Fasting Until Noon Triggers Increased Postprandial Hyperglycemia and Impaired Insulin Response After Lunch and Dinner in Individuals With Type 2 Diabetes: A Randomized Clinical Trial

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OBJECTIVE

Skipping breakfast has been consistently associated with high HbA_{1c} and postprandial hyperglycemia (PPHG) in patients with type 2 diabetes. Our aim was to explore the effect of skipping breakfast on glycemia after a subsequent isocaloric (700 kcal) lunch and dinner.

RESEARCH DESIGN AND METHODS

In a crossover design, 22 patients with diabetes with a mean diabetes duration of 8.4 ± 0.7 years, age 56.9 ± 1.0 years, BMI 28.2 ± 0.6 kg/m^2, and HbA_{1c} 7.7 ± 0.1% (61 ± 0.8 mmol/mol) were randomly assigned to two test days: one day with breakfast, lunch, and dinner (YesB) and another with lunch and dinner but no breakfast (NoB). Postprandial plasma glucose, insulin, C-peptide, free fatty acids (FFA), glucagon, and intact glucagon-like peptide-1 (iGLP-1) were assessed.

RESULTS

Compared with YesB, lunch area under the curves for 0–180 min ($AUC_{0–180}$) for plasma glucose, FFA, and glucagon were 36.8, 41.1, and 14.8% higher, respectively, whereas the AUC_{0-180} for insulin and iGLP-1 were 17% and 19% lower, respectively, on the NoB day ($P < 0.0001$). Similarly, dinner AUC_{0-180} for glucose, FFA, and glucagon were 26.6, 29.6, and 11.5% higher, respectively, and AUC_{0-180} for insulin and iGLP-1 were 7.9% and 16.5% lower on the NoB day compared with the YesB day ($P < 0.0001$). Furthermore, insulin peak was delayed 30 min after lunch and dinner on the NoB day compared with the YesB day.

CONCLUSIONS

Skipping breakfast increases PPHG after lunch and dinner in association with lower iGLP-1 and impaired insulin response. This study shows a long-term influence of breakfast on glucose regulation that persists throughout the day. Breakfast consumption could be a successful strategy for reduction of PPHG in type 2 diabetes.

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A slide set summarizing this article is available online.

In type 2 diabetes, postprandial hyperglycemia (PPHG) has a tremendous effect on HbA_{1c} values and is strongly associated with future development of vascular complications even when glycemic control is restored (1–3). Therefore, mitigating glycemic peaks may be a particularly important target in the initial stages of the disease to slow the progressive decline of β-cell function and improve overall outcomes.

Most of the metabolic pathways involved in postprandial glycemia, including β-cell secretory function, insulin sensitivity, muscular glucose uptake, muscle glycogen storage, and hepatic glucose output, are controlled by the circadian clock (4). As a result, PPHG displays a clear circadian pattern, with a more prolonged and higher response to identical meals in the evening than in the morning (5–10). Because meal timing is a potent synchronizer for the circadian clock, it affects the daily variations of postprandial glycemia in healthy individuals and in individuals with type 2 diabetes (4,5,8,10). Therefore, meal timing may be a crucial component if mitigation of glycemic peaks is required.

Breakfast has previously been demonstrated to be of major importance for the 24-h regulation of glucose (11). This is highly relevant, because skipping breakfast has progressively increased over the past decades in Western society (11). In fact, skipping breakfast has been shown to be associated with weight gain and other adverse health outcomes, including insulin resistance and an increased risk for developing type 2 diabetes. In addition, in individuals with type 2 diabetes, the omission of breakfast is associated with a significant increase in HbA_{1c} and all-day PPHG even without overeating in the evening (12–14). In contrast, consumption of a high-energy breakfast and a low-energy dinner results in a significant reduction of all-day postprandial glycemia (10). Similarly, 3 months of a high-energy breakfast led to a 5% (31 mmol/mol) reduction in HbA_{1c} levels in participants with type 2 diabetes (15).

