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Synergistic effect of obesity and lipid ingestion in suppressing the growth hormone response to exercise in children

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Abstract

Diet plays an important role in modulating exercise responses, including activation of the growth hormone (GH)/insulin-like growth factor-I (IGF-1) axis. Obesity and fat ingestion were separately shown to reduce exercise GH responses, but their combined effect, especially important in children, has not been studied. We therefore measured the GH response to exercise [30-min intermittent cycling, ten 2-min bouts at 80% maximal aerobic capacity ($\dot{V}o_{2max}$), separated by 1-min rest], started 45 min after ingestion of a high-fat meal (HFM) in 16 healthy [controls; body mass index percentile (BMI%ile) 51 ± 7], and 19 obese (Ob, BMI%ile 97 ± 0.4) children. Samples were drawn at baseline (premeal), and at start, peak, and 30 min postexercise. In the Ob group, a marked 75% suppression of the GH response (ng/ml) to exercise was observed (2.4 ± 0.6 vs. 10.6 ± 2.1, $P < 0.001$). This level of suppression was also significantly greater compared with age-, fitness-, and BMI-matched historical controls that had performed identical exercise in fasting conditions. Our data indicate that the reduction in the GH response to exercise, already present in obese children vs. healthy controls, is considerably amplified by ingestion of fat nutrients shortly before exercise, implying a potentially downstream negative impact on growth factor homeostasis and long-term modulation of physiological growth.

Keywords: growth hormone, exercise, high-fat meal, pediatric obesity

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PHYSICAL EXERCISE ACTIVATES a complex pattern of physiological responses, including secretion of immunomodulatory mediators (pro/anti-inflammatory cytokines, chemokines) (28, 29), counterregulatory hormones (19, 22), and growth factors, such as the growth hormone (GH)-insulin-like growth factor-I (IGF-I) axis (27, 28, 39), which are collectively responsible for the full manifestation of the health effects associated with exercise. As the GH → IGF-I axis is particularly important to ensure proper growth and development during childhood and adolescence, its exercise

modulation during this age is considered a critical component of overall healthy growth (12). Basal GH concentrations are determined by the pulsatile release of the hormone from the anterior pituitary, with maximal secretion occurring during deep sleep (23, 45). Baseline secretion levels are acutely amplified by intervening stimuli, among which exercise is one of the most important. During exercise, GH can rapidly increase 10- to 20-fold over basal levels (18, 22, 27). As children spontaneously and repeatedly engage in all sorts of structured and unstructured exercise (4), the resulting frequent peaks in GH secretion are now considered a necessary component of overall growth homeostasis; conversely, insufficient activation of the GH → IGF-I axis early in life has been shown to result in impaired bone elongation and muscle growth (3, 25). Height gain, however, is only one of the phenotypic outcomes of GH effects (37). Another important action involves modulation of adipose tissue metabolism (10). GH in fact affects proliferation and differentiation of preadipocytes, as well as hydrolyzation of circulating triglycerides (via inhibition of lipoprotein lipase) and release of triglycerides stored in adipocytes (via stimulation of hormone-sensitive lipase). Further, GH interacts with inflammatory mediators; several proinflammatory cytokines (IL-6, IL-1β, TNF-α) have been shown to alter GH signaling (31), either directly or via activation of suppressor of cytokine signaling (SOCS) molecules (1). These two sets of effects are especially relevant to pediatric obesity, in which altered adipocyte metabolism is a crucial issue, and subclinical chronic inflammation is common and considered responsible for early endothelial function impairment.

Among the several factors known to modulate GH homeostasis (which also include acute stress, hypoglycemia, and repeated, high-intensity exercise), obesity and high-fat diets are especially common in Western society. Obesity has been clearly demonstrated to affect, through multiple biochemical pathways, several aspects of GH metabolism and function (15, 24). More specifically, the GH response to exercise is markedly reduced in both obese children and adults (21, 41, 42), with the magnitude of blunting proportional to the severity of obesity (30). Further, even in healthy-weight subjects, the ingestion of a high-fat meal shortly before exercise has been shown to acutely induce a strong GH suppression (9, 20, 35).

Obesity and excessive fat ingestion are commonly just two facets of the same phenomenon and are therefore likely to occur together very frequently. Their combined effect on GH responses in children, which we hypothesize to be at least cumulative, and possibly synergistic, has not, however, to date been studied. We therefore designed the present study to measure, in 16 healthy and 19 obese children, the GH response to a standardized, moderate-intensity exercise protocol performed 45 min after ingestion of 1.5 g of fat per kg body weight.

MATERIALS AND METHODS

Subjects. This study was conducted at the University of California-Irvine (UCI) Institute for Clinical and Translational Science (ICTS). The UCI Institutional Review Board approved all protocols, and all study participants and their parents/legal guardians signed assent/consent forms. Thirty-five children, aged 8–17 yr of age, participated in the study and were separated into two groups according to age- and sex-adjusted body mass index percentile (BMI%ile): controls (CTL, 9 females/7 males), BMI%ile < 85% (avg 51 ± 7); and obese (Ob, 13 females/6 males), BMI%ile > 95% (avg 97 ± 0.4). Except for overweight status in the Ob group, participants were in good health, free of chronic or acute pathologies, and not taking any medication. Anthropometric characteristics are shown in Table 1.

