitine Concentrations of Blood and Organs in Rats

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Abstract

Males and females exhibit different rates of central obesity, cardiovascular disease and diabetes. Furthermore, altered concentrations of sex steroid hormones can lead to altered rates of these diseases in the afflicted populations, suggesting these hormones can affect metabolism and, in the long term, have clinical repercussions. Carnitine, an amino acid derivative involved in fat oxidation, was used to examine differences in metabolism between the sexes based on changes in the hormonal milieu. Rats (178 males and 176 females) were administered one of the following treatments: estradiol injection, testosterone injection, castration, and hypophysectomy. Total carnitine was measured in plasma, liver, heart, muscle, and epididymis. In both sexes, estradiol appears to increase liver carnitine while decreasing plasma, muscle and heart carnitine; testosterone, on the other hand, increases plasma, muscle and heart carnitine. In males, estradiol decreases and testosterone increases epididymis carnitine. Hypophysectomy decreased carnitine in all compartments for males and all compartments except for heart and muscle in females. This study demonstrates that estradiol, testosterone and the pituitary gland greatly influence carnitine concentrations of the body and are key to the observed sex differences in carnitine.

Introduction

- Men and women exhibit different incidences of clinical abnormalities:
  - ♂ Men are more prone to visceral fat accumulation and cardiovascular disease
  - ♀ Women's incidences of visceral fat accumulation and cardiovascular disease increase after menopause
- There are also differences in substrate utilization during endurance exercise between the sexes:
  - ♂ Men have higher carbohydrate oxidation rates
  - ♀ Women have higher lipid oxidation rates
- Sex steroid hormones have effects on metabolism:
  - ♂ Testosterone stimulates lipolysis in adipose tissue
  - ♀ Estradiol can directly inhibit complexes I and V of the mitochondrial electron transport chain
- Carnitine:
  - is an amino acid derivative which shuttles long-chain fatty acids into the mitochondria for β-oxidation
  - can serve as an indicator of metabolic state and mitochondrial acyl-CoA content
  - was examined in this project in blood and organs of rats undergoing various hormonal treatments

Legend

- HYPOX
- CAST
- CARN
- ESTRA
- TEST
- HYPOX/ESTRA
- CAST/ESTRA
- HYPOX/CAST
- HYPOX/CAST/ESTRA
- HYPOX/TEST
- CAST/TEST
- HYPOX/CAST
- HYPOX/CAST/TEST

Materials & Methods

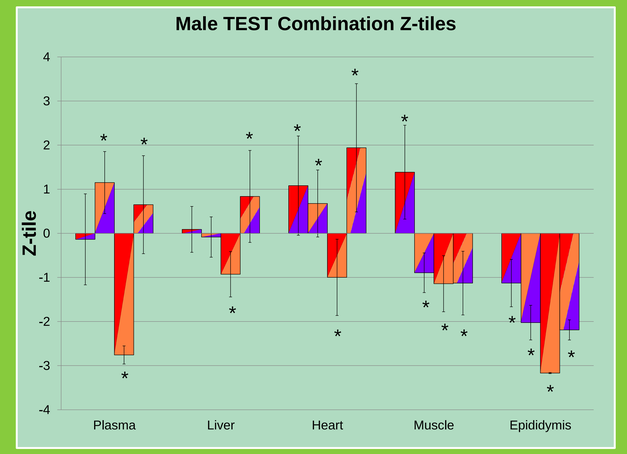
326 male and 325 female rats were randomly assigned to one or a combination of the following treatments:

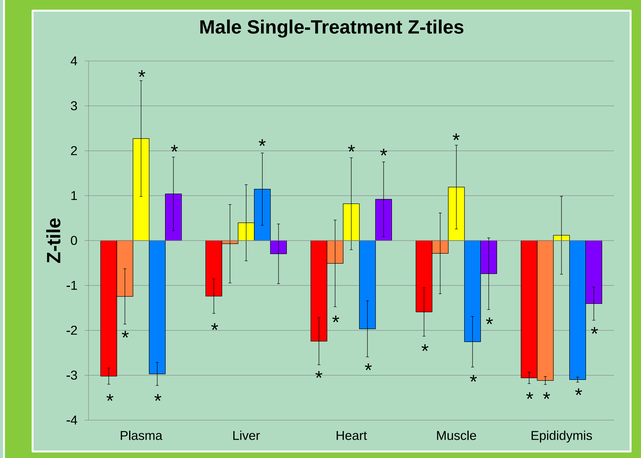
- Carnitine supplementation (CARN) – 2g carnitine per liter drinking water, begun 60 ± 3 days before sacrifice
- Estradiol (ESTRA) – daily injections approximating natural female production begun 61 ± 1 days before sacrifice
- Testosterone (TEST) – daily injections approximating natural male production begun 62 ± 1 days before sacrifice
- Hypophysectomy (HYPOX) – pituitary surgically removed 41 ± 13 days before sacrifice
- Castration (CAST) – testes (male) or ovaries (female) removed 63 ± 4 days before sacrifice
- No treatment (control)

