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Glucose Response to an Oral Glucose Tolerance Test Predicts Weight Change in Non-diabetic Subjects

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Abstract

Objective—Glucose exerts a dual action in the regulation of energy balance, consisting of inhibition of energy intake and stimulation of energy expenditure. Whether blood glucose affects long-term regulation of body weight in humans remains to be established. We sought to test the hypothesis that the post-challenge glucose response is a predictor of weight change.

Research Methods and Procedures—We performed a prospective analysis of the impact of glucose response to an oral glucose tolerance test (OGTT) and a mixed-meal test (MT) on subsequent changes in body weight (BW) on 253 Pima Indians (166 men and 87 women) with normal glucose regulation at baseline and follow-up (follow-up: 7 ± 4 years). Main outcome measures included BW change (total, percent, and annual), plasma glucose and insulin concentrations during OGTT and MT [total and incremental areas under the curve (AUCs)], resting metabolic rate (RMR; indirect calorimetry), and insulin action (euglycemic-hyperinsulinemic clamp).

Results—Total and incremental glucose AUCs during the OGTT (but not the MT) were negatively associated with BW change (total, percent, and annual), both before and after adjusting for sex, age, initial BW, follow-up time, insulin action, RMR, fasting plasma glucose and insulin concentrations, and insulin response. Total and incremental glucose AUCs during the OGTT were independent determinants of final BW with age, initial BW, follow-up time, fasting plasma insulin concentrations, and RMR.

Discussion—Higher post-challenge glucose response protects against BW gain in subjects with normal glucose regulation. We propose that this action may be because of the effect of glucose on food intake and/or thermogenesis.

Keywords

post-load glucose response; weight regulation; predictors; Pima Indians

Introduction

An epidemic of overweight and obesity has developed in the United States over the past 20 years, with nearly two thirds of U.S. adults now overweight or obese (1). Although the pathogenesis of overweight and obesity is clearly complex, factors influencing energy intake are thought to play a pivotal role (2). Multiple internal (physiological) and external (environmental) factors are known to interact with each other to regulate energy intake and maintain energy homeostasis (3). Among the internal factors, blood glucose is an important

determinant of energy intake, primarily because of its tight regulation, limited storage, and dominant role as an energy source for the central nervous system (4). This hypothesis, referred to as the glucostatic theory, suggests that hunger and spontaneous meal initiation are stimulated, at least in part, by changes in circulating glucose. This has been shown in controlled experimental settings in animals (5) and humans (6). Glucose may also act as a biomarker of satiety (3). Human studies have shown that acute changes in blood glucose concentrations are associated with reciprocal changes in appetite sensations and food intake (7–10).

In addition, it is well known that both glucose administration and food intake are associated with an increase in energy expenditure (EE)¹ above the resting level, referred to as the thermic effect of food (TEF) (11,12). TEF is reduced in obese compared with lean subjects (11) and was shown to remain so in a group of obese women after weight reduction (13), pointing to a possible role for a reduced TEF as a risk factor for body weight (BW) gain.

These data indicate a dual role for glucose in the regulation of energy balance, including the stimulation of EE and the inhibition of energy intake. To test the hypothesis that the post-challenge glucose response is a predictor of BW change, we analyzed the impact of the glucose response during an oral glucose tolerance test (OGTT) and a mixed-meal test (MT) on subsequent changes in BW in a group of Pima Indians. Only subjects who had normal glucose regulation (NGR) at baseline and who did not develop diabetes during the follow-up were included in this analysis.