Physical assessment and fitness testing. Children were admitted at the UCI ICTS, where staff nurses obtained preparticipation history and conducted a physical exam. A direct assessment of body composition was then performed using dual-energy X-ray absorptiometry (DEXA), to confirm that

elevated BMI data were due to increased adiposity. Subsequently, a standard incremental test was performed to assess individual maximal aerobic capacity ($\dot{V}_{O_{2max}}$) using an ergonometric bicycle (SensorMedics Ergoline 800S, Yorba Linda, CA). As the patient cycled, power output was increased every minute by 10% of the total estimated maximum, as derived by standard predictive equations ([13]). The total duration of the test, therefore, including initial warm-up period, was 12–14 min. Each subject exercised to their maximum tolerance and was allowed to raise their hand and ask to stop for any reason. Exercise characteristics are shown in [Table 2]. During exercise, gas exchange was measured via a commercial metabolic cart (Sensor Medics, Yorba Linda, CA), which, in addition to $\dot{V}_{O_{2max}}$, allowed determination of individual anaerobic threshold (AT). After exercise, patients rested and were monitored until heart rate returned to preexercise values. The results from this session were used to decide which patients were to be recalled for the next exercise session. Children with a $\dot{V}_{O_{2max}}$ between 20 and 45 ml $O_2 \cdot kg^{-1} \cdot min^{-1}$ were asked to return.

Main exercise study. Patients were admitted in the morning at our research center after a 10-h fast, and an indwelling catheter was placed in an antecubital vein by a trained physician or nurse, allowing for repeated blood draws without further adrenergic stimulation. After sitting comfortably for 30 min, children were fed a flavored semiliquid meal containing 1.5 g of fat/kg body wt and only negligible amounts of other nutrients. Forty-five minutes after ingestion of the meal, subjects performed a standard 30-min exercise challenge (ten 2-min bouts of cycling at constant power output, with 1-min rest between bouts). The power output was set at a value corresponding to the midpoint between their predetermined anaerobic threshold and $\dot{V}_{O_{2max}}$, which on average was 75% of $\dot{V}_{O_{2max}}$. This ensured that the exercise was tailored to each child's physical capability, and that relative work intensity was homogeneous across subjects. Blood samples were drawn at baseline (immediately before meal ingestion); preexercise (immediately before exercising, and 45 min after meal ingestion); end exercise (during the last minute of the exercise challenge); and at 30 min postexercise (30 min after exercise cessation) ([Fig. 1]).

Sample processing. The first 0.4 ml of each blood draw was microcentrifuged and plasma glucose was measured using a Beckman Glucose Analyzer II (Beckman Coulter, Fullerton, CA) utilizing the glucose oxidase method. The rest of the blood was collected in EDTA tubes and centrifuged at 3,000 rpm in a refrigerated centrifuge; plasma was aliquotted into 1-ml microcentrifuge tubes and placed in a −80°C freezer for later analysis. Enzyme-linked immunoabsorbent assays (ELISAs) were utilized for GH [Diagnostic Systems Laboratories (Webster, TX): intra-assay coefficient of variation (CV) was 3.3–4.3%, interassay CV was 6.3–6.6%, and assay sensitivity was 0.03 ng/ml] and insulin [LINCO Research (St. Charles, MO): intra-assay CV was 4.6–7.0%, interassay CV was 9.1–11.4%, and assay sensitivity was 2 μU/ml]. A standard colorimetric method was used to assay free fatty acids (Zen-Bio, Research Triangle Park, NC) and triglyercides (Bio Assay Systems, Hayward, CA). L-Lactate concentrations were quantified using the YSI 2300 STAT PLUS Glucose and Lactate Analyzer (YSI, Yellow Springs, OH).

Statistical analysis. Data are shown as group means ± SE. For variables measured at baseline only (such as anthropometric characteristics) differences across groups were determined with unpaired, two-tailed Student's t-tests. For variables measured at multiple time points (baseline, preexercise, end exercise, and 30 min postexercise), within- and across-group differences were determined using a standard, parametric, two-way repeated-measures analysis of variance (ANOVA). When overall significance was revealed by ANOVA, post hoc analysis was used to determine the level of significance at individual time points; differences in response to exercise between groups was performed with comparisons of absolute deltas compared with baseline. A value of $P < 0.05$ indicated significant

RESULTS

Demographic characteristics of patient populations. CTL and Ob children differed significantly in body weight (41 ± 2.9 vs. 68.9 ± 4.3 kg, $P < 0.05$), BMI%ile (51 ± 7.1 vs. 97.1 ± 0.04, $P < 0.05$), and whole body $\dot{V}_{O_{2max}}$; however, $\dot{V}_{O_{2max}}$ was similar if normalized by lean body mass (51.6 ± 1.6 vs. 50.3 ± 4.0 ml·min^{-1}·kg lean mass^{-1}) (Table 1).

