Effects of Chemical Diabetes and Starvation on Blood and Organ Carnitine Concentrations in Rats

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Abstract

Carnitine (CARN) is known for shuttling fatty acids across the mitochondrial membrane, but its role in carbohydrate (CHO) metabolism is less well defined. This study examines the effect of altered CHO metabolism on CARN status. Age-stratified rats received one of the treatments in Table 1. Total CARN was measured in plasma, red blood cells (RBC), liver, heart, muscle, and epididymis.

Table 1: Male and Female Carnitine Concentrations

Treatment	Male	Female
Control	0.9 ± 0.4	1.3 ± 0.3
Alloxan (acute)	2.7 ± 1.3	2.7 ± 0.9
Streptozotocin (acute)	3.5 ± 1.5	2.4 ± 0.6
Alloxan (chronic, 35 days)	0.9 ± 0.3	0.8 ± 0.3
CARN supplementation	1.5 ± 0.2	2.7 ± 0.8
Alloxan (acute) + CARN supp.	8.9 ± 6.7	7.9 ± 2.6
Starvation (4 days)	1.8 ± 0.4	2.1 ± 0.7

Generally, acute diabetes led to elevated blood glucose and ketones; CARN concentrations decreased in plasma and RBC, increased in liver and muscle, and changed little in cardiac and epididymal tissues. CARN supplementation yielded 1.5- to 2-fold increases in blood and most organs. Acute diabetes altered CARN status more than chronic diabetes or starvation. Liver and muscle, with greater capacity for glycogen utilization, accreted CARN when glucose was unavailable but CARN supplementation was required for accretion in other organs. Though many associate CARN only with fat metabolism, this study shows that alterations in CHO metabolism change the distribution of CARN.

Introduction

Carnitine is most widely known for its role in shuttling fatty acids across the mitochondrial membrane for β-oxidation; however, its involvement in carbohydrate metabolism is often overlooked. By buffering the acyl-CoA/CoA ratio within cells, carnitine can regulate the feedback mechanism of pyruvate dehydrogenase, the enzyme that converts pyruvate to acetyl-CoA (see Figure 1)[1]. Alterations in carbohydrate metabolism (Type 1 and Type 2 diabetes, starvation, inborn errors in metabolism, etc.) have been shown to lead to changes in fat metabolism, likely due to the interrelation of the pathways involved. Therefore, carnitine should have a role in overall metabolism. This study sets out to investigate changes in blood and organ carnitine concentrations in rats that were starved or in which chemical diabetes was induced.

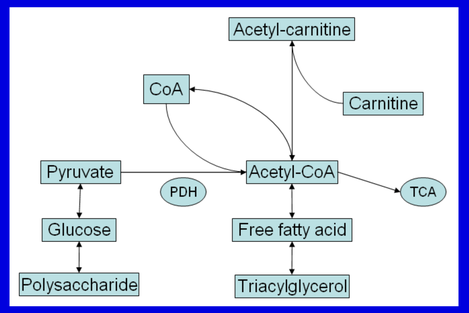


Figure 1: Carnitine's role in overall metabolism. Abbreviations – pyruvate dehydrogenase (PDH); tricarboxylic acid cycle (TCA).

Materials & Methods

304 male and 294 female rats were randomly assigned to the following treatments:

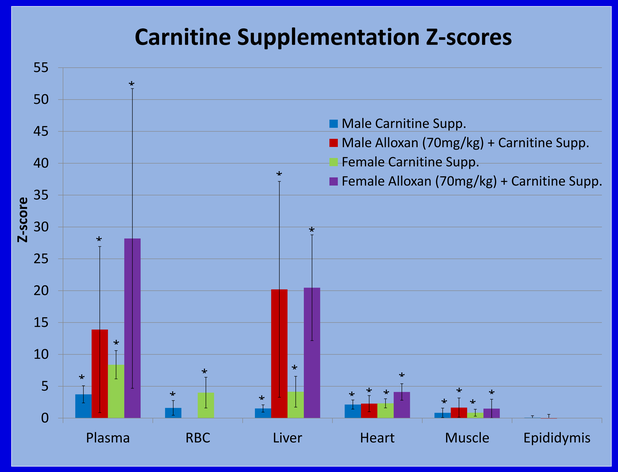
Table 2: Male Rat Groups

Treatment	Treatment duration (days)	Age (days)	Number of rats
Control	N/A	89 ± 6	96
Alloxan (70mg/kg)	2	91 ± 7	44
Streptozotocin (70mg/kg)	2	98 ± 12	10
Carnitine supplemented	2	90 ± 4	12
Alloxan (70mg/kg) + carn. supp.	2	90 ± 5	34
Alloxan (35mg/kg)	17	93 ± 4	13
Alloxan (35mg/kg)	23-24	86 ± 3	13
Alloxan (35mg/kg)	28-29	91 ± 2	16
Alloxan (35mg/kg)	35	85 ± 1	10
Starvation	1	84 ± 4	13
Starvation	2	86 ± 5	16
Starvation	3	78 ± 6	11
Starvation	4	100 ± 16	16

Table 3: Female Rat Groups

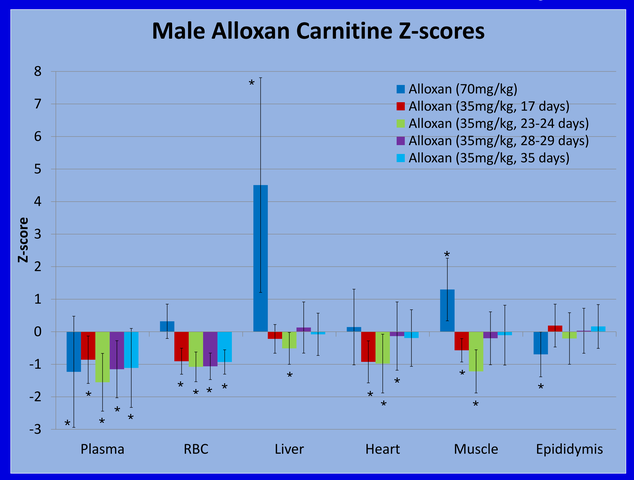
Treatment	Treatment duration (days)	Age (days)	Number of rats
Control	N/A	87 ± 5	86
Alloxan (70mg/kg)	2	89 ± 9	38
Streptozotocin (70mg/kg)	2	109 ± 0	10
Carnitine supplemented	2	89 ± 4	12
Alloxan (70mg/kg) + carn. supp.	2	88 ± 5	22
Alloxan (35mg/kg)	17	92 ± 4	12
Alloxan (35mg/kg)	21-25	85 ± 2	27
Alloxan (35mg/kg)	29	87 ± 0	6
Alloxan (35mg/kg)	35	86 ± 0	10
Starvation	1	86 ± 5	14
Starvation	2	91 ± 7	26
Starvation	3	94 ± 22	16
Starvation	4	92 ± 17	15

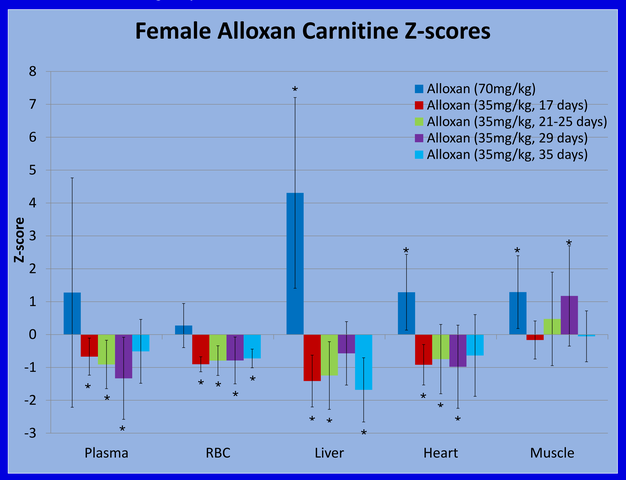
Carnitine-supplemented rats were given 2 grams carnitine per liter of drinking water. Plasma, red blood cell (RBC), liver, heart, muscle, and epididymis samples were obtained, processed and frozen. Carnitine concentrations were determined using a radioenzymatic assay[2]. Z-scores were calculated with the control groups as the reference populations.

