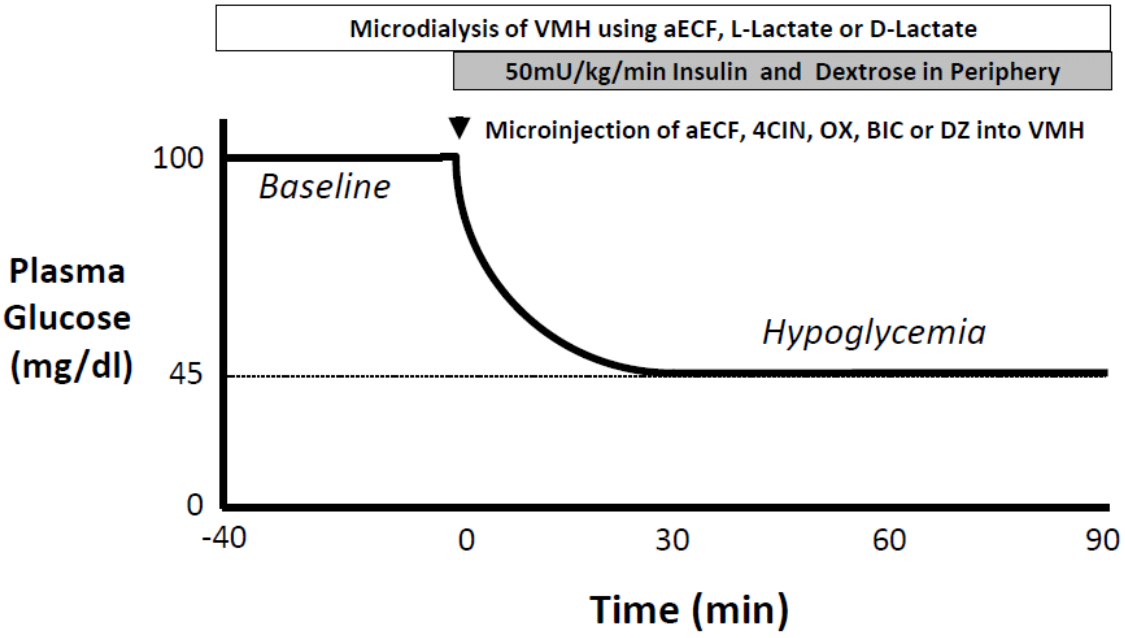
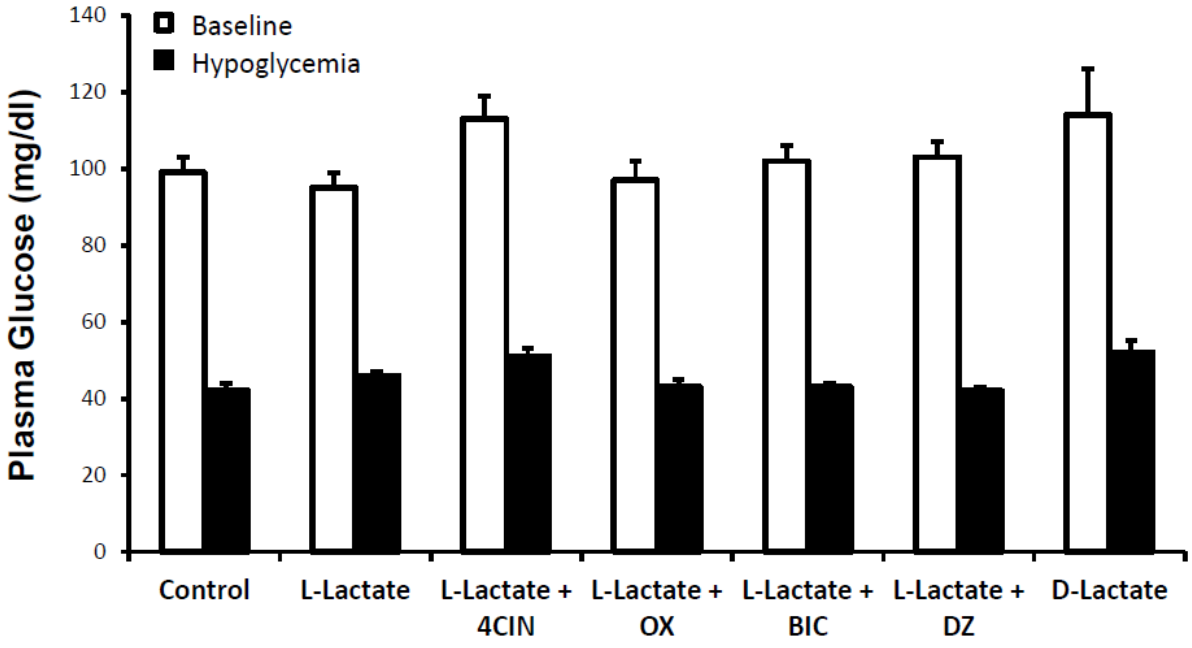
SUPPLEMENTARY DATA