Metabolic variables. Plasma glucose levels were not different between CTL and Ob children throughout the study, and within each group did not change over time. Plasma insulin displayed a consistent pattern in both groups (Fig. 2): it increased significantly after fat ingestion, dropped back to near-basal levels at peak exercise, and again increased significantly 30 min after exercise cessation. At each time point, however, insulin was significantly higher in Ob vs. CTL (baseline, 82 ± 11 vs. 35 ± 9, $P < 0.05$; preexercise, 159 ± 23 vs. 91 ± 22, $P < 0.01$; peak exercise, 81 ± 10 vs. 42 ± 9, $P < 0.01$, 30-min postexercise, 136 ± 17 vs. 57 ± 15 pM, $P < 0.001$). Free fatty acids (FFAs, µM) and triglycerides (TGs, mmol) were also consistently higher in Ob vs. CTL (FFAs: baseline, 523 ± 40 vs. 310 ± 45, $P < 0.001$; preexercise, 464 ± 33 vs. 320 ± 41, $P < 0.001$; peak exercise, 438 ± 38 vs. 246 ± 37; 30-min postexercise, 619 ± 45 vs. 429 ± 63, $P < 0.01$; TGs: baseline, 1.6 ± 0.2 vs. 0.4 ± 0.03, $P < 0.0001$; preexercise, 1.8 ± 0.2 vs. 0.5 ± 0.04, $P < 0.0001$; peak exercise, 2.2 ± 0.2 vs. 0.6 ± 0.1, $P < 0.0001$; 30 min postexercise, 2.0 ± 0.2 vs. 0.6 ± 0.1 mmol/l, $P < 0.0001$). Total cholesterol and low-density lipoprotein (LDL) were not significantly different between CTL and Ob children; however, high-density lipoprotein (HDL) was significantly lower in Ob (baseline, 49.0 ± 4.5 vs. 84.7 ± 6.6 mg/dl, $P < 0.0001$) (Table 3). Lactate levels were not different between CTL and Ob children at any time point, documenting that relative exercise intensity was similar across groups.

GH exercise response. Plasma GH (ng/ml) was similar across groups at rest (CTL 0.2 ± 0.1, Ob 0.1 ± 0.1) and increased significantly in both at peak exercise (to 10.6 ± 2.1 in CTL, $P < 0.0001$, and to 2.4 ± 0.6 in Ob, $P < 0.01$). The exercise-induced GH peaks, however, either expressed as absolute GH values or as GH increase over baseline (2.1 ± 0.6 vs. 10.0 ± 2.2), were significantly lower in Ob vs. CTL ($P < 0.001–0.0001$). In both groups, 30 min after exercise cessation, GH concentrations had reverted to values close to baseline (Fig. 3).

Data were then compared with the GH exercise response in a group of obese and healthy children with identical number of participants, and one-on-one matching for sex, age, and BMI status (Table 1), who had undergone an identical exercise protocol without fat ingestion in a previous study (30) (Fig. 4). Not surprisingly, through this comparison, the greatest GH response was recorded in fasting healthy children. The GH response then appeared to be blunted by 10% in healthy children after ingestion of a high-fat meal, and by an additional 20% in fasting obese children. Remarkably, in the obese children who had ingested a high-fat meal, the magnitude of GH blunting reached over 85% compared with fasting healthy controls, i.e., much greater than could have been expected by the additive effect of obesity and fat ingestion alone, and therefore suggesting a possible synergistic effect of these two factors.

DISCUSSION

To our knowledge, this is the first study examining the combined effects of pediatric obesity and acute high-fat ingestion prior to an exercise challenge. The central finding of our study is the observation that acute ingestion of a lipid-rich meal in obese children resulted in almost complete suppression of the GH response during subsequent exercise. Our experimental paradigm was designed to reproduce

conditions that would likely occur in everyday real-life situations. The timing and caloric high-fat composition of the meal was chosen to mimic a convenient high-fat fast food meal on the way to sports practice, a common event in Western societies.

The relationship between pediatric excess adiposity and adult body size remains incompletely defined. Current evidence seems to indicate that the effect on final and adult height of pediatric weight status is not strong ([44](#)); however, overweight and obese children may be taller in childhood, and later show relatively slower growth in height during adolescence. Independent of linear growth, obese children seem to display greater lean body mass, most likely because their muscles and bone are constantly being loaded ([36](#)). In addition, Bakker et al. ([2](#)) found lean mass was positively correlated with bone mineral density in adulthood, and Uusi-Rasi et al. ([46](#), [47](#)) demonstrated heavier children had bones with larger cross-sectional areas in adulthood. These studies, however, while providing valuable descriptive information, did not correlate findings with growth factor levels.

Physical activity promotes physiological growth via activation of the GH-IGF-I axis ([18](#), [34](#)). Each exercise bout, even of moderate intensity, induces a clear spike in GH secretion, which can easily reach levels 10- to 20-fold greater than basal values during normal, everyday life activities ([22](#)). If allowed to participate in spontaneous play, children naturally engage in repeated, short, and often intense bursts of exercise, strongly activating GH release ([4](#)). Increasing evidence indicates that these repeated GH peaks are not just by-products of an otherwise healthy activity, but indeed part of why the activity in itself is healthy, physiologically modulating growth and development ([12](#)). Borer et al., in fact, documented how regulating the amount of exercise in an animal model could accelerate somatic growth via increased GH pulse frequency and amplitude ([6](#), [7](#)). Conversely, as early deficiencies in this axis result in impaired bone elongation and muscle growth in children ([25](#)), insufficient exercise during childhood has been associated, later in life, with osteoporosis and sarcopenia through reduced bone mineralization ([5](#)) and muscle mass development ([38](#)). The metabolic effects of GH, however, go well beyond regulation of linear growth; relevant to the field of obesity these effects include regulation of lipolysis and differentiations of preadipocytes ([10](#)), as well as interaction with multiple inflammatory mediators ([1](#), [31](#)) now identified as key effectors in the early stages of obesity-related vascular defects. Any condition, therefore, featuring a reduction in the expected GH response to physiological stimuli (including exercise during childhood and adolescence) is likely to interfere with the coordinated pattern of growth-related events. While this may not consistently result in a reduction in linear growth (as indeed seems not to be the case in our study population, in which obese children were not shorter than matched controls), it is certainly likely to have marked metabolic repercussion, possibly severely affecting long-term body composition.

