

SUPPLEMENTARY DATA

Supplementary Table 1. Characteristics of the experimental groups before and during the pancreatic clamp studies during acute infusions of either vehicle or proline into the MBH.

	Vehicle	Proline
Basal		
Body weight (g)	308±2	319±2
Insulin (ng/ml)	1.9±0.3	0.9±0.1*
Glucagon (pg/ml)	83±10	85±6
Clamp		
Glucose (mM)	8.3±0.4	7.8±0.5
Insulin (ng/ml)	1.2±0.1	1.2±0.3
Glucagon (pg/ml)	33±7	39±7
Adiponectin (ng/ml)	3.7±0.3	3.7±0.2
MBH, mediobasal hypothalamus. Data are means±s.e.m.; n=4-6. Asterisk denote p<0.05 versus vehicle.		

Supplementary Table 2. Metabolic characteristics of the experimental groups before and during the pancreatic clamp studies in animals receiving systemic infusions of either vehicle or proline plus central (MBH) vehicle or LDH inhibitor.

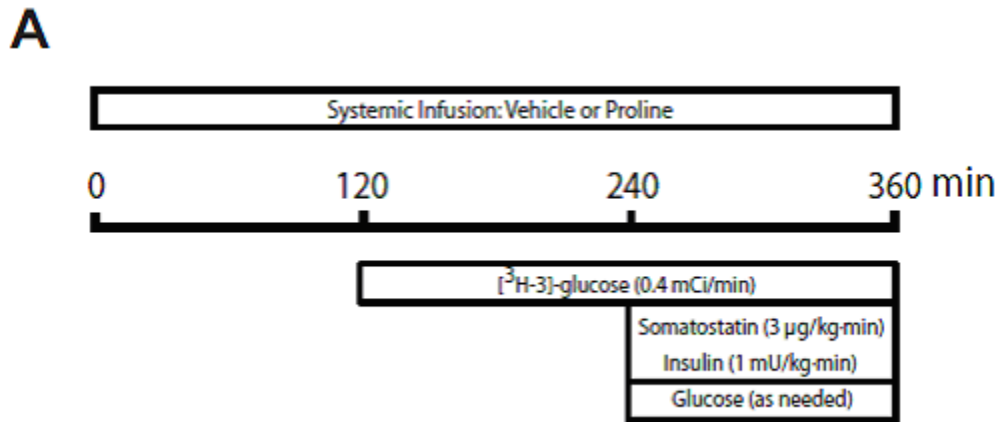
	Veh/Veh^a	Veh/Proline	LDHi/Proline
Basal			
Body weight (g)	330±10	328±9	330±8
Insulin (ng/ml)	1.3±0.2	0.9±0.2*	1.3±0.2
Glucagon (pg/ml)	89±15	93±6	85±10
Clamp			
Glucose (mM)	8.4±0.1	8.2±0.1	8.3±0.2
Insulin (ng/ml)	1.0±0.1	1.0±0.1	0.9±0.3
Glucagon (pg/ml)	69±15	67±15	63±12
Adiponectin (ng/ml)	1.2±0.2	1.1±0.2	1.2±0.4
MBH, mediobasal hypothalamus. ^a Infusions: MBH/Systemic. Data are means±s.e.m.; n=6-7. Asterisk denote p<0.05 versus veh/veh.			