Despite the growing evidence showing the beneficial effects of breakfast consumption on overall PPHG and HbA_{1c} levels, very little is known regarding the relationship between breakfast skipping and all-day glycemic excursions in patients with type 2 diabetes. Although omission of breakfast has been demonstrated to be associated with a higher glycemic response after a liquid preload (16) or lunch in healthy individuals (17) and in individuals with type 2 diabetes (10,18,19), postprandial glycemia after other meals ingested later during the day has never been assessed. A recent study showed that breakfast skipping resulted in a higher postprandial glycemic response after lunch and dinner in healthy individuals (20). However, in this study, the skipped breakfast was compensated for by extra calories at lunch and dinner, making it difficult to determine whether the high glycemic response was a consequence of breakfast omission or the extra calories. We hypothesize that skipping breakfast will increase PPHG after both lunch and dinner and lead to impaired insulin response in patients with type 2 diabetes. Therefore, we explored the postprandial glycemic response to identical lunch and dinner meal tests, with or without breakfast, in patients with type 2 diabetes.

RESEARCH DESIGN AND METHODS

Participants

The study population initially included 26 individuals with type 2 diabetes. Participants had diabetes duration of <10 years and glycated hemoglobin (HbA_{1c}) levels of 7–9% (53–75 mmol/mol) on recruitment. Individuals who habitually ate breakfast, aged 30–70 years with a BMI 22–35 kg/m^2, were included. None of the patients had impaired thyroid, renal, or liver function; none had anemia or pulmonary, psychiatric, immunological, or neoplastic diseases; none had severe diabetes complications, such as cardiovascular disease, cerebrovascular disease, proliferative diabetic retinopathy, or gastroparesis; and none had undergone bariatric surgery. Participants had not worked shifts within the last 5 years and had not crossed time zones within the last month of the study. Participants usually woke up between 0600 and 0700 h and went to sleep between 2200 and 2400 h. All participants were insulin-naïve, and patients taking oral hypoglycemic agents other than metformin were excluded. Those on GLP-1 analogs, anorectic drugs, or steroids were not allowed to participate. The study was approved by the Institutional Helsinki Ethics Committee, and written informed consent was obtained from each participant.

Study Design

This was a randomized, open-label, crossover-within-subject clinical trial. The participants were recruited from the outpatient clinic at the Diabetes Unit in the Hospital de Clinicas, Caracas, Venezuela, and were randomized by a person not involved in the study using a coin flip. The participants underwent two separate all-day meal tests with washout of 2–4 weeks between test days. On the day with breakfast (YesB), participants consumed three identical standard meals that were provided in the clinic as breakfast at 0800 h, lunch at 1330 h, and dinner at 1900 h. On the day with no breakfast (NoB), breakfast was omitted and the individuals continued their overnight fast until lunch at 1330 h, and only two identical standard meals were provided, lunch at 1330 h and dinner at 1900 h. The energy and content of all test meals had the same macronutrient content and composition (701 $\pm$ 8 kcal; 20% fat, 54% carbohydrates, 26% protein, 7% fiber). Patients ingested their last oral therapy 24 h before the test day.

Patients were asked to follow the meal schedule at home 2 days preceding the test. For the 2 days preceding the YesB day, patients were provided with three meals for each day and were instructed to eat breakfast between 0600 and 0830 h, lunch between 1230 and 1430 h, and dinner between 1830 and 2030 h. On the 2 days preceding the NoB test day, the patients were given only two meals for each day and were instructed to eat lunch between 1230 and 1430 h and dinner between 1830 and 2030 h. On the morning of each test day, the assessment of compliance at home was based on an oral report to the dietitian. In addition, participants were asked to avoid alcohol and excessive physical activity 6 days preceding each test day.

Meal Tests

On the day of the meal tests, each participant arrived at the Diabetes Unit at 0700 h after an overnight fast. Anthropometric data were collected in the morning, and only the YesB group received breakfast. At 0730 h, a catheter was placed in the antecubital vein of the nondominant arm and remained in the patient until 2200 h. Venous blood samples were collected just before breakfast at 0800 h (t = 0 min) and at 15, 30, 60, 90, 120, 150, and 180 min after eating commenced. In the NoB

group, blood samples were taken at the same time. The same procedure was repeated after lunch at 1330 h and dinner at 1900 h. The primary outcome was the assessment of postprandial glycemia after lunch and dinner in the YesB versus NoB groups. The secondary outcome was the assessment of plasma insulin, C-peptide, intact GLP-1 (iGLP-1), free fatty acids (FFA), and glucagon levels after lunch and dinner on YesB versus NoB days.