In this context, pediatric obesity represents an especially vulnerable state, as it compounds the possible effects of multiple factors known to individually influence GH metabolism. First, the presence of obesity per se, independent of circulating lipid levels, has been clearly associated with reduced GH secretion ([17](#), [30](#)); if chronic hyperlipidemia is also present, especially elevated free fatty acids, there is further induction of somatostatin-mediated suppression of pituitary GH release ([11](#)). This suppressive effect may be acutely exacerbated each time excessive fat ingestion causes overlapping hyperlipidemic peaks (as obesity is commonly associated with high-fat feeding, this is a common event). While it is intuitive that these factors may have a cumulative effect on GH secretion, ours is the first systematic attempt to quantify the effect in controlled conditions. Interestingly, the hypothesis has been raised that, at least in some instances, an inappropriate GH response to a stimulus may precede weight gain ([14](#)). In this situation, a vicious cycle would be established: the initial reduced GH response would favor onset of obesity, which in turn would further reduce at least the GH response to exercise (as seen in our study).

The actual applicability and overall relevance of this mechanism to the broader pediatric obesity population, however, remain to be determined.

In the attempt to meaningfully compare the effect of high-fat feeding to otherwise similar, fasting conditions, we compared our study results to prior data from our laboratory. The comparison was performed using results from a group of children who had previously performed an identical exercise protocol, and who were individually matched by age, sex, and BMI%ile to the 35 children in this study ([Fig. 4](#)). Through this comparison it became apparent that CTL children had the greatest GH response to exercise in fasting conditions, which was slightly reduced after fat ingestion. Ob children, even in fasting conditions, displayed a GH response that was already lower than in CTL fed a high-fat meal. Finally, when Ob children ingested a high-fat meal, their GH response was almost completely suppressed, i.e., was 85% lower than in the fasting CTL. Based on the levels of suppression observed in the other two groups, i.e.,   10% in the CTL children after high-fat feeding, representing the effect of fat ingestion alone, and   30% in the fasting Ob children, representing the effect of obesity alone, this 85% suppression appears disproportionate, unless a synergistic effect of obesity and fat ingestion is present.

While our study was not designed to clarify the underlying pathophysiological mechanism by which obesity and acute high-fat ingestion caused the observed exercise-induced GH blunting, the FFA model of GH modulation conforms to our findings. FFAs have been shown to directly suppress GH secretion via inhibition of pituitary somatotrophs and through the indirect regulation of the secretion of somatostatin ([11](#), [32](#)). Our data showed that the Ob group, at all time points, had significantly greater concentrations of FFA than the CTL group. The contributory role of FFAs is also supported by the observation that when lipolysis is pharmacologically prevented during an antecedent exercise bout, subsequent GH secretion is not suppressed, or even increased, proportionally to systemic FFA levels ([43](#)). Furthermore, even in normal-weight subjects, acute increases in FFA through ingestion of a high-fat meal 30–45 min before exercise can reduce the GH response by 40–50%. This was first demonstrated in adults performing a 10-min exhaustive exercise bout ([9](#)) and more recently confirmed in our laboratory in children undergoing an intermittent exercise protocol identical to that used in the present study ([20](#), [30](#)). Insulin has also been shown to independently modulate GH function via cross activation of intracellular signaling pathways, such as the phosphatidylinositol 3-kinase and ERK1/2 pathways, which are activated by both the GH and the insulin receptors ([49](#)). Prolonged hyperinsulinemia, in particular, has been shown to inhibit GH-induced signaling at the receptor and postreceptor level ([48](#)). In our study, high-fat ingestion, even in the absence of carbohydrate ingestion and with no movement of glycemic values, resulted in marked hyperinsulinemia in both groups (insulin concentrations roughly doubled over baseline values 45 min after the meal). At all time points, however, plasma insulin was consistently greater, more specifically, about twice as high, in obese compared with normal-weight children, which may have contributed to the reported blunted GH secretion.