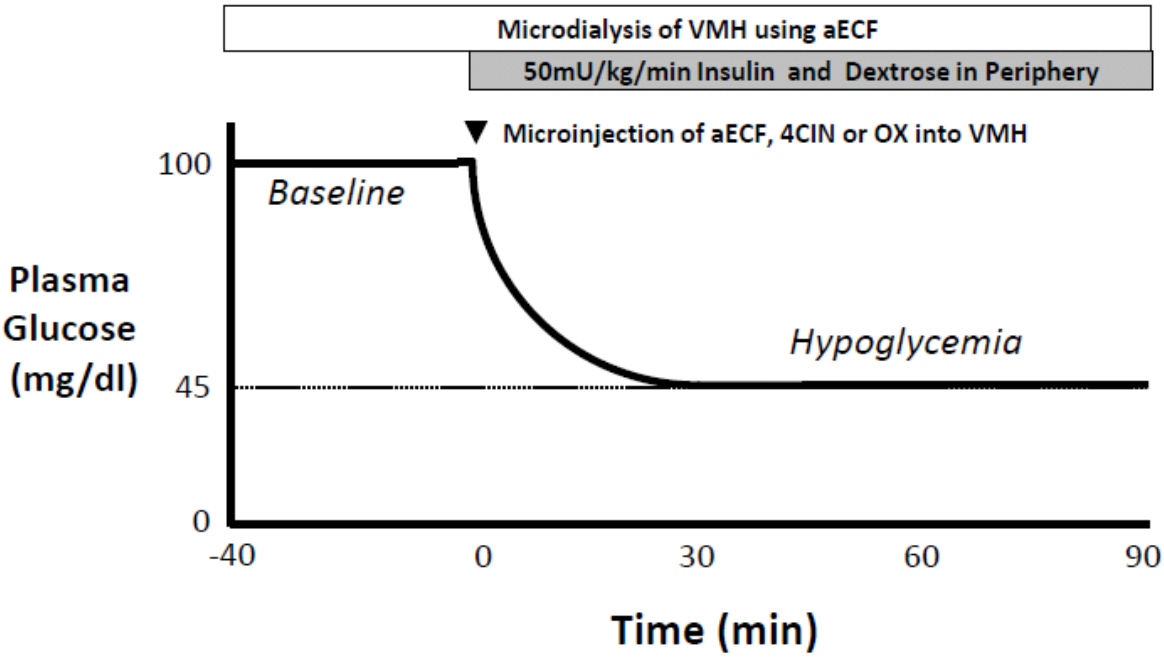
Supplementary Figure 1. Top panel: Schematic diagram showing glucose clamp protocol for *acute hypoglycemia* studies. Lower panel: Plasma glucose concentrations under baseline conditions (white bars) and during the hypoglycemic clamp (black bars). Control animals were perfused with aECF (Control; n=5). L-lactate animals received 100mM L-lactate by microdialysis and were microinjected with either aECF (L-Lactate; n=10), alpha-4-cyano-hydroxycinnate (L-Lactate+4CIN; n=6), oxamate (L-Lactate+OX; n=5), bicuculline (L-Lactate+BIC; n=8), or diazoxide (L-Lactate+DZ; n=5). A separate group of rats received 100mM D-lactate (D-Lactate; n=5) by microdialysis as an osmolarity control. No significant differences in plasma glucose levels were observed between treatment groups.