Research Methods and Procedures

Subjects

Subjects selected for this prospective analysis were Pima (or closely related Tohono O'Odham) Indians from the Gila River Indian Community near Phoenix, AZ. Members of this community have been participating since 1982 in an ongoing longitudinal study on the pathogenesis of type 2 diabetes (14), under a protocol approved by the Institutional Review Board of the National Institute of Diabetes and Digestive and Kidney Diseases and by the Tribal Council of the Gila River Indian Community. Participants in the longitudinal study were admitted for 8 to 15 days to the Clinical Research Unit of the NIH in Phoenix. Before participation, volunteers were fully informed of the nature and purpose of the study, and written informed consent was obtained. On admission to the metabolic ward, subjects were placed on a standard weight maintenance diet (20%, 30%, and 50% of daily calories provided as protein, fat, and carbohydrate, respectively) for 3 days before testing. Subsequently, volunteers underwent a metabolic assessment, including measurements of glucose tolerance, insulin action, and EE. For this prospective analysis, we selected only subjects who 1) were free of disease, according to physical examination, medical history, and laboratory testing; 2) had normal glucose regulation, defined as fasting plasma glucose <100 mg/dL and 2-hour glucose (OGTT) <140 mg/dL (15); 3) underwent both an OGTT and an MT; 4) had measurements of metabolic variables previously identified as predictors of weight gain in this population, namely insulin action (16) and resting metabolic rate (17); and 5) had at least one follow-up visit with an assessment of glucose tolerance. The follow-up exam was the last non-diabetic (as assessed by OGTT) visit that took place at least 6 months after the initial exam. Subjects were not receiving treatment for any chronic illnesses at the time of the follow-up visit. Only subjects with NGR at baseline who did not develop diabetes during the follow-up were included in this analysis, because impaired glucose homeostasis would be expected to confound the

¹Nonstandard abbreviations: EE, energy expenditure; TEF, thermic effect of food; BW, body weight; OGTT, oral glucose tolerance test; MT, mixed-meal test; NGR, normal glucose regulation; M, insulin-stimulated glucose disposal; AUC, area under the curve.

relationship between post-challenge glucose response and BW regulation, because of its effects on resting metabolic rate and insulin action (18).

Body Composition

Body composition was estimated by underwater weighing, with determination of residual lung volume by helium dilution, or by total body DXA (DPX-L; Lunar Radiation, Madison, WI), as previously described (14).

OGTT

After a 12-hour overnight fast, subjects underwent a 75-gram OGTT (19). Plasma samples were drawn at baseline and after 30, 60, 120, and 180 minutes for determination of plasma glucose and insulin concentrations. Glucose tolerance was classified according to the 2006 American Diabetes Association diagnostic criteria (15).

MT

After a 12-hour overnight fast, subjects consumed a standardized test meal containing 35% of their calculated 24-hour energy requirements distributed as 40% of total calories from fat, 40% from carbohydrate, and 20% from protein. All subjects finished the meal within 15 minutes. Blood samples for determination of plasma glucose and insulin concentrations were drawn at 0, 30, 60, 90, 120, 150, and 180 minutes. A complete meal test was available for 205 of 253 subjects (137 men and 68 women).

Hyperinsulinemic–Euglycemic Glucose Clamp

Insulin action was assessed by a hyperinsulinemic–euglycemic glucose clamp, and the rate of total insulin-stimulated glucose disposal (M) was calculated, as previously described (14).

Indirect Calorimetry

After an overnight fast, resting metabolic rate was measured for 45 minutes using a ventilated hood system, as previously described (20).

Analytical Measurements

Plasma glucose concentrations were measured using the glucose oxidase method (Beckman Instruments, Fullerton, CA). Plasma insulin concentrations were measured by three different radioimmunoassays, which have been used over time in our laboratory: a modified Herbert-Lau assay was used from the beginning to 1986; Concept 4 (Concept 4; ICN, Costa Mesa, CA) was used from 1987 to 1998; and Access (Beckman Instruments) has been used from 1999 to the present. All measurements of insulin were normalized to the original radioimmunoassay by using regression equations.

Statistical Methods

The total and incremental areas under the curve (AUCs) for plasma glucose and insulin concentrations during the OGTT and MT were determined by the trapezoidal method. The total weight change was calculated as final weight minus initial weight. The percentage weight change was calculated as final weight minus initial weight divided by initial weight multiplied by 100. The annual percentage weight change was calculated as final weight minus initial weight divided by initial weight and number of years of follow-up multiplied by 100. All statistical analyses were performed using the software of the SAS Institute (SAS version 8.2; SAS Institute, Cary, NC). Simple and partial Spearman correlation analyses were used to evaluate the relationships of total weight change, percent weight change, and annual percentage weight change with the other study variables while adjusting for confounders. General linear

regression models were used to examine the relationships between post-challenge glucose response and final body weight (log-transformed to approximate a normal distribution) while adjusting for age, sex, initial BW, follow-up time, post-challenge insulin secretion, M, resting metabolic rate, and fasting concentrations of glucose and insulin.