Many of the downstream effects of GH are believed to be mediated by IGF-I, its main anabolic effector ([8](#)). While it would appear intuitive that blunted GH responses should also result in parallel blunting of IGF-I concentrations, the kinetics of the two hormones appear to be significantly different, and several prior studies from our and other laboratories reported substantially unchanged IGF-I levels in the face of significantly reduced GH concentrations ([30](#), [39](#), [40](#)). IGF-I, unfortunately, due to limitations in available sample volume, could not be measured in this study. While we have no reason to believe that its concentration profile should differ from what was previously reported, it is possible that the exceptionally strong suppressive effect on GH secretion, caused by the combination of obesity and fat ingestion, may actually have altered IGF-I levels. On the other hand, existing reports on IGF's response

to stimulus, including exercise, are often nonconclusive, even conflicting, likely due to the extreme complexity of the related biochemical mechanisms (intracellular signaling, secretion patterns, targeted effects), and large number of players involved, including multiple IGF receptors and binding proteins (16), and various IGF-I precursor isoforms (33), expressions of several of which appear to be differently regulated by mechanical stress on skeletal muscle (26). Further elucidating these issues will be an interesting rationale for future studies.

In summary, our data for the first time document the simultaneous effects of pediatric obesity and acute consumption of a high-fat meal on GH secretion during a subsequent exercise challenge, an experimental setting reproducing a common scenario in Western society lifestyle. Our data show that in obese children, who already display reduced GH adaptation to exercise, ingestion of fat nutrients shortly before exercise greatly amplifies this blunting effect. As pediatric obesity is largely due to high-fat content diets, this blunting may be a recurrent or continuous condition in many subjects, with a potentially negative impact in growth factor homeostasis, and possible long-term effects on growth and development. Our observations provide a strong rationale for future studies aimed at better defining the complex interplay of human growth factors and their regulatory proteins, and underscore the necessity of optimizing the timing and nutrient compositions of preexercise meals to maximize the full health benefits of physical activity.

GRANTS

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: S.R.O. and P.R.G. conception and design of research; S.R.O., J.S.R., and F.P.Z. performed experiments; S.R.O., J.S.R., and P.R.G. analyzed data; S.R.O., S.R.H., and P.R.G. interpreted results of experiments; S.R.O. and S.R.H. prepared figures; S.R.O., S.R.H., and P.R.G. drafted manuscript; S.R.O. and P.R.G. edited and revised manuscript; S.R.O., S.R.H., and P.R.G. approved final version of manuscript.

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Figures and Tables

Table 1.

Demographic characteristics of patients

	CTL	Ob	Matched Fasting CTL	Matched Fasting Ob
Sex	9 F, 7M	13F, 6M	9 F, 7M	13F, 6M
Age, yr	12.0 ± 0.6	12.1 ± 0.6	12.1 ± 1.0	12.0 ± 0.6
Height, cm	148.2 ± 3.9	152.1 ± 3.1	151.5 ± 10.0	151.9 ± 3.1
Weight, kg	41.0 ± 2.9	68.9 ± 4.3[*]	44.5 ± 4.3	72.5 ± 7.5[*]
Tanner	2.2 ± 0.4	2.5 ± 0.3	2.6 ± 0.4	3.0 ± 0.3
LBM, g	31,013 ± 2,621	39,880 ± 2,829[*]	36,458 ± 5,493	46,135 ± 4,081
Total body fat, g	9,413 ± 687	26,863 ± 2,347[*]	8,843 ± 1,102	33,583 ± 4,704[*]
% Body fat	23.4 ± 1.4	38.5 ± 1[*]	20.5 ± 2.8	40.7 ± 2.1[*]
BMI %ile	51.0 ± 7.1	97.1 ± 0.4[*]	57.0 ± 6.2	97.1 ± 0.6[*]

Data are means ± SE. CTL, control; Ob, obese; BMI, Body mass index; LBM, lean body mass.
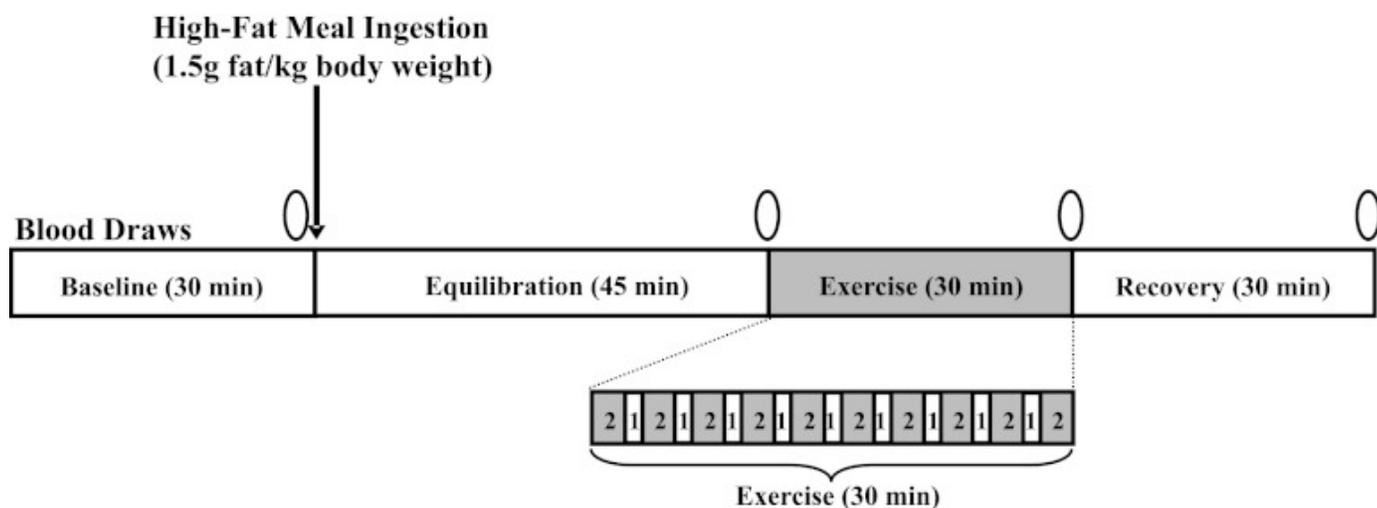
[*]$P < 0.05$, Ob vs. CTL.