Biochemical and Hormonal Blood Analyses

Plasma glucose was immediately analyzed on Olympus AU 2700 analyzer (Beckman Coulter, Inc., Brea, CA). Serum and plasma EDTA tubes for insulin and C-peptide were left on ice for 30 min. Blood samples for determining iGLP-1 were collected into chilled tubes containing EDTA, aprotinin, and diprotin A (0.1 mmol/L). Samples were centrifuged at 3,000 rpm at 4°C for 10 min and stored at −80°C. Insulin, C-peptide, and iGLP-1 were assayed as previously described (10). Plasma FFA was measured using an enzymatic colorimetric assay (Wako Diagnostics, Richmond, VA), and plasma glucagon was measured using ELISA (R&D Systems, Inc., Minneapolis, MN).

Sample Size and Power Analysis

With a sample size of 22 participants in each treatment group, the current study provided 80% power to detect 5% difference between groups in the overall postprandial plasma area under the curve (AUC) for iGLP-1, insulin, glucose, C-peptide, and glucagon. To allow discontinuation, 26 participants were recruited.

Statistical Analyses

The study enrolled 26 subjects, and 4 subjects dropped out. They were excluded from the analyses; therefore, the results are based on 22 subjects. AUCs of the early response interval (0–30 min) and whole meal (0–180 min) were calculated by the trapezoidal rule and were used as an estimate of response to the meal consumption. The results are expressed as mean ± SEM. For time series, a two-way ANOVA (time × diet) was performed, and a least-significant difference *t* test post hoc analysis was used for comparison between the diets at each interval. A Student *t* test was used for comparing the AUC at different time intervals. In addition, a multivariate ANOVA for repeated measurements was performed assessing effects for diet and time between and within subjects. A P value of ≤ 0.05 was considered statistically significant. Statistical analysis was performed with JMP 11 software (SAS Institute, Inc., Cary, NC).

RESULTS

Participants

The study enrolled 26 individuals who habitually ate breakfast, with 22 participants completing. The period of recruitment and follow-up was between October 2012 and January 2014. After the first all-day meal test, four dropped out (1 of NoB and 3 of YesB) because of difficulties getting to the clinic. Twenty-two patients (12 men and 10 women) completed the study. These patients were 56.9 ± 1.0 years old and had controlled type 2 diabetes for 8.4 ± 0.7 years, had 7.7 ± 0.1% (61 ± 0.8 mmol/mol) HbA_{1c}, and were overweight or obese, with an average BMI of 28.2 ± 0.6 kg/m^2. Ten patients were treated with diet alone, whereas 12 were treated with diet and metformin. On the meal test days, glucose and insulin levels were not statistically different between those who were and were not on metformin ($P > 0.05$ by *t* test). Seven patients had a history of hypertension and were treated with ACE inhibitors and/or calcium antagonists.

Effect of Breakfast or Its Omission on Plasma Glucose, Hormones, and FFA

Fasting plasma glucose, insulin, C-peptide, iGLP-1, glucagon, and FFA did not differ significantly between the two test days ($P > 0.05$) (Fig. 1). As expected, $AUC_{0–180\ min}$ values were 35.7%, 68.6%, 62.1%, and 52.9% higher for glucose, insulin, C-peptide, and iGLP-1, respectively, after breakfast compared with no breakfast ($P < 0.0001$). Plasma levels were 16.5%, 45%, 50%, and 33% higher for glucose, insulin, C-peptide, and iGLP-1, respectively, before lunch in the YesB versus NoB group ($P < 0.0001$) (Fig. 1*A*–*D*). Fasting FFA levels were similar in both YesB and NoB groups. On the NoB day, the $AUC_{0–180\ min}$ value for the plasma FFA level was 1,787.1% higher compared with the YesB day (Fig. 1*E* and Table 1). After breakfast, the $AUC_{0–30\ min}$ value for glucagon levels was higher, but during the late interval, the $AUC_{60–180\ min}$ value was lower and reached 12.5% before lunch on the YesB day versus the NoB day (Fig. 1*F*). Thus, as expected, skipping breakfast led to retained high levels of glucagon and FFA and reduced levels of glucose, insulin, C-peptide, and iGLP-1, whereas breakfast consumption led to a reverse metabolic state.