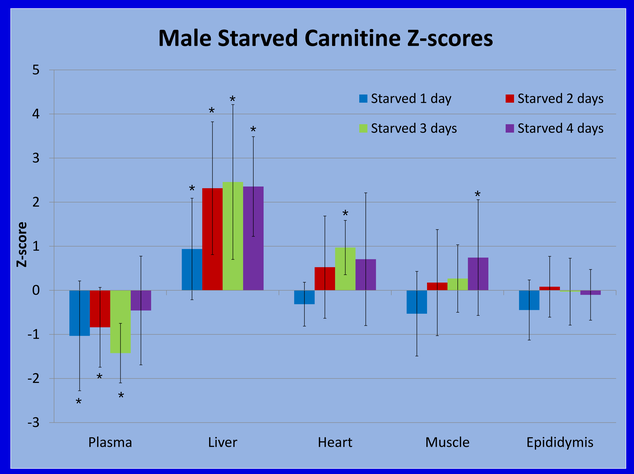


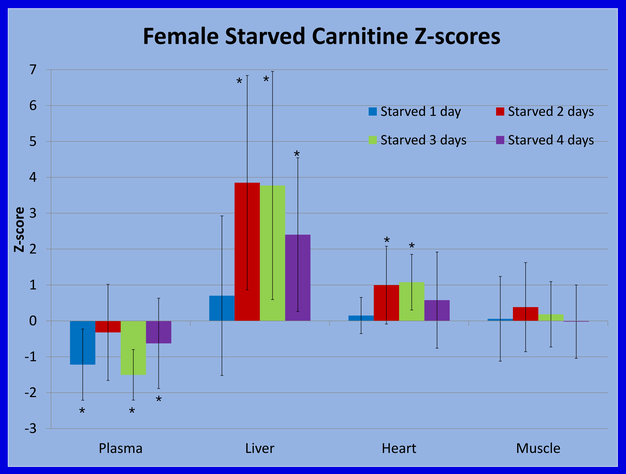
Results

* Indicates significant difference from control group









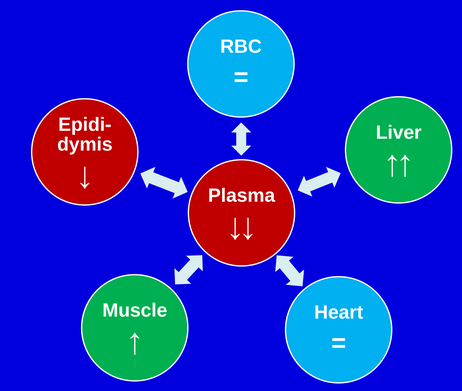


Figure 2: Blood and organ carnitine change comparison for males treated with alloxan (70mg/kg).

Conclusions

- Altering glucose metabolism associated with a change in carnitine concentrations
- Males and females had different carnitine trends
  - Ex. Trend in starved rats' muscle carnitine
- Carnitine compartments reacted differently (Figure 2)
  - Liver and muscle may need more carnitine to facilitate increased movement of fatty acids across the cell membranes and process ketones
  - Heart has a greater metabolic "preference" for fat so changing glucose metabolism may not have as much of an effect

References

[1]De Simone C, Famularo G. Carnitine Today. Chapman and Hall: New York. 1997.

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