Table 2.

Exercise characteristics of patients

	CTL	Ob	Matched Fasting CTL	Matched Fasting Ob
$\dot{V}_{O_2max}$, l/min	1.71 ± 0.2	1.88 ± 0.1	1.58 ± 0.2	1.71 ± 0.1
$\dot{V}_{O_2max}$, ml · min^{-1} · kg^{-1}	40.6 ± 2.0	27.8 ± 0.9[*]	36.1 ± 2.8	25.7 ± 1.4[*]
$\dot{V}_{O_2max}$/LBM, ml · min^{-1} · lean kg^{-1}	54.0 ± 1.8	48.8 ± 2.7	46.3 ± 5.1	40.5 ± 1.8
RER max test	1.11 ± 0.01	1.10 ± 0.01	1.14 ± 0.1	1.09 ± 0.01
HR max test, beats/min	189.6 ± 2.8	184.0 ± 5.8	187.6 ± 11.9	190.4 ± 3.2
PO max test, W	123.1 ± 12.2	127.9 ± 7.9	130.7 ± 14.8	126.2 ± 6.9
Mean HR (10 × 2 Exe), beats/min	179.3 ± 2.0	175.0 ± 2.5	175.5 ± 10.9	178.8 ± 3.1
Mean PO (10 × 2 Exe), W	91.4 ± 8.6	91.9 ± 6.9	99.0 ± 12.9	92.8 ± 5.5

Data are means ± SE. $\dot{V}_{O_2max}$, maximal aerobic capacity; RER, respiratory exchange ratio; HR, heart rate; PO, power output; Exe, exercise.

[*]$P < 0.05$, Ob vs. CTL.

Fig. 1.

High-Fat Meal Ingestion
(1.5g fat/kg body weight)

Blood Draws

| Baseline (30 min) | Equilibration (45 min) | Exercise (30 min) | Recovery (30 min) |

2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2

Exercise (30 min)

Experimental design. Subjects rested for 30 min after establishment of intravenous line for blood draws. A high-fat meal was then ingested (1.5 g fat/kg body wt of a semiliquid preparation containing 99% dairy fat) followed by a 45-min equilibration. The exercise paradigm consisted of 2-min cycling at 80% $\dot{V}_{O_2max}$ followed by 1-min rest, completed 10 times (30 min total, 20 min of actual cycling and 10 min rest in between). Blood samples were drawn at baseline, 45 min after meal ingestion, peak exercise, and 30-min post exercise. White circles, blood draw for all analytes; large black arrow, high-fat ingestion; exercise: gray bar, cycling; white bar, resting period.

Fig. 2.
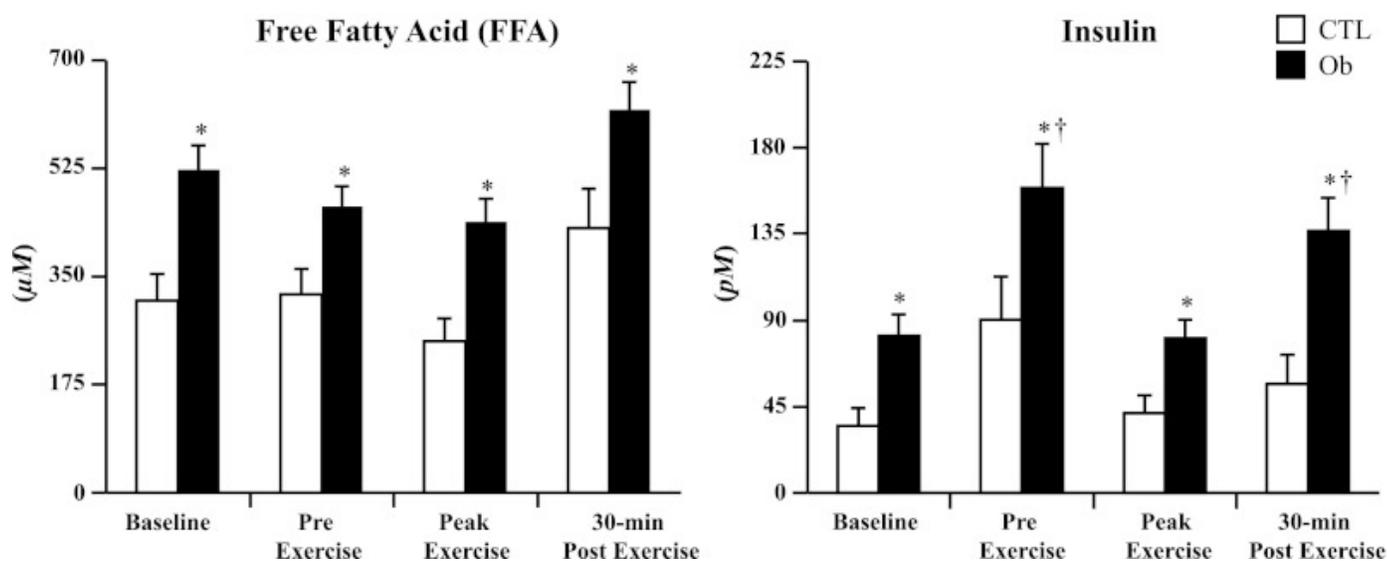
Plasma free fatty acid (FFA) and insulin response to 30 min of intermittent exercise at 80% maximal aerobic capacity ($\dot{V}_{O_2max}$) following ingestion of a high-fat meal. Obese (Ob) children displayed significantly higher levels of circulating FFA and insulin throughout the study. Data are means ± SE. $*P < 0.05$, Ob vs. controls (CTL); $†P < 0.05$ vs. baseline within same group.

