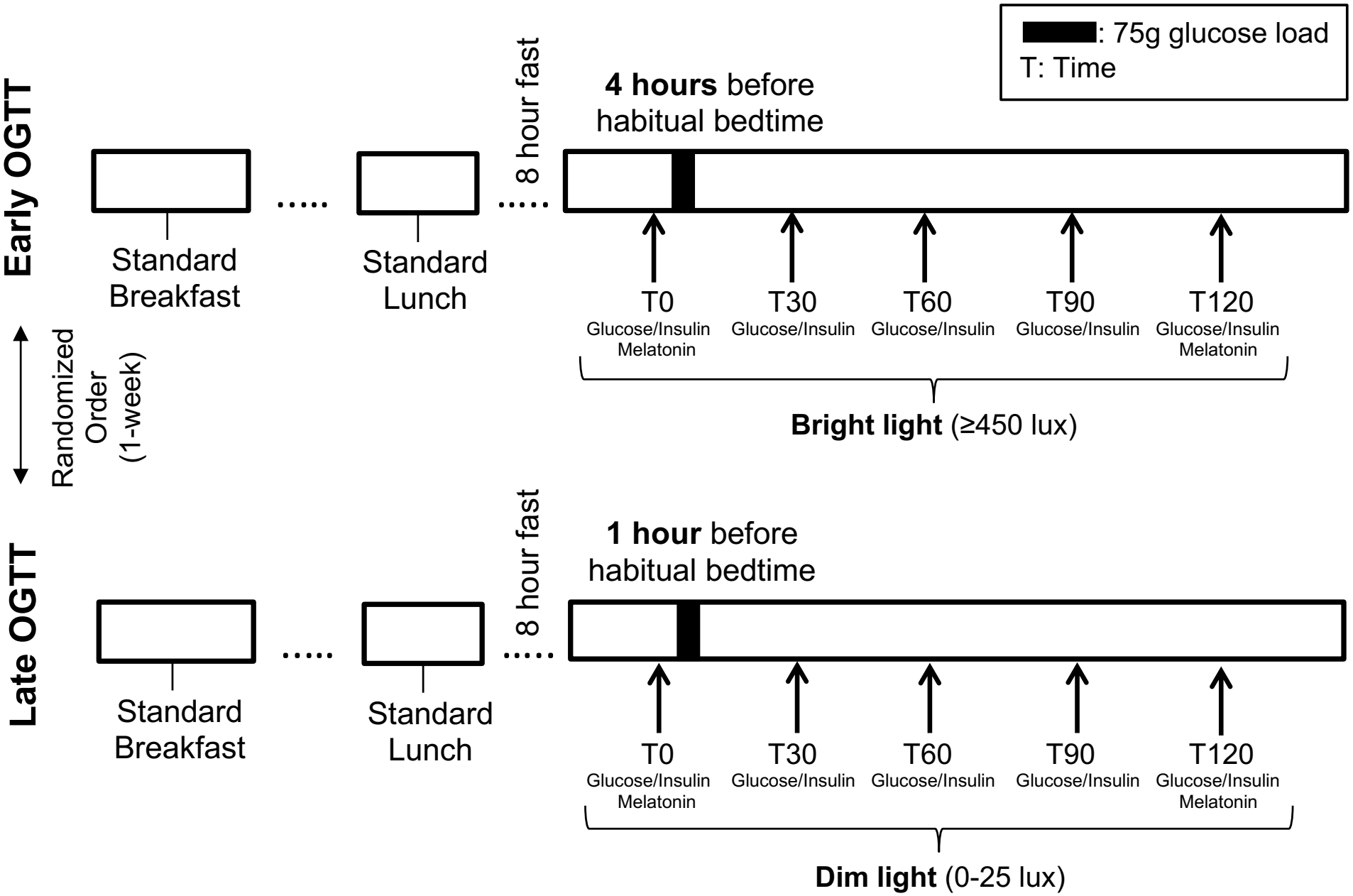
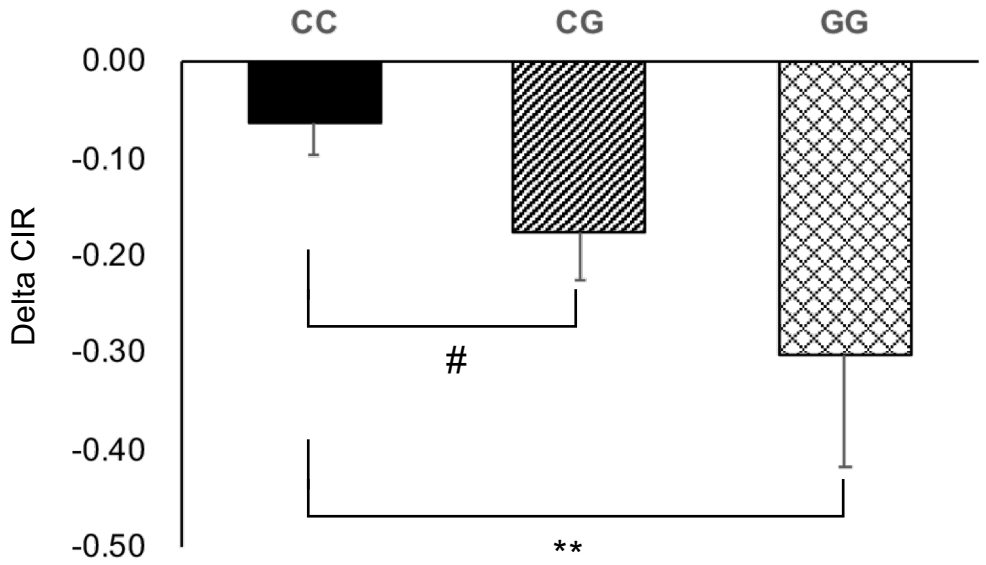
Supplemental Figure S1