Results

Baseline Characteristics

The subjects (166 men and 87 women) were young adult (age: 18 to 44 years) Pima Indians spanning a wide range of adiposity (body fat: 10% to 49%). Mean duration of follow-up was 7 ± 4 years, and over this period of time, BW increased by a mean of 9 kg (10%), corresponding to an average increase in BW of 2% per year (Table 1).

Uni- and Multivariate Linear Regression Analyses of Baseline Post-load Glucose Response

The total AUCs for plasma glucose concentrations during the OGTT (OGTT_{Total AUC glucose}) and the MT (MT_{Total AUC glucose}) were positively correlated with age ($r: 0.17, p = 0.005$; and $r: 0.20, p = 0.003$, respectively), body fat ($r: 0.20, p = 0.001$; and $r: 0.28, p < 0.0001$, respectively), fasting plasma glucose concentrations ($r: 0.41, p < 0.0001$; and $r: 0.64, p < 0.0001$, respectively), fasting plasma insulin concentrations ($r: 0.21, p = 0.0008$; and $r: 0.27, p = 0.0002$, respectively), and the total AUC for plasma insulin concentrations ($r: 0.33, p < 0.0001$; and $r: 0.34, p < 0.0001$, respectively) and were negatively associated with M ($r: -0.31, p < 0.0001$; and $r: -0.27, p < 0.0001$, respectively). The incremental AUCs for plasma glucose concentrations during the OGTT (OGTT_{Incremental AUC glucose}) and the MT (MT_{Incremental AUC glucose}) were positively correlated with the incremental AUC for plasma insulin concentrations ($r: 0.33, p < 0.0001$; and $r: 0.23, p = 0.001$, respectively) and negatively associated with M ($r: -0.23, p = 0.0002$; and $r: -0.17, p = 0.01$, respectively). All these associations remained significant also after adjustment for sex, age, and percentage body fat by general linear regression modeling (data not shown).

Univariate Linear Regression Analysis of Changes in Body Weight

The relationships between changes in body weight and the variables of interest are shown in Table 2. The total weight change, percent weight change, and annual percentage weight change were negatively associated with age ($p = 0.05, p = 0.03$, and $p = 0.04$, respectively) and fasting plasma insulin concentrations ($p = 0.08, p = 0.0002$, and $p = 0.09$, respectively). M was significantly associated with the percentage weight change ($r: 0.20, p = 0.002$). Both OGTT_{Total AUC glucose} and OGTT_{Incremental AUC glucose} (Figure 1), but neither MT_{Total AUC glucose} nor MT_{Incremental AUC glucose}, were negatively associated with the total weight change ($p = 0.002$ and $p = 0.002$, respectively), percent weight change ($p = 0.0004$ and $p = 0.002$, respectively), and annual percentage weight change ($p = 0.03$ and $p = 0.005$, respectively).

Multivariate Analyses of Changes in Body Weight

Two statistical approaches were used to analyze the adjusted effects of both OGTT_{Total AUC glucose} and OGTT_{Incremental AUC glucose} on BW regulation. The first approach consisted of partial correlation analyses of OGTT_{Total AUC glucose} and OGTT_{Incremental AUC glucose} vs. total weight change, percent weight change, and annual percentage weight change, with possible confounders as partial variables. Both OGTT_{Total AUC glucose} and OGTT_{Incremental AUC glucose} remained negatively associated with the total weight change (partial $r: -0.20, p = 0.002$; and partial $r: -0.18, p = 0.004$, respectively), percent weight change (partial $r: -0.20, p = 0.002$; and partial $r: -0.18, p = 0.004$, respectively), and annual percentage weight change (partial $r: -0.16, p = 0.01$; and partial $r: -0.15, p = 0.02$, respectively), after

adjusting for sex, age, initial BW, follow-up time, M, resting metabolic rate, fasting plasma concentrations of glucose and insulin, and OGTT_{Total AUC} insulin or OGTT_{Incremental AUC} insulin, respectively.

The second approach consisted of general linear regression models adjusted for age, sex, initial BW, follow-up time, fasting plasma concentrations of glucose and insulin, M, resting metabolic rate, and the post-load insulin response, to determine independent predictors of final BW. These multivariate analyses revealed that both OGTT_{Incremental AUC} glucose (Table 3) and OGTT_{Total AUC} glucose (data not shown) were independent, negative determinants of final BW, along with age (negative), initial BW (positive), follow-up time (positive), fasting plasma insulin concentrations (negative), and resting metabolic rate (negative).

