

ONLINE APPENDIX

Supplemental Table 1. Baseline demographic values of non diabetic subjects and patients with type 1 diabetes

Units And Normal ranges	AGE Year	BMI kg/m ²	HbA1c % 4.0 - 6.5	Hgb g/dL M -14.0-18.1 F 11.8-16	K+ mEq/L 3.5 - 5.1	Total Bilirubin mg/dL 0.70 - 1.5	Creatinine mg/dL 0.2 - 1.2	AST U/L 4.0 - 40	ALT U/L 4.0 - 40	BP mmHg	Type 1 DM on insulin Pump %	Type 1 DM On multiple insulin injections%	Duration of diabetes
Healthy eugly	32±2	28±2	5.5±0.1	14±2	3.9±0.1	0.98±0.1	0.9±0.04	26±2	24 ±4	117/69±3/2	-	-	-
Healthy hypo	33±2	25±1	5±0.1	14±1	4±0.1	0.78±0.09	0.9±0.04	28±2	23 ±2	115/72±3/2	-	-	-
T1DM eugly	29±3	28±2	8±0.5	14±0.5	4.1±0.2	0.48±0.04	0.79±0.04	27±4	31±4	119/76±6/3	60	40	19±4
T1DM hypo	33±3	25±1	7.5±0.2	15±0.2	4±0.1	0.56±0.05	0.85±0.04	26±3	23±3	118/75±6/3	66	34	18±3

Hypo-hypoglycemia

Eugly-euglycemia

Hgb- hemoglobin

AST-Aspartate Aminotransferase

ALT-Alanine Aminotransferase

Supplemental Table 2. Comparison of baseline concentrations of cardiovascular markers in full cohort of non diabetic and type 1 diabetic subjects who participated in either euglycemic or hypoglycemic studies.

	Non Diabetic Subjects		Type 1 Diabetic Subjects	
	Eugly	Hypo	Eugly	Hypo
(ng/ml)	Baseline	Baseline	Baseline	Baseline
ICAM	89±7	79±7	88±3	73±4*
VCAM	844±42	675±39*	969±42	871±47
E-selectin	21±2	17±2	20±2	21±2
P-selectin (pg/mL)	75±8	61±8	89±13	67±9
PAI-1	29±4	24±4	40±6	23±3*
tPA	5.3±0.9	5.3±0.8	4.1±0.4	3.5±0.3
IL-6 (pg/mL)	15±4	14.5±4	8±3	16±7
TNF- α	2.3±0.4	2.7±0.5	1.3±0.3	2.4±0.5
VEGF (pg/mL)	27±8	17±5	19.5±7	13±7
Adiponectin	10660±617	10600±634	13370±924	14350±803

*p<0.05 –Hypoglycemia baseline values compared to euglycemia baseline

Supplemental Table 3. Comparison of baseline concentrations of cardiovascular markers before euglycemic and hypoglycemic clamps in non diabetic subjects and type 1 diabetic subjects undergoing both protocols.

	Non Diabetic Subjects		Type 1 Diabetic Subjects	
	Eugly	Hypo	Eugly	Hypo
(ng/ml)	Baseline	Baseline	Baseline	Baseline
ICAM	90±12	86±7	86±3	78±7
VCAM	862±53	728±67	999±42	990±58
E-selectin	24±4	20±3	22±4	21±5
P-selectin (pg/mL)	90±13	64±15	71±21	67±9
PAI-1	24±5	14±4	36±7	18±4*
tPA	5.2±2	4.4±2	4±1	3±1
IL-6 (pg/mL)	19±6	21±10	3±1	3±1
TNF- α	3±0.5	3±0.5	2±0.4	2±0.8
VEGF (pg/mL)	42±16	18±10	34±12	33±17
Adiponectin	9855±1061	9310±1277	13613±1692	15869±1732

*p<0.05 –Hypoglycemia baseline values compared to euglycemia baseline.

Figure A1. Effects of hyperinsulinemic euglycemia and hypoglycemia in overnight fasted healthy controls (n=10) and type 1 DM (n=7) subjects whom underwent both clamps on vascular biologic markers. Responses of V-CAM, E-selectin and VEGF were significantly increased during hypoglycemia as compared to euglycemia in healthy controls. Responses of VCAM, E-selectin and VEGF are significantly increased during hypoglycemia as compared to euglycemia in T1DM. Statistical difference with two-way ANOVA during the 120 min clamp experiments is marked in each graph panel.