Effect of Lunch and Dinner on Plasma Glucose, Hormones, and FFA on YesB or NoB Day

Compared with the YesB day, on the NoB day, the peaks of plasma glucose after lunch and dinner were 39.8% and 24.9% higher, respectively ($P < 0.0001$) (Table 1). The $AUC_{0–180\ min}$ values for glucose were 36.8% and 26.6% higher, respectively ($P < 0.0001$). The whole interval, $AUC_{0–180\ min}$, for insulin after lunch and dinner was 17% and 7.9% lower, respectively, on the NoB day compared with the YesB day ($P < 0.0001$) (Table 1). On the NoB day, after lunch and dinner, insulin levels peaked 30 min and 60 min later and were 24.7% and 10.8% lower, respectively ($P < 0.0001$) (Table 1 and Fig. 1*B*). The responses of C-peptide and its AUC values mirrored those of insulin after lunch and dinner (Table 1). After lunch, iGLP-1 peaked 60 min later and was 21.5% lower compared with the peak of iGLP-1 on the YesB day ($P < 0.0001$) (Fig. 1*D* and Table 1). The $AUC_{0–30\ min}$ and $AUC_{0–180\ min}$ values for plasma iGLP-1 after dinner were 17.4% and 16.5% lower, respectively, on the NoB day ($P < 0.0001$) (Table 1). After lunch and dinner, glucagon levels increased, resulting in 14.8% and 11.5% higher $AUC_{0–180\ min}$ values, respectively, on the NoB day ($P < 0.0001$) (Table 1). $AUC_{0–180\ min}$ values for FFA after lunch and dinner were 41.1% and 29.6% higher, respectively, on the NoB day ($P < 0.0001$) (Table 1). The $AUC_{0–180\ min}$ value for glucose after lunch and dinner correlated with the $AUC_{0800–1330\ h}$ value for FFA (R^2 = 0.888, $P < 0.0001$) and inversely correlated with the $AUC_{0800–1330\ h}$ values for glucose (R^2 = 0.888, $P < 0.0001$), insulin (R^2 = 0.587, $P < 0.0001$), and iGLP-1 (R^2 = 0.622, $P < 0.0001$). Thus, skipping breakfast led to higher glycemic index response and high levels of glucagon and FFA and to reduced levels of insulin, C-peptide, and iGLP-1 after lunch and dinner, whereas breakfast consumption led to a reverse metabolic state.

