The protective effect of exercise on diabetic nephropathy: the role of histidine containing dipeptides

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Background: Histidine-containing dipeptides such as carnosine and anserine are protective towards development of diabetic nephropathy in rodents. In humans, these dipeptides are hydrolyzed by the enzyme serum carnosinase 1 (hCN1), hindering the protective properties of these dipeptides, especially in people with high CN1 activity. Physical exercise is thought to enhance the levels of circulating histidine containing dipeptides. Therefore we hypothesize that the development of diabetic nephropathy will be attenuated by exercise, especially when hCN1 activity is low. **Methods:** BTBR ob/ob mice show fast progression towards advanced nephropathy, closely resembling the human phenotype of diabetic nephropathy. Both BTBR ob/ob mice that are genetically determined to produce the active hCN1 enzyme (n=7) and non-transgenic BTBR ob/ob mice that lack the active hCN1 enzyme (n=8) were subjected to a chronic exercise intervention (running at 10m/min, 5 days per week) from the age of 4 weeks to the age of 24 weeks. **Results:** Treadmill running increased circulating carnosine and anserine levels, which was completely abolished in hCN1 transgenic mice. The latter show a significantly (+17.7%, $p<0.001$) greater glomerular hypertrophy compared to the mice lacking hCN1. In both groups, exercise has a moderately tampering effect on glomerular hypertrophy (non-transgenic: -5.8%, transgenic: -0.5%). **Conclusion:** Despite preliminary, both exercise and especially low hCN1 activity tend to evoke protective effects against diabetic nephropathy at histological level. The study is currently expanded (n=82) and more results on blood, urine, muscle and kidney analyses of both sexes will be presented the congress.