Endurance exercise training suppressed cardiac and renal damage in diabetic rats.

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INTRODUCTION

Diabetes mellitus causes damage in both heart and kidneys, leading to the cardiorenal syndrome that is associated with increased complications and mortality.

Additionally, it causes mitochondrial dysfunction; that is responsible for several metabolism parameters.

Although the specific molecular mechanisms underlying DM are not well understood, perhaps the most important pathway regulating metabolism in muscle is mitochondrial biogenesis.

The Mitofusin 2 is a important protein to mitochondrial fusion. Additionally, muscle mitochondrial metabolism is regulated by a group of morphogenesis machinery proteins which are important for mitochondrial fusion and fission events and also for their independent effects on bioenergetics.

Although, exercise training is a well described method to prevent DM damages, it is not clear how exercise training influences on mitofusin 2. Also, exercise training is an interesting strategy for reversing the effects of mitochondrial dysfunction that might be through the regulation of mitochondrial protein transcription and biogenesis.

AIM

To verify whether endurance exercise training could improve renal and cardiac parameters and increase Mitofusin2 expression in cardiac myocytes in experimental diabetes.

METHODS

Male Wistar (8 weeks-old) rats were divided into 4 groups: control non-exercise (CS=8), control exercised (CE=8), diabetic non-exercise (DS=8), diabetic exercised (DE=8).

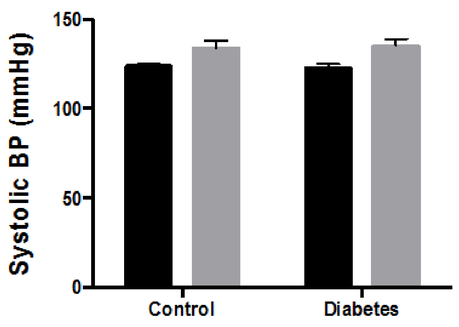
Diabetes was induced by STZ (50mg/kg), all diabetic rats had the glycemia >250mg/dL. Trained groups were submitted to a progressive exercise training protocol on a treadmill (1h/day; 5day/week; 8 wk).

SBP, HR were analyzed using a data acquisition system (PowerLab). Renal function were evaluated using proteinuria (codas) and Albumin excretion was analyzed by the Rat Albumin ELISA Quantification Set (Bethyl Laboratories, Inc. Montgomery, TX). The urinary volume was colleted by metabolic gate.

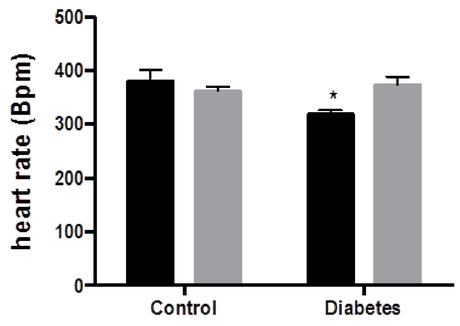
The tissue weight/tibia length ratio was used to determinate the cardiac and kidney hypertrophic index . The expression of the following proteins were analyzed by western blotting: mitofusin 2 (cell signaling; 1:1000); AMPK (cell signaling; 1:1000); p-AMPK (cell signaling; 1:1000) and α-tubulin (Sigma ,1:1000).