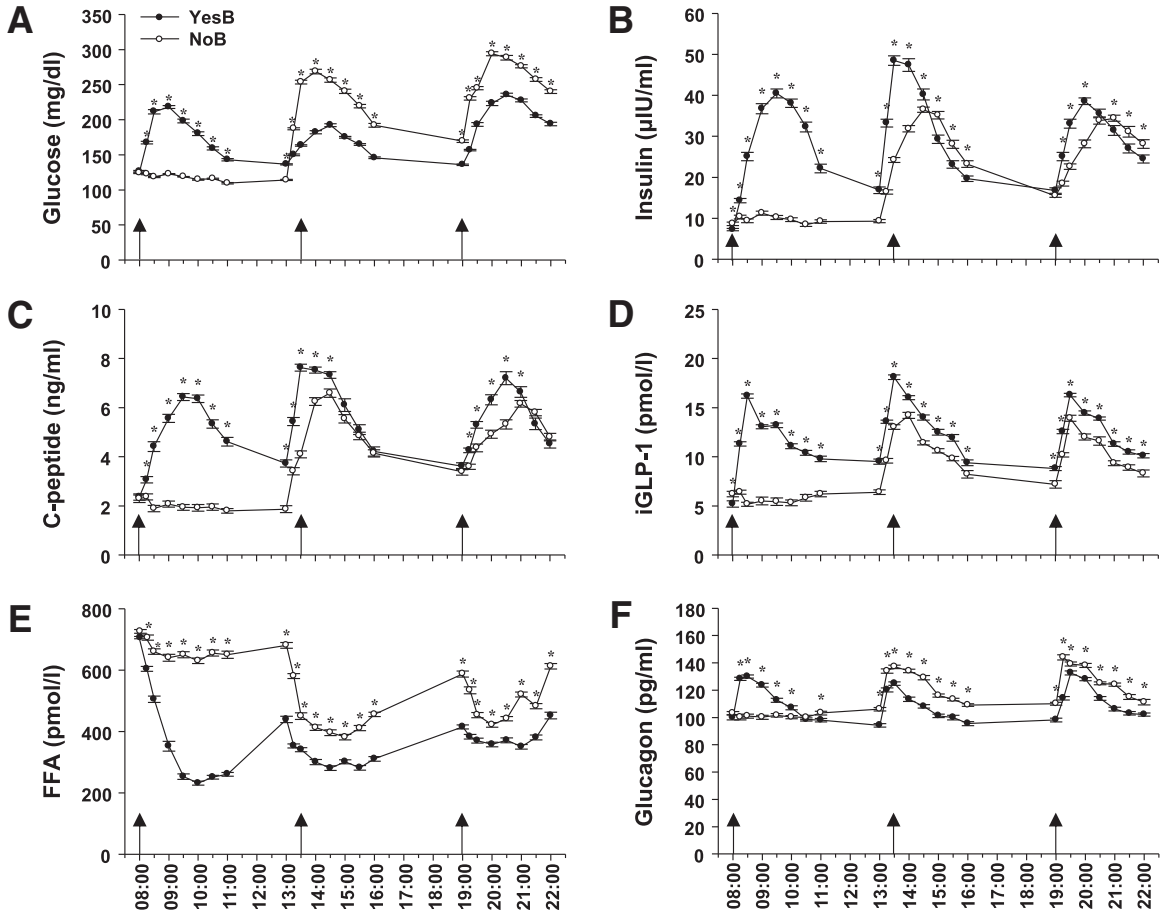

Figure 1—All-day graphs for (*A*) glucose, (*B*) insulin, (*C*) C-peptide, (*D*) iGLP-1, (*E*) FFA, and (*F*) glucagon. *$P < 0.0001$.

CONCLUSIONS

In the current study, we report that the omission of breakfast in patients with type 2 diabetes is associated with a significantly higher glycemic response after subsequent lunch and dinner compared with the glycemic response after an identical lunch and dinner when breakfast is consumed. The omission of breakfast also resulted in impaired insulin secretion after lunch and dinner, as reflected by the delayed peak insulin and reduced concentrations of plasma insulin and C-peptide. In addition, iGLP-1 responses after lunch and dinner were lower when breakfast was omitted compared with when breakfast was consumed. In contrast, plasma FFA and glucagon levels were significantly higher after lunch and dinner when breakfast was omitted. The study, therefore, shows that breakfast is of major importance for glucose homeostasis, including islet function and incretin hormones, throughout the day. Our results are consistent with a previous study performed in healthy individuals showing higher glucose excursions after lunch and dinner on the day breakfast was omitted (20). However, unlike in our study, the caloric intake of lunch and dinner was not identical, making it difficult to determine whether the high glycemic response was a result of the increased intake or the omission of breakfast.

Reduced glycemia and enhanced insulin after lunch with prior consumption of breakfast is a phenomenon that was coined the "second meal phenomenon" (10,18). This has been explained by enhanced β-cell responsiveness at the second meal as induced by the first meal (21,22). This explanation is based on the findings that the first and the second phase of insulin release are both influenced by β-cell memory, and the magnitude of insulin release is enhanced significantly by previous glucose exposure (22). However, we show that this effect is not only restricted to the subsequent meal but also is extended to dinner (i.e., has a much longer duration than previously anticipated). In fact, omission of breakfast indeed worsened the postprandial glucose and impaired insulin secretion, as reflected by both delayed insulin peak and lower insulin response at lunch and also at dinner. The absence of glucose elevation because of fasting until noon may diminish β-cell responsiveness and memory, leading to a reduced and delayed insulin response after lunch and dinner on the NoB day. Indeed, a recent study reported that lower insulin release by β-cells in response to nutrient depletion or starvation induces lysosomal degradation of nascent secretory insulin granules and that this is controlled by protein kinase D, a key player in secretory granule biogenesis (23). The recovery of the responsiveness of the β-cell's secretory function on nutrient availability likely requires some hours, explaining the prolonged depression of the insulin secretory response after lunch and dinner on the NoB day. The impaired insulin secretion at lunch and dinner, as dependent on breakfast, may also be due to perturbed incretin regulation, because β-cell memory and sensitivity to glucose are both

