Patients with acromegaly exhibit altered mitochondrial function despite successful treatment

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Introduction

Acromegaly [1] results from excessive growth hormone (GH) by an adenoma of the pituitary gland and is amongst other symptoms associated with myopathy, alterations of energy expenditure and insulin action which are mediated by insulin-like growth factors (IGFs). It is unclear to which extent these abnormalities remain after treatment. Thus, we examined glucose metabolism, intracellular fat deposition and mitochondrial function in patients with acromegaly (AM) [2].

Methods

Six AM (4f/2m, age: 49±10 years, BMI: 27±3 kg/m^2) with an at least 7-years history of successful treatment and age-/BMI-matched healthy volunteers (CON: 3f/3m, 43±12 years, 26±4 kg/m^2) were studied. Insulin sensitivity (OGIS) and first-phase insulin secretion were assessed from the frequently sampled OGTT (insulinogenic index, ISEC). Fasting mitochondrial function was assessed from the Pi to ATP synthetic flux (fATP) using ^{31}P MRS of calf muscle on a 3 T Bruker MEDSPEC, 80 cm bore and a 10 cm linear polarized surface coil, TR=15 s. Intracellular lipid contents of tibialis anterior (IMCLt) and soleus muscles (IMCLs) as well as liver (HCL) were measured with STEAM-localized ^{1}H MRS (IMCL: 24 cm diameter circular polarized birdcage coil, TM=30 ms, TE=20 ms, TR=4 s; HCL: linear polarised surface coil, TM=30 ms, TE=15, 20, 30, 50, 70 ms, TR=2.5 s). The protocol was approved by the local institutional ethics board.

Results

IGF-1 did not differ between groups (AM: 177±88 ng/ml; CON: 145±51 ng/ml). Fasting plasma glucose was ~16% higher in AM (99±8, CON: 85±6 mg/dl, p<0.05), OGIS was comparable (395±74, CON: 415±14), but ISEC was ~87% lower in AM (0.9±0.9, CON: 6.7±4.3, p<0.05). fATP was ~22% lower in AM (10.1±1.5 vs. 12.9±2.4 mmol.l^{-1}.min^{-1}, p<0.05) and related positively to ISEC (r=0.687, p<0.01). IMCLt and IMCLs and HCL were not different between groups. IMCLs correlated negatively to insulin sensitivity (r=-0.745, p=0.005).

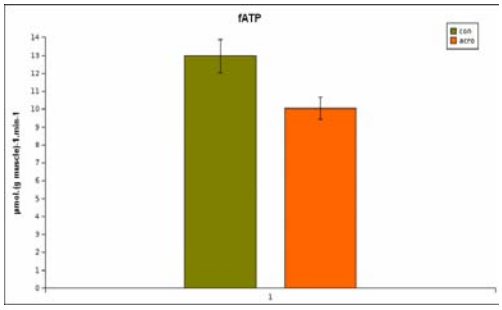

Figure 1: Calf muscle ATP synthesis rates of acromegalics and Controls

Conclusion

Successfully treated acromegaly patients exhibit reduced insulin secretion and muscle ATP synthesis despite normal insulin sensitivity. The impairment of mitochondrial function could be explained by previous long-term GH/IGF exposure and/or chronically increased plasma glucose concentrations resulting from impaired ß cell function.

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[2] Petersen KF, Befroy D, Dufour S, Dziura J, Ariyan C, Rothman DL, DiPietro L, Cline GW, Shulman GI: Mitochondrial dysfunction in the elderly: possible role in insulin resistance. *Science* 300:1140–1142, 2003.