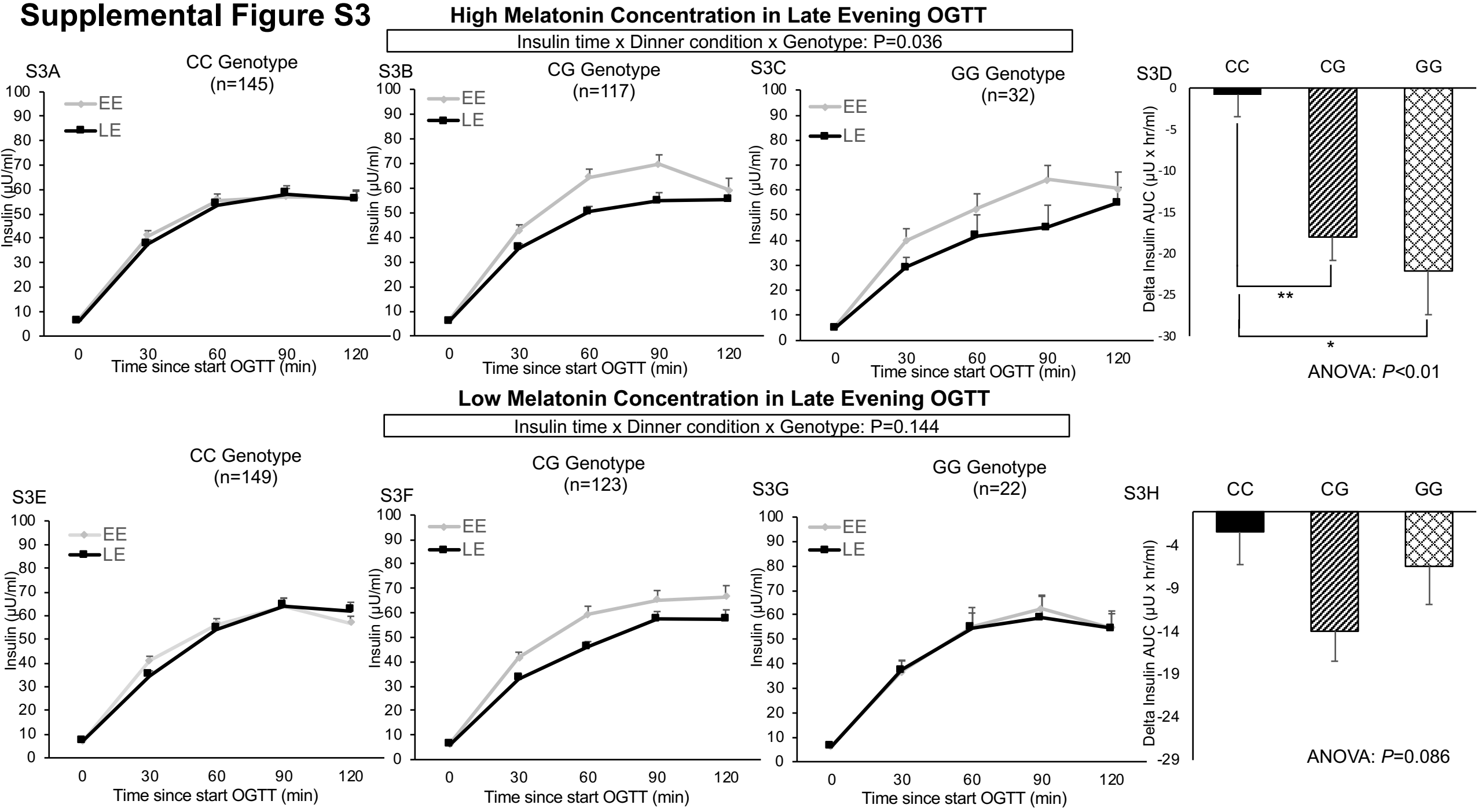


Supplemental Figure S2

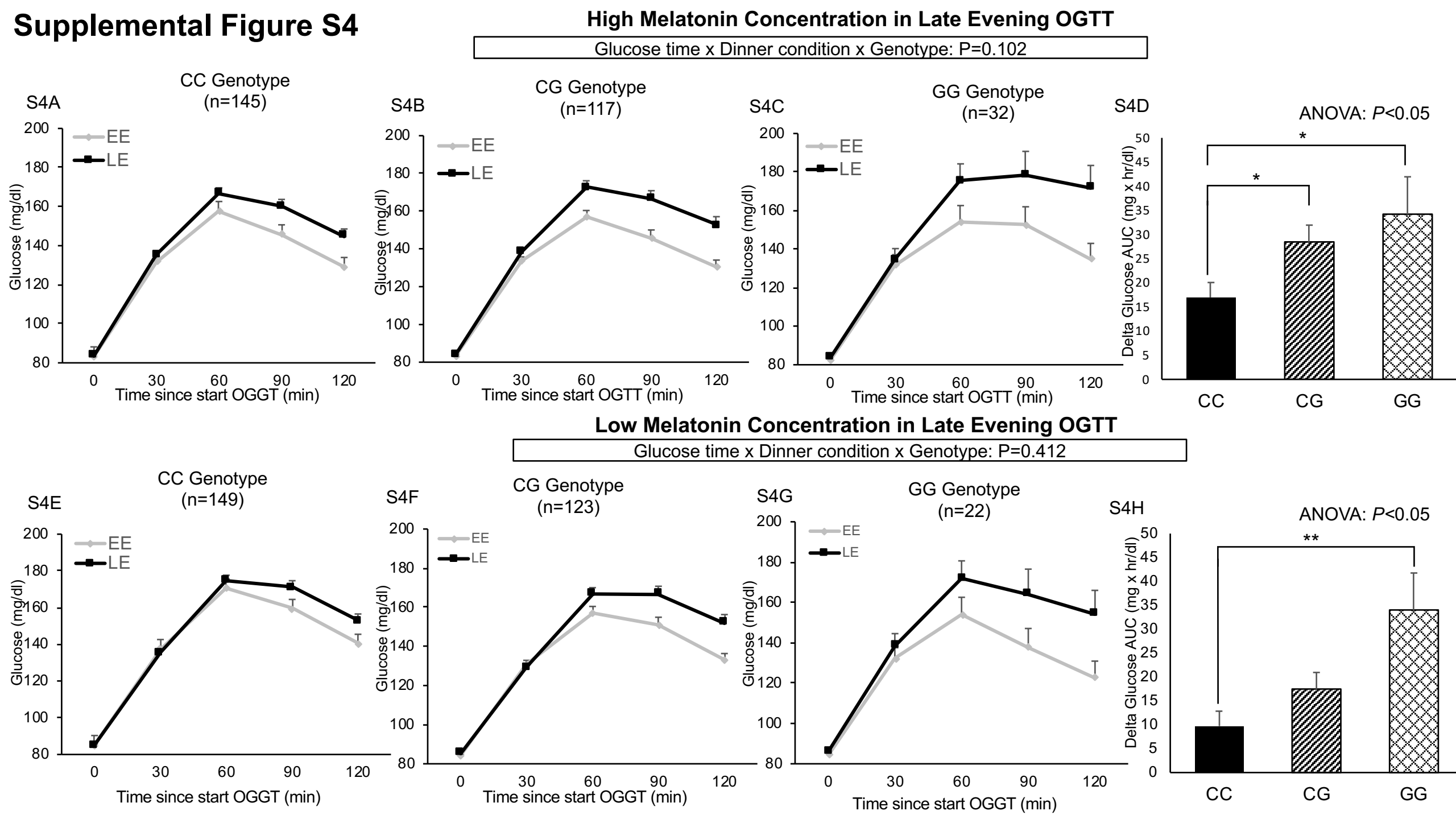


ANOVA: $P<0.05$

Supplemental Figure S3



Supplemental Figure S4



Supplemental Table S5.