Table 3.

Lipid characteristics of patients

| | CTL | Ob |

Lactate, mmol/l		
Baseline	2.3 ± 0.1	2.5 ± 0.1
Preexercise	2.0 ± 0.1	$2.2 \pm 0.1^{\dagger}$
Peak exercise	$5.4 \pm 0.4^{\dagger}$	$5.5 \pm 0.4^{\dagger}$
30-min postexercise	2.5 ± 0.2	2.6 ± 0.2
TG, mmol/l		
Baseline	0.4 ± 0.03	$1.6 \pm 0.2^{*}$
Preexercise	0.5 ± 0.04	$1.8 \pm 0.2^{*}$
Peak exercise	$0.6 \pm 0.1^{\dagger}$	$2.2 \pm 0.2^{*}$
30-min postexercise	$0.6 \pm 0.1^{\dagger}$	$2 \pm 0.2^{*}$
Total cholesterol, mg/dl		
Baseline	156.8 ± 5.7	152.1 ± 7.6
HDL, mg/dl		
Baseline	84.7 ± 6.6	$49 \pm 4.5^{*}$
LDL, mg/dl		
Baseline	64.6 ± 3.6	74.1 ± 5.7

Data are means ± SE. TG, triglycerides; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

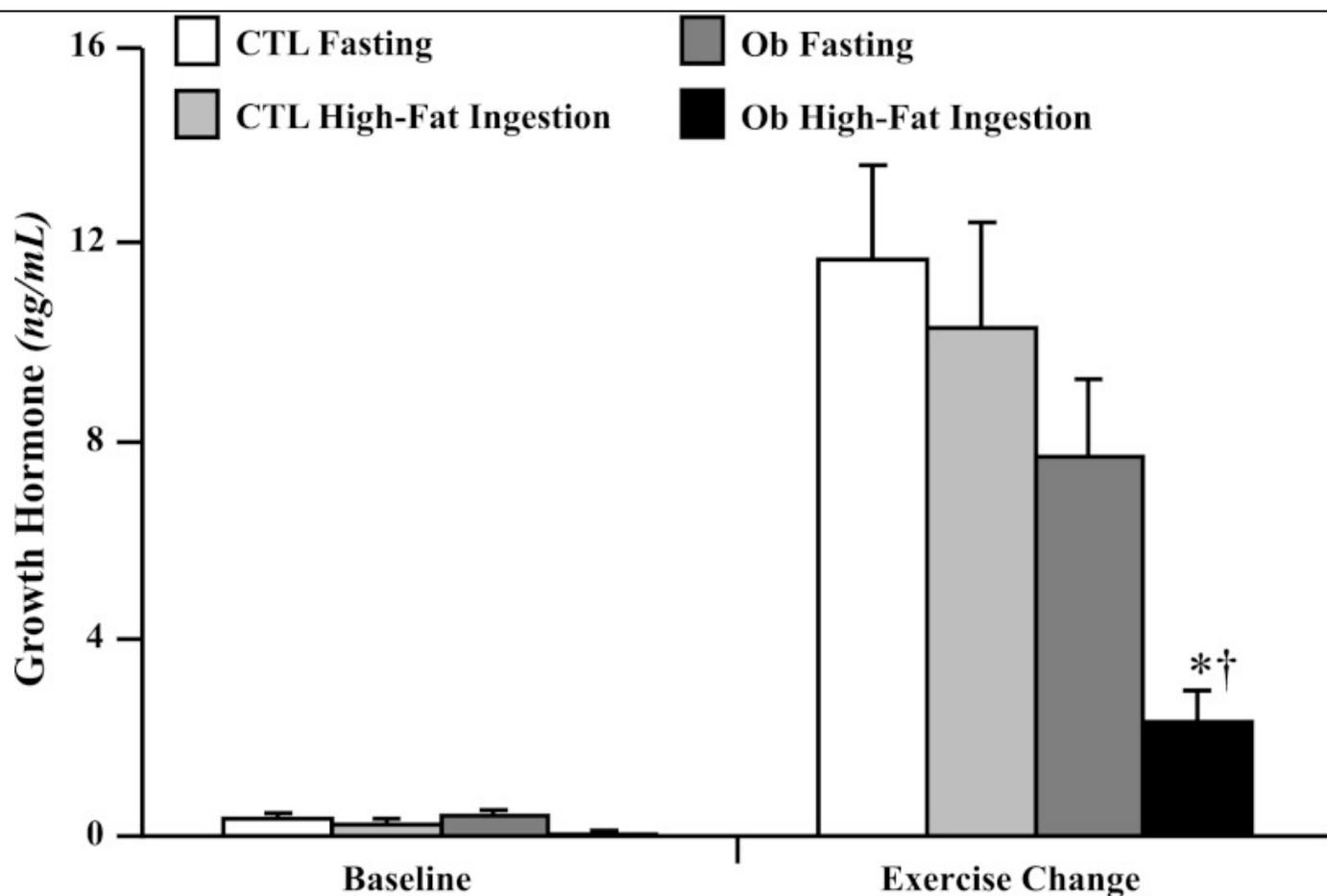$^{*}P < 0.05$, Ob vs. CTL between-groups difference;
$^{\dagger}P < 0.05$, time point vs. baseline within groups.