Discussion

A higher plasma glucose response during an OGTT was associated with lower BW gain in this study, independent of potential confounding variables known to be predictors of BW change, including resting metabolic rate (17) and insulin action (16). The effect of post-load increases in plasma glucose on long-term BW change may be related to the role of blood glucose as a biomarker of satiety (3). Central and peripheral chronic infusions of glucose are known to reduce food intake and BW in rats (21,22). Changes in blood glucose concentrations can affect appetite sensations and short-term food intake in humans, independent of insulin concentrations (8). Clamp studies carried out under euglycemic and hyperglycemic conditions indicate that higher glucose concentrations are associated with lower hunger scores and higher satiety scores (9). Similarly, glucose preloads have been shown to lower energy intake during a subsequent meal; moreover, the glucose AUC was negatively correlated with the subjective ratings of appetite and food intake (23). Likewise, a higher blood glucose response was associated with longer intermeal intervals in a study of meal patterns in time-blinded men (6). Finally, interstitial glucose concentrations (mirroring blood glucose concentrations) were found to be a significant determinant of meal size in normal subjects (24).

The physiological underpinnings of this effect of glucose are multifaceted. Glucose-sensing neurons are located in brain areas involved in the control of neuroendocrine function and nutrient metabolism (25). The integrated output of these neurons is relayed to neurohumoral and autonomic effector areas involved in the regulation of overall energy homeostasis (26). In addition to the role of central glucose sensing in the regulation of food intake and BW, changes in plasma glucose concentrations can also affect gastrointestinal motility. Elevations of blood glucose within the normal postprandial range have been shown to slow gastric emptying compared with euglycemia (27). The magnitude of the postprandial rise in blood glucose has been negatively correlated with gastric emptying in healthy subjects (28). Hyperglycemia has also been found to enhance the perception of gut stimuli, such as gastric distension (29), and has been associated with reduced perception of postprandial hunger (30) in normal subjects.

These findings indicate that postprandial increases in plasma glucose can prompt meal termination and affect subsequent food intake. Interestingly, Bady et al. (31) have recently shown that central glucose sensing is a critical physiological regulator of food intake by showing a loss of feeding regulation by glucose and concomitant increase in food intake in rats lacking glucose transporter 2-dependent glucose sensors. On this basis, we speculate that the negative association between the post-load blood glucose response and BW change, independent of insulin action, insulin secretion, and resting metabolic rate, is the result of the proposed role of glucose as a satiety signal, in that a delayed decline in blood glucose can postpone meal initiation, thus leading to lower overall food intake and BW gain over time. In fact, when we examined the associations between the annual percentage weight change and blood glucose response from fasting to each of the subsequent time-points of the OGTT, after

adjustment for sex, age, and the respective insulin response (data not shown), there was a progressive increase in the strength of these correlations; viz., the change in plasma glucose between fasting and 30 minutes and the glucose AUC from fasting to 60 minutes were not correlated with the annual percentage weight change; there was a borderline association with glucose AUC from fasting to 120 minutes; and there was a stronger association, as reported above, with the glucose AUC from fasting to 180 minutes. These findings lend further support to the hypothesis that a longer blood glucose response may prolong satiety and delay initiation of the following meal, thus contributing to BW regulation. The fact that only the post-load glucose response, but not fasting plasma glucose concentrations, was an independent predictor of BW change in this study is not surprising because the pattern of blood glucose over time, rather than glucose concentration per se, represents the critical signal prompting meal initiation/termination (3).

The effect of postprandial increases in plasma glucose on long-term BW change may also be related to the TEF. Oral ingestion of glucose is associated with an increase in EE (13). TEF is positively related to satiety and negatively associated with hunger scores (32–34). Therefore, a higher TEF may be associated with lower rates of BW gain over time, either directly (i.e., by increasing total EE) or indirectly (i.e., by leading to earlier satiety). TEF is reportedly lower in obese compared with lean subjects (35) and has been shown to remain so after weight reduction (13), indicating that a reduced TEF may precede obesity and possibly contribute to its pathogenesis. Although these have not been unanimous findings (36–39), we speculate that the higher BW gain in subjects with lower post-load blood glucose response, independent of insulin action, insulin secretion, and resting metabolic rate, may also reflect lower rates of TEF, thus leading to lower total EE and higher BW gain over time.

