The effects of GLP-1 on microvascular recruitment in human and rat muscle

K.A. Sjøberg,[1] J.J. Holst,[2] S. Rattigan,[3] E.A. Richter[1] and B. Kiens,[1] [1]Section of Molecular Physiology, Department of Nutrition, Exercise and Sports , University of Copenhagen, Universitetsparken 13, DK-2100 Copenhagen, Denmark, [2]NNF Center for Basic Metabolic Research, Department of Biomedical Sciences, University of Copenhagen, Blegdamsvej 3, DK-2200 Copenhagen, Denmark and [3]Menzies Research Institute Tasmania, University of Tasmania, 17 Liverpool St, Hobart, TAS 7000, Australia.

The insulinotropic gut hormone, glucagon-like-peptide-1 (GLP-1) has been proposed to have positive effects on vascular function and glucose disposal which might be beneficial for glucose homeostasis. We hypothesized that GLP-1 increases microvascular recruitment (MVR) and glucose uptake. To test this, GLP-1 was infused in the femoral artery in overnight fasted healthy young men. Microvascular recruitment in the *vastus lateralis* muscle was measured with real time contrast-enhanced ultrasound with microbubbles. Leg glucose uptake was measured by the leg balance technique.

GLP-1 caused a rapid increase (P<0.05) of 20%±12% (mean ± SE) in muscle MVR after 5 min of arterial infusion which increased to 60%±8% at the end of the 60 min infusion. Although plasma insulin concentration transiently increased above fasting levels during GLP-1 infusion, leg glucose uptake was not increased.

It has previously been shown that increased plasma fatty acid availability induces impairment of the insulin-mediated MVR and subsequently a decreased muscle glucose uptake in rats.

Another interesting finding was that acute infusion of GLP-1 increased the MVR in insulin resistant rats without increasing the skeletal muscle glucose uptake. However, when GLP-1 was co-infused with insulin during a euglycemic hyperinsulinemic clamp (3 $mU \cdot min^{-1} \cdot kg^{-1}$), this effect of GLP-1 was associated with a restoration of both whole body insulin sensitivity and increased insulin-mediated glucose uptake in skeletal muscle after 5 days high fat diet but not after 8 weeks.

It is concluded that GLP-1 in physiological concentrations causes a rapid increase in muscle MVR which is independent of insulin, but GLP-1 does not affect muscle glucose uptake directly in overnight fasted healthy, young men or in rats. Furthermore, despite of diet induced insulin resistance GLP-1 increases MVR in rat skeletal muscle and subsequently reverses early stages of HF diet induced insulin resistance *in vivo* when co-infused with insulin.