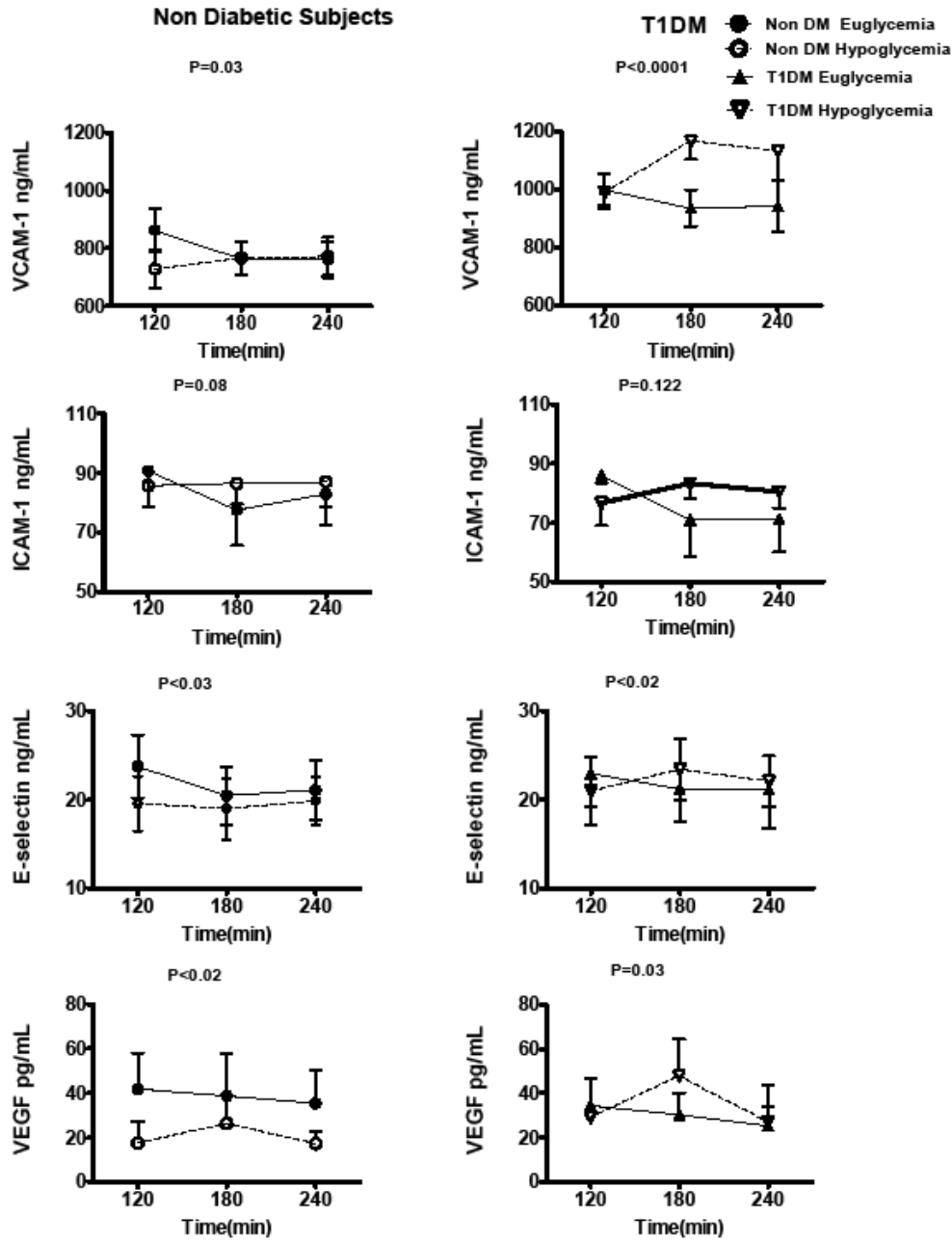


Figure A2. Effects of hyperinsulinemic euglycemia and hypoglycemia in overnight fasted healthy controls (n=10) and type 1 DM (n=7) subjects whom underwent both clamps on vascular biologic markers. Responses of PAI-1, P-selectin and adiponectin were significantly increased during hypoglycemia as compared to euglycemia in healthy controls. Statistical difference with two-way ANOVA during the 120 min clamp experiments is marked in each graph panel.