One might speculate that, because all subjects were given the same challenge during the OGTT, i.e., 75 grams of glucose, individuals with smaller body size may have had a higher plasma glucose response and gained less weight over time. This was not the case, however, in this study. In fact, initial weight was related neither to the glucose response during the OGTT nor to the degree of weight change (data not shown), thus making the above possibility unlikely. The stimulus used for the OGTT, i.e., glucose ingestion, evokes a greater postprandial response than a conventional mixed-meal, as previously discussed (40). The MT consists of a bacon-and-egg sandwich that is consumed over a 15-minute period. The OGTT is performed by administering 75 grams of glucose dissolved in water over a 3-minute period. Therefore, the glucose patterns during the two procedures were quite different (i.e., lower during the MT) because of the lower absolute amount of carbohydrate and the presence of complex carbohydrates (as opposed to a simple sugar), as well as other macronutrients, in the MT. This leads to profound differences in digestion, absorption, and processing of nutrients. In fact, the glucose AUC during the MT was not a significant predictor of BW change, as opposed to the glucose AUC during the OGTT. As such, results from this and other studies that have used oral glucose as an experimental model may overestimate the observed effect of glucose compared with real-life conditions. Alternatively, one can speculate that higher increases in plasma glucose concentrations, such as those elicited by an OGTT, are needed to detect the effects of glucose on food intake (i.e., glucose sensing) and/or metabolic rate (i.e., TEF) and, consequently, BW regulation in this setting.

This study involved only Pima Indians, a population with an extremely high prevalence of obesity and type 2 diabetes (41). Therefore, it has to be taken into account that the protective role of a higher post-load glucose response against weight gain may be unique to this population. Hence, these findings need to be confirmed by studies including a more heterogeneous population to indicate a general physiological mechanism.

This study also confirmed the previously reported role of EE and insulin action in the regulation of BW (16,17), even though M did not maintain an independent association with final BW in the fully adjusted model. In addition, fasting plasma insulin concentrations were an independent, negative predictor of both final BW and BW change. This finding is in keeping with a previous study (42) in which this observation was interpreted as supporting the notion that insulin resistance is associated with lower rates of BW gain (42). Only ~50% of the variability in the fasting plasma insulin concentration, however, can be accounted for by insulin sensitivity (43). Therefore, fasting insulinemia may have a role in BW regulation, independent of insulin resistance. In fact, the negative association between fasting plasma insulin concentrations and BW change in this study was retained after adjustment for confounders, including insulin action. Although the peripheral actions of insulin are anabolic (i.e., increasing energy storage and potentially increasing body weight), its central action is fundamentally catabolic (i.e., reducing food intake and body weight) (44), through its effects on central nervous system areas involved in the regulation of energy balance (45).

In conclusion, lower post-load blood glucose response predisposed to BW gain in a prospective study of Pima Indians with normal glucose regulation. This effect was independent of the previously reported associations of higher insulin sensitivity and reduced resting metabolic rate with higher rates of BW gain in this population. In light of the role of glucose sensing in food intake regulation and the ability of glucose to stimulate EE, we propose that the protective effect of a higher post-load blood glucose response within the normal range against BW gain may be mediated by lower food intake and/or higher glucose-induced thermogenesis.

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Figure 1.

Relationships of the incremental AUC for plasma glucose concentrations during the OGTT with the total weight change (A), percent weight change (B), and annual percentage weight change (C) in the study population.

Table 1

Characteristics of the study subjects

	Mean $\pm$ standard deviation	Range
Sex (M/F)	166/87	—
Age (years)	27 $\pm$ 6	18 to 44
Body fat (%)	31 $\pm$ 8	10 to 49
Fasting glucose (mg/dL)	86 $\pm$ 7	60 to 98
Fasting insulin (μ U/mL)	38 $\pm$ 19	10 to 123
Resting metabolic rate (kcal/24 h)	1777 $\pm$ 330	718 to 3120
M (mg/kg EMBS/min)	2.9 $\pm$ 1.2	1.4 to 8.4
OGTT _{Total AUC} glucose (mg/dL per 180 minutes)	20376 $\pm$ 2602	12,720 to 26,835
OGTT _{Incremental AUC} glucose (mg/dL per 180 minutes)	4961 $\pm$ 2354	-1755 to 10,755
MT _{Total AUC} glucose (mg/dL per 180 minutes) *	580 $\pm$ 50	432 to 709
MT _{Incremental AUC} glucose (mg/dL per 180 minutes) *	61 $\pm$ 42	-60 to 199
Initial weight (kg)	92 $\pm$ 22	46 to 177
Final weight (kg)	101 $\pm$ 26	45 to 184
Weight change (kg)	9 $\pm$ 11	-21 to 47
Weight change (%)	10 $\pm$ 11	-31 to 46
Weight change (%/year)	2 $\pm$ 2	-4 to 11
Follow-up (years)	7 $\pm$ 4	0.5 to 14

