GLP-1 ANALOGUE EXENATIDE MODIFIES PARAMETERS OF MITOCHONDRIAL RESPIRATION IN RAT HEPATOCYTES

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INTRODUCTION
The incretin hormone glucagon-like peptide-1 (GLP-1) exhibits protective effects on pancreatic β-cells and affects metabolism of hepatocytes. Exenatide (Ex4) is a GLP-1 analogue with longer half-life compared to GLP-1. In our previous study, we described that Ex4 significantly diminishes an early phase of liver regeneration after 2/3 partial hepatectomy (PHx, see Fig 1a-1b). To elucidate a potential role of the mitochondrial respiration in the decline of regenerative response, we evaluated the effect of Ex4 on mitochondrial respiration parameters in liver homogenates obtained from male Wistar rats pretreated with Ex4.

METHODOLOGY
Animals were submitted either to PHx or sham laparotomy (LAP) and received 3 doses of Ex4 (42 μg/kg) or saline (S) intraperitoneally (1± dose 24 hrs before the surgery, 2± dose 12 hrs before the surgery and 3± dose immediately after the surgery. Animals were sacrificed 24 hrs after the surgery. Liver samples were homogenized in sucrose-mannitol medium. Oxygen uptake in liver homogenates (n = 4) was measured using High Resolution Oxygraph 2K. We assessed oxidation of glutamate-malate (G/M) and palmitoyl carnitine-malate (PC/M) and calculated the respiratory control index (RCI). Integrity of the outer mitochondrial membrane was assessed by means of respirometry after addition of cytochrome C (cyt C).

RESULTS (* p < 0.05)

CONCLUSION
Treatment with the GLP-1 analogue Exenatide modifies mitochondrial respiration in rat liver homogenates, with an opposite effect on hepatocytes isolated from laparotomized and hepatectomized animals.

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