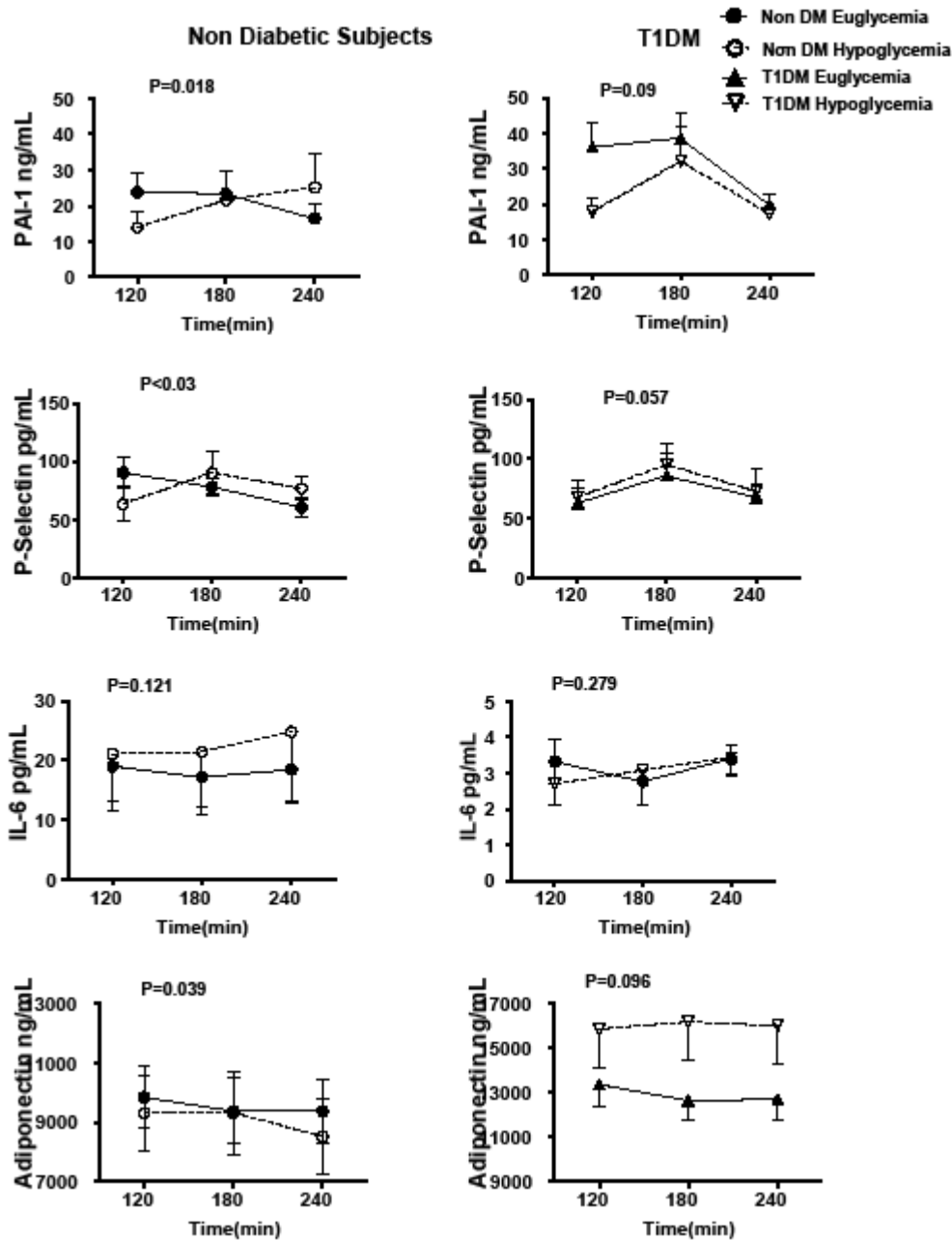


Figure A3. Glucose and insulin levels during the 2 hr hyperinsulinemic (9pmol/kg/min) euglycemic and hypoglycemic clamps in control and T1DM patients. Values are mean \pm SE.