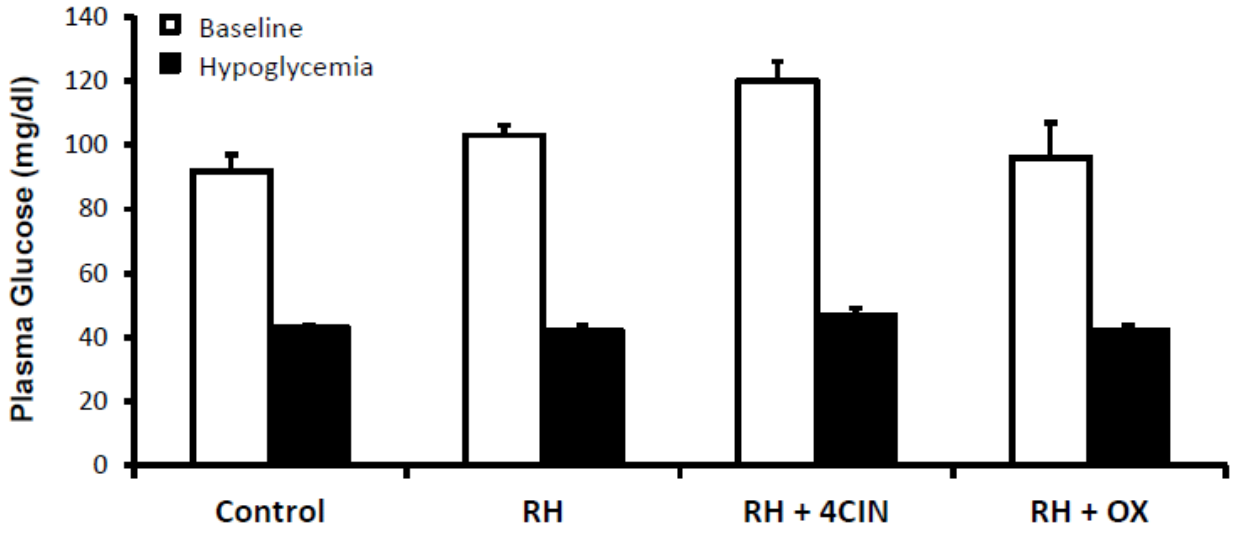




SUPPLEMENTARY DATA

Supplementary Figure 2. Top panel: Schematic diagram showing glucose clamp protocol for the *recurrent hypoglycemia* studies. Microdialysis was used to deliver either artificial extracellular fluid (aECF) or lactate into the VMH of the animals and microdialysate samples were taken throughout the clamp study to assess changes in GABA. Following microinjection of either aECF, alpha-4-cyano-hydroxycinnamic acid (4CIN) or oxamate (OX) into the VMH, a constant insulin and variable dextrose infusion were started and plasma glucose levels were lowered and maintained at 45±5mg/dL for the remainder of the study. Lower panel: Average plasma glucose levels under baseline conditions (white bars) and during hypoglycemia (black bars). Data presented as mean ± S.E.M. * $P<0.001$ vs. Control. # $P<0.02$ vs. Control.





SUPPLEMENTARY DATA

Supplementary Figure 3. Top panel: Schematic diagram showing glucose clamp protocol for *diabetes* studies. Microidlaysis was used to sample for GABA in the VMH of the animals during the clamp study. Following collection of baseline samples at -180 minutes, a constant insulin and variable dextrose infusion were used to lower plasma glucose levels of diabetic animals (dotted line) to euglycemic levels (115±10mg/dl) for 30 minutes. Non-diabetic controls (solid line) were maintained at euglycemia from the start of the study. Then, either aECF, alpha-4-cyano-hydroxycinnamic acid (4CIN) or oxamate (OX) was microinjected into the VMH, and plasma glucose levels were lowered and maintained at 45±5mg/dL for the remainder of the study. Lower panel: Average plasma glucose concentrations of normal, non-diabetic (Control; n=5), streptozotocin-diabetic (STZ; n=5) and streptozotocin-diabetic rats microinjected with either alpha-4-cyano-hydroxycinnate (STZ+4CIN; n=4) or oxamate (STZ+OX; n=5) under baseline (white bars), hyperinsulinemic-euglycemic (grey bars) and hypoglycemic clamp (black bars) conditions. Data presented as mean ± S.E.M.