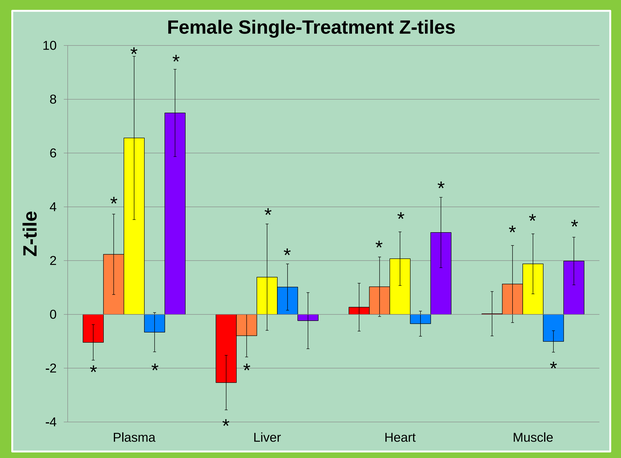
Plasma, liver, heart, muscle, and epididymis samples were obtained, processed and frozen. Carnitine concentrations were determined using a radioenzymatic assay[1]. Z-tiles were calculated with the control groups as the reference populations.

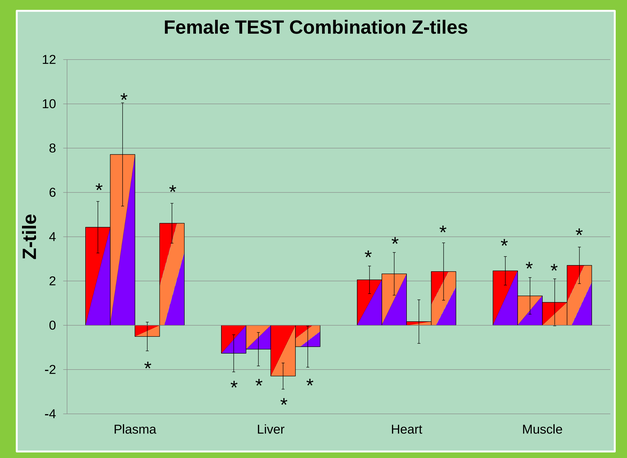
Results

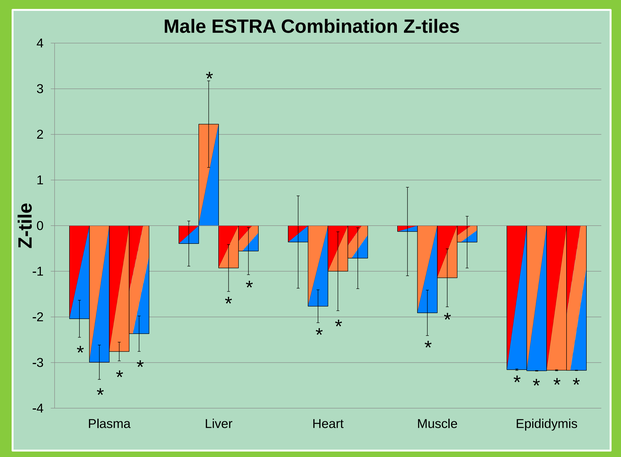
* Indicates significant difference from control group

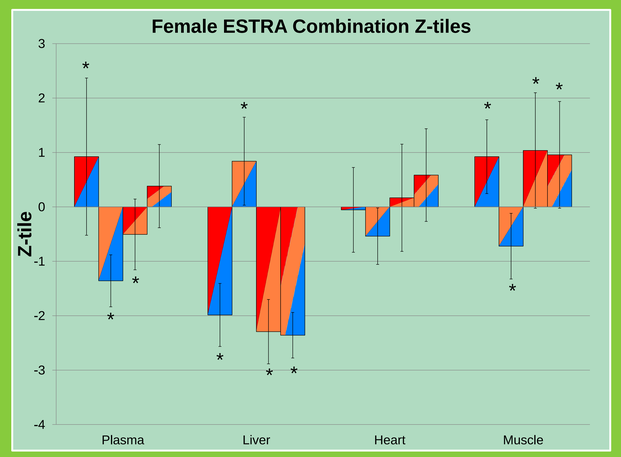












Conclusions

- Carnitine supplementation consistently increased carnitine in plasma and all organs except liver
- Testosterone increased carnitine in plasma and organs except liver where it had little effect
  - Speculation: some decreases seen in male muscle may be due to aromatization of testosterone to estradiol
- Estradiol decreased carnitine in plasma and organs except liver where it increased carnitine
- Pituitary function elevated carnitine in almost all compartments
- Testosterone present in larger amounts than estradiol is necessary for epididymal carnitine to be on the same order of magnitude as control rats

References

[1]Borum, PR. Carnitine: determination of total carnitine using a radioenzymatic assay. J. Nutr. Biochem. 1990 Feb;1(2):111-4.