Data are *n* or means $\pm$ standard deviation and range. EMBS, estimated metabolic body size.

* Men (*n* = 137); women (*n* = 68).

Table 2
Correlation analyses between changes in body weight and other characteristics of interest

	Weight change		
	Kilograms	Percent	Percent/year
Age (years)	<i>r</i> : -0.12 <i>p</i> = 0.05	<i>r</i> : -0.14 <i>p</i> = 0.03	<i>r</i> : -0.13 <i>p</i> = 0.04
Body fat (%)	<i>r</i> : 0.05 <i>p</i> = 0.4	<i>r</i> : -0.07 <i>p</i> = 0.3	<i>r</i> : -0.01 <i>p</i> = 0.9
Fasting glucose (mg/dL)	<i>r</i> : -0.003 <i>p</i> = 0.9	<i>r</i> : -0.06 <i>p</i> = 0.3	<i>r</i> : 0.08 <i>p</i> = 0.2
Fasting insulin (μU/mL)	<i>r</i> : -0.11 <i>p</i> = 0.08	<i>r</i> : -0.23 <i>p</i> = 0.0002	<i>r</i> : -0.10 <i>p</i> = 0.09
M (mg/kg EMBS/min)	<i>r</i> : 0.07 <i>p</i> = 0.3	<i>r</i> : 0.20 <i>p</i> = 0.002	<i>r</i> : 0.07 <i>p</i> = 0.2
Adjusted resting metabolic rate (kcal/d)	<i>r</i> : -0.10 <i>p</i> = 0.1	<i>r</i> : -0.10 <i>p</i> = 0.1	<i>r</i> : 0.03 <i>p</i> = 0.7
OGTT _{Total} AUC glucose (mg/dL per 180 minutes)	<i>r</i> : 0.19 <i>p</i> = 0.002	<i>r</i> : -0.22 <i>p</i> = 0.0004	<i>r</i> : -0.13 <i>p</i> = 0.03
OGTT _{Incremental} AUC glucose (mg/dL per 180 minutes)	<i>r</i> : -0.19 <i>p</i> = 0.002	<i>r</i> : -0.19 <i>p</i> = 0.002	<i>r</i> : -0.17 <i>p</i> = 0.005
MT _{Total} AUC glucose (mg/dL per 180 minutes) *	<i>r</i> : -0.05 <i>p</i> = 0.4	<i>r</i> : -0.09 <i>p</i> = 0.2	<i>r</i> : 0.02 <i>p</i> = 0.7
MT _{Incremental} AUC glucose (mg/dL per 180 minutes) *	<i>r</i> : -0.09 <i>p</i> = 0.2	<i>r</i> : -0.09 <i>p</i> = 0.2	<i>r</i> : -0.05 <i>p</i> = 0.5

EMBS, estimated metabolic body size.

* Men (*n* = 137); women (*n* = 68).

Table 3Determinants of final body weight ($\log_{10}$)*

	β	p
Intercept	1.611	<0.0001
Sex (M)	0.003	0.6
Age (years)	-0.001	0.008
Initial body weight (kg)	0.005	<0.0001
Follow-up (years)	0.002	0.03
Fasting glucose (mg/dL)	0.0001	0.8
Fasting insulin (μ U/mL)	-0.0006	0.005
M (mg/min)	0.001	0.6
RMR (kcal/d)	-0.00003	0.02
OGTT _{Incremental AUC} insulin (μ U/mL per 180 minutes)	0.0000004	0.1
OGTT _{Incremental AUC} glucose (mg/dL per 180 minutes)	-0.000004	0.004

* Using general linear regression modeling (R^2 : 0.84, $p < 0.0001$).