

Public Abstract

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Title:

Roles of Sex and Insulin on Microvascular Exchange Function

A characteristic of endothelial dysfunction, which is observed in the beginning stages of type 2 diabetes, is the alteration of the microvascular barrier, affecting the microvascular permeability. We measured the venular leakage and clearance of albumin in response to suffusion with high-dose insulin ($10e-7M$) in the autoperfused mesentery in the adult male (AM), adult female (AF), and juvenile male (JM) rats. Insulin suffusion lead to increased venular albumin leakage by 63% in AM rats. Albumin and total protein clearance decreased with insulin treatment and hence, had an inverse relationship. In the JM rats, venular albumin leakage increased by 103% with insulin suffusion. The total protein clearance in JM was unchanged, while the albumin clearance increased with insulin suffusion, resulting in an uncoupling of the responses. In the AM rats, venular albumin leakage was unchanged with insulin suffusion. Insulin also decreased the total protein clearance, but not the albumin clearance. We demonstrated that not only can insulin result in changes in macromolecule exchange in intact, mesenteric microvasculature, but that these changes were dependent on the sex and the sexual maturity of the animal. We determined that the venular leakage response at the single vessel does not reflect the overall protein clearance of the mesenteric network. The uncoupling of the relationship between albumin and total protein clearance response with insulin provides evidence that albumin movement from the vessel and through the tissue is regulated via different mechanisms compared to other plasma proteins. The implication from our studies suggest that the treatment and progression of diseases need to be considered with the genomic and phenotypic backgrounds in mind.