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Autor(en) des Beitrags: Simões, MV; Egert, S; Ziegler, S; Miyagawa, M; Reder, S; Lehner, T; Nguyen, N; Charron, MJ; Schwaiger, M

Titel des Beitrags: Delayed response of insulin-stimulated fluorine-18 deoxyglucose uptake in glucose transporter-4-null mice hearts.

Abstract: OBJECTIVES: We sought to evaluate the time course of insulin-stimulated myocardial glucose uptake (MGU) in mice that had undergone ablation of glucose transporter-4 (GLUT4).

BACKGROUND: The relative importance of GLUT4, the most abundant insulin-responsive glucose transporter, to modulate myocardial glucose metabolism is not well defined. METHODS: Myocardial glucose uptake was assessed at various time points after glucose (1 mg/g) and insulin (8 mU/g) injection in GLUT4-null (G4N) (n = 48) and wild-type (WT) (n = 48) mice with (18)F-2-deoxy-2-fluoro-d-glucose (FDG) using in vivo positron emission tomography (PET), in vitro gamma-counter biodistribution, and isolated, perfused hearts. RESULTS: Baseline assessment with PET imaging showed comparable MGU in G4N (0.66 +/- 0.12) and WT (0.67 +/- 0.11, p = 0.70) mice. Early after insulin injection, WT mice demonstrated a 3.5-fold increase in MGU (2.45 +/- 0.45, p = 0.03), whereas G4N mice presented no increase (1.11 +/- 0.24, p = 0.28). At 60 min, MGU was comparable in G4N (3.19 +/- 0.60) and WT (2.66 +/- 0.47, p = 0.28) mice. In vitro gamma-counter biodistribution evaluation confirmed in G4N mice a lack of MGU increase early after insulin, but a slow response over 120 min. The isolated, perfused hearts of G4N mice during short-term (15 min)
insulin stimulation displayed no increase in MGU (0.08 +/- 0.01 ml/g/min), whereas WT mice presented a threefold increase (0.22 +/- 0.01 ml/g/min, p< 0.01). With long-term (60 min) insulin stimulation, similar MGU was found in G4N (0.31 +/- 0.02 ml/g/min) and WT (0.33 +/- 0.04 ml/g per min, p = 0.04) mice. CONCLUSIONS: The G4N mice displayed an increase of MGU in response to insulin similar to that of controls, but with a markedly delayed time response. Our findings underscore the important role of GLUT4 in the rapid adaptive response of myocardial glucose metabolism.