CARDIAC CHANGES AND DECREASED CARDIAC EXPRESSION OF FOXP2 MEDIATED BY DIET-INDUCED MODERATE OBESITY CANNOT BE AFFECTED BY MAO-B INHIBITION.

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Obesity is a major risk factor for the development of cardiovascular diseases, which is associated with oxidative stress and chronic inflammation. Monoamine oxidases (MAOs) are major sources of mitochondrial reactive oxygen species. We have shown previously that MAO-B selective inhibitor selegiline reduces visceral adiposity in obesity, however, it has not been assessed if selegiline can alleviate cardiac oxidative stress. Therefore, we investigated the effects of selegiline on cardiac redox homeostasis and cellular damage in a high-fat high-sucrose diet (HFD)-induced obesity model of rat. We demonstrate that specific MAO-B inhibition by selegiline reduces cardiac mitochondrial ROS production in healthy, but not in HFD obese rats. Although HFD did not affect pro-survival, pro-death and oxidative stress-related mechanisms, it decreased sequestosome-1 level and B-cell lymphoma 2-associated X protein/B-cell lymphoma 2 (Bax/Bcl-2) ratio, and increased TNF and NF-kB expressions. Selegiline did not affect any of these HFD-induced alterations. Simulated hypercholesterolemic treatment disrupted mitophagy in H9c2 cardiomyocytes which was not restored by selegiline. Both SERCA2a and its upstream modulators were affected by HFD and selegiline, however it did not manifest in altered cytosolic calcium dynamics. In addition, we identified a previously unknown cardiac signaling molecule, forkhead box P2 gene (Foxp2), which was decreased in obesity, but not restored by selegiline. In conclusion, MAO-B inhibition is of no significant therapeutic value to alleviate cardiac consequences of obesity.

Keywords: cardioprotection, obesity, MAO-B, selegiline