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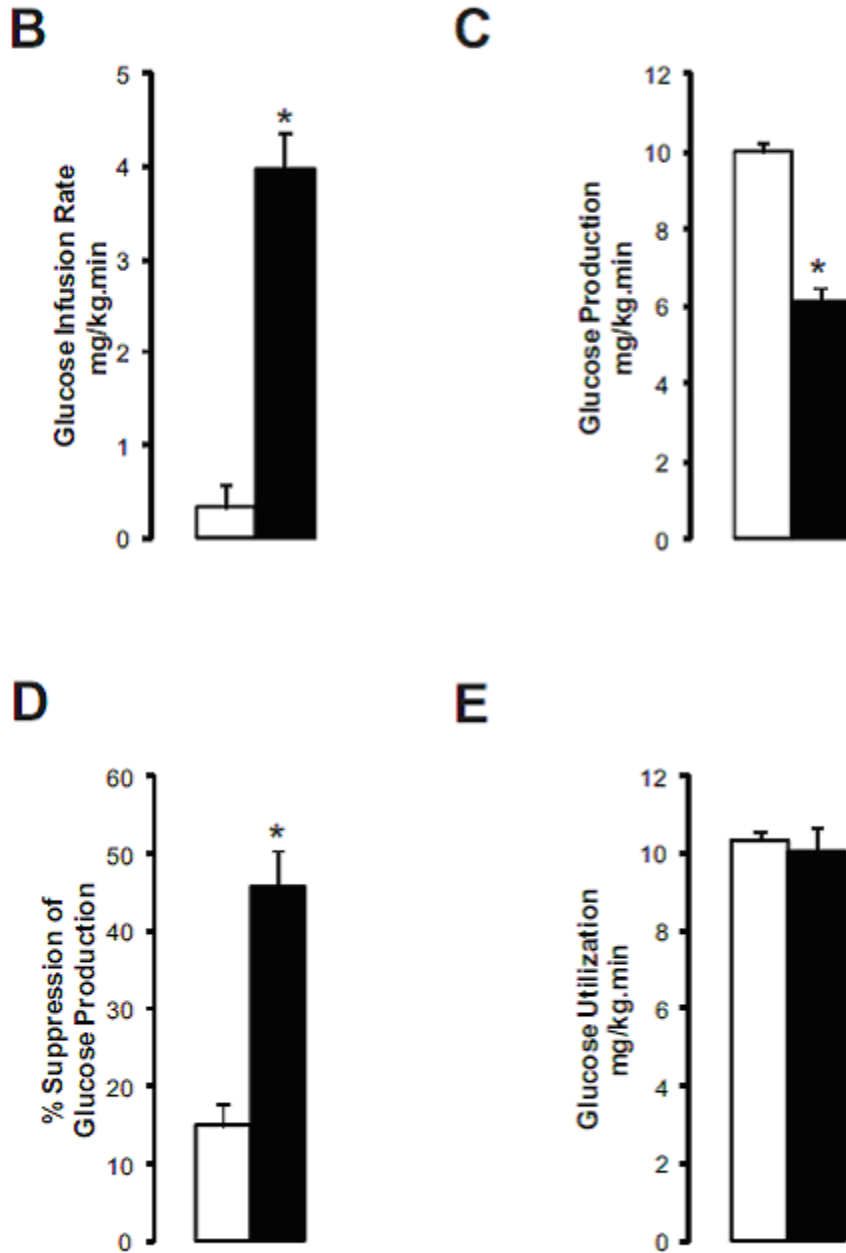
Supplementary Table 3. Metabolic parameters of animals injected with shRNA vectors in the MBH during the basal period and the pancreatic clamp studies receiving either vehicle or proline into the MBH.

	Vehicle		Proline	
	Ctrl	LdhA	Ctrl	LdhA
Basal				
Body weight (g)	327±5	324±6	330±8	329±9
Insulin (ng/ml)	1.3±0.2	1.3±0.2	1.0±0.1*	1.6±0.2
Glucagon (pg/ml)	79±22	82±21	105±18	100±22
Clamp				
Glucose (mM)	8.7±0.2	8.6±0.1	8.3±0.2	8.7±0.2
Insulin (ng/ml)	0.9±0.1	0.9±0.1	0.9±0.2	1.1±0.1
Glucagon (pg/ml)	43±14	45±7	67±16	59±16
Adiponectin (ng/ml)	2.5±0.4	2.5±0.3	1.9±0.3	2.0±0.3
MBH, mediobasal hypothalamus; Ctrl, non-silencing shRNA vector; LdhA, LdhA-shRNA vector. Data are means±s.e.m.; n=5-6. Asterisk denote p<0.05 versus the appropriate LdhA value.				

Supplementary Figure 1. Circulating proline regulates hepatic glucose production in animals with intact brains. **A**, Schematic of pancreatic clamp procedure in rats receiving systemic infusions of either proline or vehicle. The animals did not have cannulae implanted in the mediobasal hypothalamus (MBH). **B-E**, Effect of the systemic administration of either vehicle (n=6, white bars) or proline (n=6, black bars) on glucose infusion rate (**B**), glucose production (**C, D**), and glucose utilization (**E**). Asterisk denotes p<0.05 vs vehicle. All values are mean±s.e.m.



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Supplementary Figure 2. LDH-B expression is not affected by LDH-A specific knock down. LDH isoform expression was determined by Western blot analysis of HTC cells transfected with sequence specific LDH-A silencing RNA and probed with either LDH-A or LDH-B antibodies. Ab, antibody.

