



Insulin infusion increases brain blood flow in healthy Sprague Dawley rats

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Insulin has key physiological roles to increase microvascular blood flow in peripheral organs to stimulate increased nutrient (e.g. glucose) uptake. While studies report high abundance of insulin receptors in all regions of the brain (1, 2), whether insulin alters brain blood flow is not well understood. The aim of this project was to determine whether acute insulin infusion increase brain blood flow *in vivo* in otherwise healthy rats.

Male Sprague Dawley rats were anaesthetised with pentobarbitone (84 mg/kg) and underwent microvascular surgery to isolate two jugular veins and a carotid artery for cannulation. After successful cannulation, animals were equilibrated for 60 min to stabilise blood pressure and heart rate before entering a hyperinsulinaemic euglycemic clamp protocol. Briefly, rats were infused with either saline (n=3) or insulin (n=4, 10 mU/mi;n/kg) for 120 minutes. Exogenous glucose was infused to maintain steady blood glucose levels throughout the procedure. We then intravenously infused phospholipid microbubbles and quantified continuous blood flow at baseline and 30 min post-infusion using transcranial Contrast Enhanced Ultrasound (CEU), as published (4). All animals had similar blood pressure and heart rate throughout the procedure. We found that insulin increased cortical CBF at baseline vs. 30 minutes post-infusion by ~45%, ($p=0.048$), while no change was observed in the saline treated group ($p=0.785$). Next, we used destruction-refill kinetics to measure changes in vascular perfusion (AI/sec). Our preliminary data suggests that insulin appears to increase vascular perfusion by 2.5 fold compared to 1.8 fold increase in the saline group ($p = 0.133$).

In summary, our data suggests that cortical blood flow is greater following insulin infusion for 30 minutes and that insulin appears to increase vascular perfusion (AI/sec) following destruction-refill kinetics compared to saline. These findings give an important insight into understanding the brain vascular responses to insulin and will be the first to provide scalable knowledge on the role of insulin in cortical cerebral blood flow.