Table 1—Peak and AUC at different intervals of YesB-Day versus NoB-Day

		Breakfast			Lunch			Dinner		
		YesB	NoB	Δ%	YesB	NoB	Δ%	YesB	NoB	Δ%
Glucose (mg/dL · min)	Peak	218.2 ± 2.1	124.4 ± 1.3*	−43.0	192.32.1	268.8 ± 3.3*	39.8	235.5 ± 2.4	294 ± 3.1*	24.9
	$AUC_{0–30}$	5,041.4 ± 42.4	3,658.6 ± 272.6*	−27.4	4,499.7 ± 22.7	5,566 ± 26.4*	23.7	4,818.4 ± 29.4	6,565.9 ± 43.9*	36.3
	$AUC_{0–180}$	33,033.4 ± 243.9	21,248.9 ± 65.9*	−35.7	30,566.3 ± 185.1	41,804.7 ± 310.9*	36.8	37,368.4 ± 247.3	47,310 ± 288.4*	26.6
Insulin (μIU/mL · min)	Peak	40.5 ± 1.1	11.3 ± 0.5*	−72.1	48.5 ± 1.2	36.5 ± 0.6*	−24.7	38.6 ± 0.8	34.4 ± 0.7	−10.8
	$AUC_{0–30}$	457.1 ± 11.9	290.7 ± 7.5***	−36.4	989.9 ± 17.7	497.7 ± 10.7*	−49.7	749.9 ± 22.8	456.3 ± 14.3*	−39.2
	$AUC_{0–180}$	5,593.6 ± 113.1	1,757.5 ± 50.6*	−68.6	6,212.9 ± 115.7	5,156.3 ± 85.8*	−17.0	5,593.4 ± 146.9	5,150.3 ± 98.8*	−7.9
C-peptide (ng/mL · min)	Peak	6.4 ± 0.1	2.4 ± 0.1*	−63.3	7.6 ± 0.1	6.6 ± 0.2**	−13.6	7.2 ± 0.3	6.2 ± 0.1**	−14.5
	$AUC_{0–30}$	96.8 ± 2.7	66.5 ± 2.8**	−31.2	166.5 ± 3.3	95.7 ± 2.6*	−42.5	130.6 ± 2.5	111.9 ± 2.7*	−14.3
	$AUC_{0–180}$	942.7 ± 16.9	357.6 ± 8.9*	−62.1	1,126.1 ± 21.6	916 ± 16.4*	−18.7	1,042.3 ± 19.6	914.4 ± 17.7*	−12.3
iGLP-1 (pmol/L · min)	Peak	16.2 ± 0.2	6.4 ± 0.2*	−60.5	18.1 ± 0.2	14.2 ± 0.3*	−21.5	16.3 ± 0.2	13.9 ± 0.3*	−14.5
	$AUC_{0–30}$	330 ± 4.9	181.4 ± 4.8*	−45.0	410.8 ± 4.5	289.4 ± 3.9*	−29.5	376.8 ± 4.4	311.4 ± 4.9*	−17.4
	$AUC_{0–180}$	2,152.4 ± 21.3	1,014.6 ± 24.4*	−52.9	2,456.6 ± 24.9	1,989.4 ± 20.5*	−19.0	2,276.1 ± 19.6	1,900.8 ± 23.1*	−16.5
FFA (mmol/L · min)	Nadir	231.4 ± 6.5	630.1 ± 8.7*	172.3	280.6 ± 7.5	381.7 ± 9.5*	36	350.5 ± 7.7	421.0 ± 7.6*	20.0
	$AUC_{0–30}$	18,099.5 ± 194.8	20,854.1 ± 148.9**	15.2	11,148.4 ± 200.3	17,189.7 ± 245.8*	54.2	11,632.2 ± 215.3	15,820.2 ± 282.4*	36.0
	$AUC_{0–180}$	6,242 ± 1,218	117,791 ± 1,368*	1,787.1	55,860.6 ± 1,034.4	78,830.1 ± 1,482.7*	41.1	67,777.2 ± 1,276.7	87,808 ± 1,251.1*	29.6
Glucagon (pg/mL · min)	Peak	130 ± 1.2	103.2 ± 1.4*	−20.6	125 ± 1.3	137.1 ± 1.2*	9.7	132.7 ± 1.5	144 ± 1.8*	8.5
	$AUC_{0–30}$	3,648.8 ± 28.5	3,032.7 ± 34.6*	−16.9	3,446.6 ± 29.7	3,834.6 ± 31.9*	11.3	3,442.2 ± 28.1	4,028.5 ± 38.9*	17.0
	$AUC_{0–180}$	20,327.4 ± 150.6	18,160.2 ± 121.2*	−10.7	19,429.8 ± 171	22,300.9 ± 145*	14.8	20,501.9 ± 143.3	22,850.1 ± 156.4*	11.5