			MTNR1B genotype								
	Total Population (n=845)		CC genotype (n=423)		CG genotype (n=342)		GG genotype (n=80)		Genotype (n=845)	Dinner timing (n=845)	Genotype X Dinner timing (n=845)
	EE	LE	EE	LE	EE	LE	EE	LE	P value	P value	P value
Test start time, hh:mm	19:49±00:40	22:48±01:00	19:47±00:39	22:44±01:14	19:51±00:04	22:50±00:42	19:50±00:39	22:50±00:39	0.100	0.0001	0.876
Fasting glucose, mg/dl	84.57±7.21	84.74±7.23	84.84±7.32	84.4±7.43	84.51±7.45	85.19±6.96	83.44±5.32	84.6±7.32	0.473	0.286	0.197
Postprandial glucose (30 min), mg/dl	132.68±25.24	136.53±25.78	134.4±26.11	136.19±24.19	131.21±23.96	135.8±26.41	129.91±25.52	141.39±30.58	0.327	0.001	**0.048**
Postprandial glucose (2 hours), mg/dl	132.71±37.80	153.07±43.13	134.52±38.87	149.60±42.23	130.67±36.15	154.34±42.92	131.85±39.04	166.03±46.39	0.097	0.001	**0.008**
Fasting insulin, µU/ml	6.46±4.3	6.07±4.1	6.7±4.61	6.32±4.51	6.25±4	5.87±3.73	6.15±3.75	5.55±3.09	0.064	0.091	0.956
Postprandial insulin (30 min), µU/ml	41.52±26.5	36.79±25.19	41.61±26.45	38.56±26.4	41.82±26.91	34.72±23.81	39.78±25.25	36.26±23.91	0.435	0.002	0.254
Glucose AUC (mgxhour/dl)	276.09±52.06	299.01±55.52	280.49±51.91	296.16±53.4	271.53±51.8	299.89±55.92	272.34±52.66	310.31±63.46	0.366	0.0001	**0.009**
Insulin AUC (µUxhour/ml)	98.25±51.55	91.67±50.13	96.27±50.41	95.99±53.21	100.71±53.35	88.04±47.62	98.21±49.82	84.36±41.5	0.599	0.005	**0.035**
Insulin/glucose AUC	6.2±3.18	5.65±3.04	5.98±3.11	5.98±3.25	6.44±3.29	5.40±2.89	6.27±3.06	4.97±2.21	0.872	0.0001	**0.023**
Insulin Sensitivity Index	7.29±4.92	7.71±5.98	7.28±5.22	7.55±6.12	7.33±4.73	7.89±5.89	7.15±3.94	7.79±5.75	0.795	0.154	0.869
Corrected Insulin Response	0.62±0.76	0.49±0.47	0.58±0.57	0.52±0.54	0.65±0.88	0.48±0.42	0.69±1	0.39±0.26	0.887	0.001	**0.022**
Disposition Index	3.89±4.38	3.15±3.15	3.49±3.04	3.26±3.51	4.28±5.48	3.07±2.53	4.39±4.96	2.93±3.53	0.293	0.001	**0.018**

EE: Early dinner timing condition. LE: Late dinner timing condition. Data are mean ± SD. AUC: Area Under the Curve.
The *P* values of the Genotype X Dinner timing interaction were calculated using a GLM Univariate Analysis (ANOVA).

Supplemental Table S6

Associations between MTNR1B risk variant and difference in glycemic outcomes between early and late dinner timing. Results are *per* additional copy of the G risk allele

	Beta (95% CI)	P value
Melatonin, baseline*‡(pg/ml)	1.42 (-3.45, 6.29)	0.569
Melatonin, 120 minutes* (pg/ml)	2.51 (-4.25, 9.27)	0.467
Glucose, fasting (mg/dl)	0.97 (0.2, 1.75)	0.014
Glucose, 30 minutes (mg/dl)	4.41 (1.7, 7.11)	<0.001
Glucose, 60 minutes (mg/dl)	6.89 (3.41, 10.36)	<0.0001
Glucose, 90 minutes (mg/dl)	7.63 (3.83, 11.43)	<0.0001
Glucose, 120 minutes (mg/dl)	9.55 (5.95, 13.16)	<0.0001
Insulin, fasting* (µU/ml)	-0.1 (-0.6, 0.4)	0.697
Insulin, 30 minutes* (µU/ml)	-2.3 (-5.26, 0.66)	0.128
Insulin, 60 minutes* (µU/ml)	-5.14 (-9.38, -0.89)	0.018
Insulin, 90 minutes* (µU/ml)	-7.37 (-12.07, -2.67)	0.002
Insulin, 120 minutes* (µU/ml)	-8.07 (-12.96, -3.18)	<0.001
Glucose, AUC (mgxhour/dl)	12.53 (8.08, 16.98)	<0.0001
Insulin, AUC* (µUxhour/ml)	-9.56 (-15.07, -4.06)	<0.001
Glucose to insulin ratio, AUC*	0.48 (0.15, 0.81)	<0.005
HOMA IR*	0 (-0.11, 0.1)	0.930
HOMA-B*	-12.69 (-29.35, 3.98)	0.136
QUICKI	0.09 (-0.28, 0.47)	0.620
Insulin sensitivity index*	0.25 (-0.45, 0.96)	0.479
Corrected insulin response*	-0.13 (-0.21, -0.05)	0.003
Disposition Index*	-0.77 (-1.28, -0.26)	0.003