RESULTS

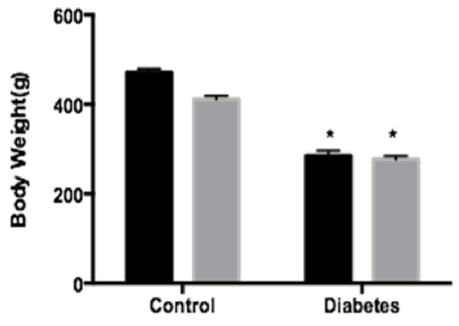
Systolic Blood Pressure



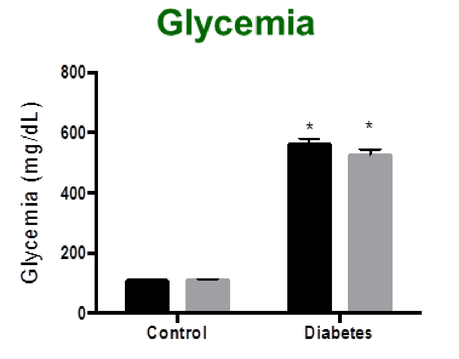
Heart Rate



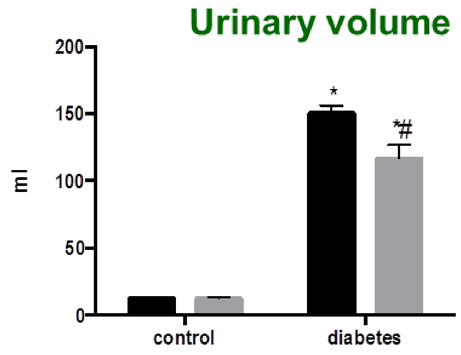
Body Weight



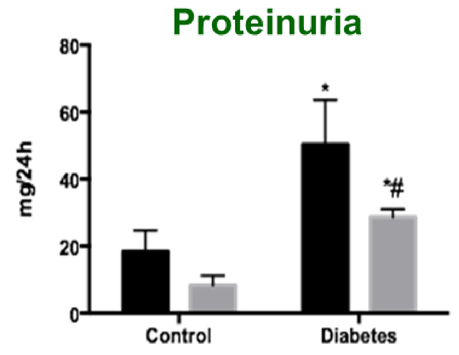
Glycemia



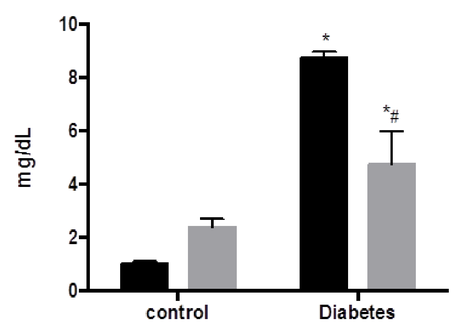
Urinary volume



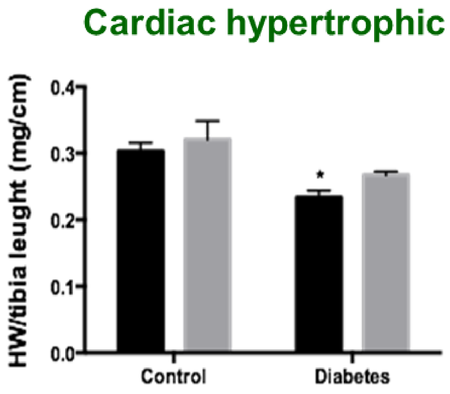
Proteinuria



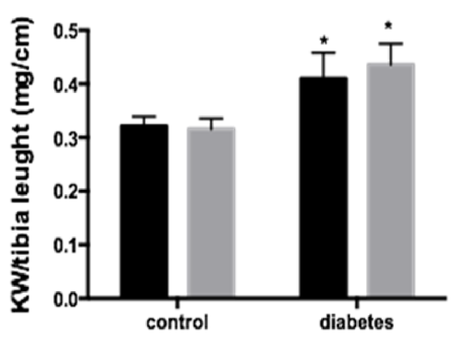
Albumin excretion



Cardiac hypertrophic index

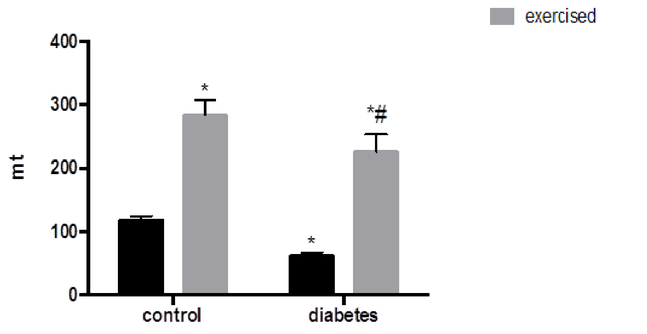


Kidney hypertrophic index



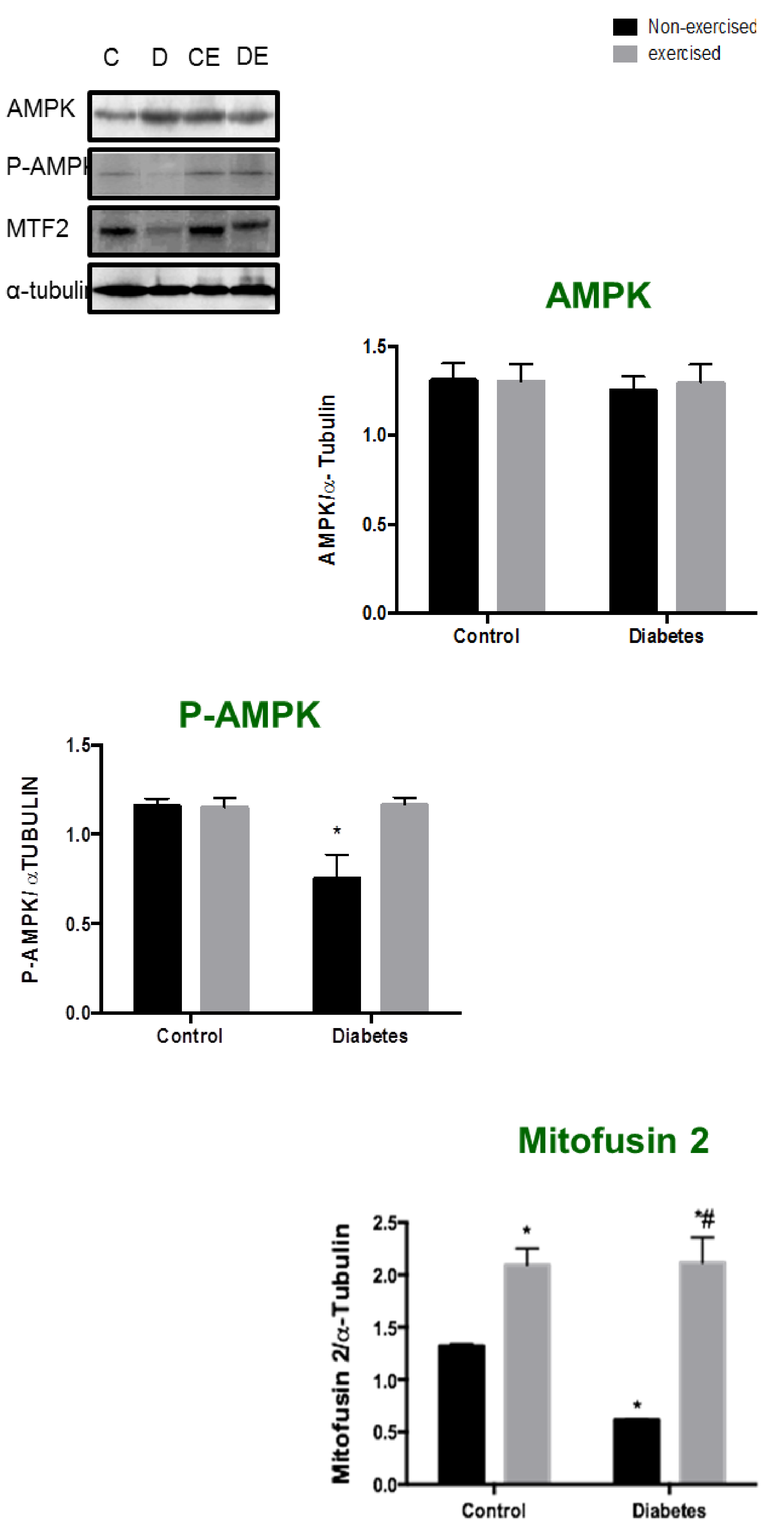
* p < 0,05 vs. Control; # p < 0,05 vs. Diabetic

Maxim run test (final



* p < 0,05 vs. Control; # p < 0,05 vs. Diabetic

WESTERN BLOT



* p < 0,05 vs. Control; # p < 0,05 vs. Diabetic

CONCLUSION

Exercise training attenuated the progression of diabetic nephropathy and cardiac dysfunction; those improvements could be a result of the increased expression of mtf2.

Exercise training was able to avoid the cardiac muscle deterioration leading to the normalization of HR; reduction the albumin excretion and the proteinuria. Those adaptation can be related with a higher expression of the biogenesis mitochondrial pathway (AMPK; P-AMPK, Mitofusin 2) and it could be associated with an improvement of cardiac metabolism. Moreover, direct influence on renal function.

These findings show that the exercise training is an important approach to avoid, both molecular and functional complications caused by diabetes.

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I) Diabetes. I1) Basic research in diabetes.

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