Statistics were between the NoB and the YesB of the same meal. *$P < 0.0001$; **$P < 0.001$; ***$P < 0.05$.

enhanced by GLP-1. Therefore, the higher levels of GLP-1 on the YesB day may explain both the enhanced insulin secretion and the reduced glycemic response after lunch and dinner.

The prolonged elevation of plasma FFA levels triggered by the extension of the overnight fast on the NoB day correlated with reduced early insulin release, higher glucose, and less suppressed glucagon and FFA levels after lunch and dinner. A similar positive correlation was observed between FFA and glucose levels after lunch in people with and without diabetes when breakfast was omitted (17–19). Acute elevation of FFA by intravenous infusion or omission of breakfast has been reported to cause inhibition of insulin-stimulated muscular glucose transport. This inhibition develops 3–4 h after plasma FFA rise, affecting the glucose response over subsequent meals (24–27). Furthermore, acute elevation of plasma FFA triggered inhibition of glycogen synthase after 4–6 h, causing a reduction in postprandial muscle glycogen storage (24–27). Acute elevation of plasma FFA also induces hepatic insulin resistance and increased hepatic glucose production in patients with type 2 diabetes and in control subjects without diabetes (24,28). The delay of 3–4 h between the rise in FFA and the development of significant insulin resistance is most likely the reason for the increased postprandial glycemia not only after lunch but also after dinner on the NoB day.

Previous studies have shown that in type 2 diabetes, α-cells, the glucagon producers, become insensitive to the inhibitory effects of glucose and/or insulin, leading to postprandial hyperglucagonemia and hepatic glucose overproduction (29–31). In this study, high nonsuppressed glucagon levels were observed throughout the NoB day, which can also explain the higher glycemic response after lunch and dinner when breakfast was omitted. Moreover, the higher plasma glucagon levels are associated with increased triglyceride breakdown in adipose tissue leading to a further increase in plasma FFA levels, aggravating the higher glycemic response described above.

Another potential explanation for our results would be an important effect of the circadian clock on glucose homeostasis. Thus, the circadian misalignment of meal timing as a result of breakfast

skipping and the prolonged fasting period on the NoB day may have aggravated postprandial glycemia throughout the day. Indeed, it has been shown in animals and humans that fasting and feeding were able to change transcript levels and circadian phase of peripheral clock genes and genes related to glucose metabolism (32,33). Loss of the positive association between postprandial glucose and insulin concentrations, characteristic of β-cell failure or loss, was reported after a few weeks of a nocturnal lifestyle in which breakfast was skipped (34). Indeed, just 10 days on a meal schedule uncoupled from the circadian cycle led to PPHG and glucose intolerance in healthy and young individuals with a normal glycemic response to an oral glucose tolerance test (35). Thus, it is plausible that the worsening of glycemic response after lunch and dinner on the NoB day is a result of the disruption of the circadian clock triggered by omission of breakfast.

One limitation of our study is that the study was restricted to subjects with type 2 diabetes. Thus, we cannot determine whether this effect is also correct for healthy people. We showed that the deleterious effects of breakfast omission triggering hyperglycemic response occurred after lunch and dinner, but the exact duration of this effect is not known. In addition, the role of insulin sensitivity, suppression of hepatic glucose production, gastric emptying, and clock gene expression remain undefined.

Herein we demonstrate that extended fasting via breakfast skipping leads to increased plasma FFA levels and hyperglucagonemia and to reduced insulin and GLP-1 levels. This, in turn, abrogates insulin- and iGLP-1–mediated sensitization and activation of β-cells. These consequences, alongside circadian clock disruption, lead to increased PPHG after lunch and dinner in individuals with type 2 diabetes. These deleterious effects on all-day glucose metabolism were reversed by breakfast consumption. These findings reiterate the crucial contribution of breakfast to prevent postprandial glucose excursions and cardiovascular complications in individuals with type 2 diabetes.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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