Association results are from linear regression models adjusted for age, sex, and BMI with an additive genetic model.
*log-transformed outcome. ‡n=556.
AUC: Area Under the Curve; HOMA-IR: Homeostatic Model Assessment of Insulin Resistance; HOMA-B: Homeostatic model assessment; QUICKI: quantitative insulin sensitivity check index.

Supplemental Figure S1. Study protocol of ONTIME-MT study.
Individualized study protocol based on participants' habitual bedtime for early and late simulated dinner conditions. In both conditions, participants of the three genotype groups (CC, CG and GG) consumed standardized breakfast and lunch on that day prior to glucose load. Glucose bolus for the OGTT was scheduled 4 hours or 1 hour before habitual bedtime to simulate early and later dinner timing conditions, respectively. Habitual bedtime was determined using a study-specific smartphone application. Blood was collected for measurements of glucose and insulin prior to (T0) and T30, T60, T90 and T120 minutes after the start of the OGTT. Furthermore, blood for melatonin assessment was collected prior to (T0) and at T120 minutes after the start of the OGTT. At approximately ~30 minutes prior to and during the 2-hour tests, participants were placed in moderately bright light (≥450 lux) for the early dinner timing condition and in dim light (0-25 lux) for the late dinner timing condition. The order of the OGTTs was randomized, and OGTTs were conducted on the same day of the week with a 1-week washout period.

Supplemental Figure S2. Comparison of delta Corrected Insulin Response (CIR) (between late and early dinner timing condition) across *MTNR1B* risk variant. A one-way ANOVA was used to compare across MTNRIB genotypes (GG, CG and CC) ($P<0.05$), and Fisher´s LSD tests were used for pairwise comparisons among genotypes (*$P<0.05$; #a trend $P=0.061$).

Supplemental Figure S3. Comparison of insulin profiles and delta AUC among *MTNR1B* genotypes in low and high melatonin concentrations. Comparison of insulin secretion and delta insulin AUC among MTNR1B genotypes separately in individuals with low and high melatonin concentrations. Comparison between early and late simulated dinner timing conditions of serum insulin among MTNR1B genotypes when the population was divided by high serum melatonin concentrations (S3A, S3B, S3C) and low melatonin concentrations (S3E, S3F, S3G). Time 0 minutes is fasting. Panels S3D and S3H represents the delta between LE and EE of the insulin Area Under the Curve (AUC), for individuals with high and low melatonin concentrations, respectively. A one-way ANOVA test was used to determine potential differences across genotypes (GG, CG and CC) in the delta between late and early conditions for insulin AUC by high and low melatonin concentration ($P<0.01$, and $P=0.086$ respectively), and Fisher´s LSD tests were used for pairwise comparisons among genotypes for high melatonin concentration only (*$P<0.05$; **$P<0.01$).

Supplemental Figure S4. Comparison of glucose profiles and delta AUC among *MTNR1B* genotypes in low and high melatonin concentrations. Comparison of glucose profiles and delta glucose AUC among MTNR1B genotypes in individuals with low and high melatonin concentrations. Comparison between early and late simulated dinner timing conditions of serum glucose among MTNR1B genotypes when the population was divided by high melatonin concentrations (S3A, S3B, S3C) and low melatonin concentrations (S3E, S3F, S3G). Time 0 minutes is fasting. Panels S3D and S3H represents the delta between LE and EE of the glucose Area Under the Curve (AUC), separated by high and low melatonin concentrations, respectively. A one-way ANOVA test was used to determine potential differences across genotypes (GG, CG and CC) in the delta between late and early conditions for the glucose AUC by high and low melatonin concentration ($P<0.05$, and $P<0.05$ respectively), and Fisher´s LSD tests were used for pairwise comparisons among genotypes by high and low melatonin concentration (*$P<0.05$; **$P<0.01$).