Fig. 3.
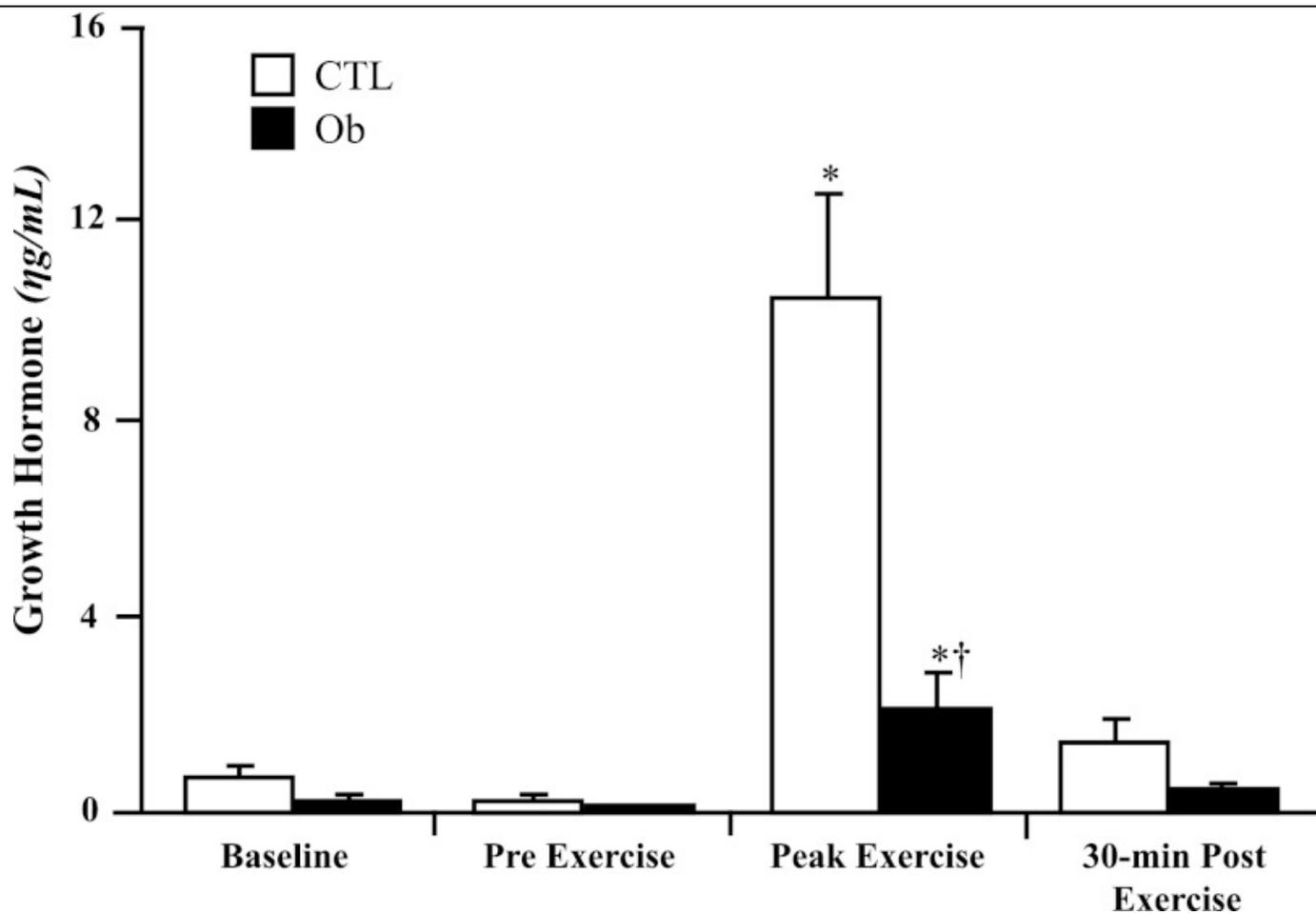
Plasma growth hormone (GH) response to 30 min of intermittent exercise at 80% $\dot{V}_{O_{2max}}$ following ingestion of a high-fat meal. Ob children displayed significant exercise-induced blunting of GH compared with CTL. Data are means ± SE. *$P < 0.05$, exercise-induced increases within groups; †$P < 0.05$, Ob vs. CTL between-groups exercise-induced increase.

Fig. 4.

Synergistic effect of obesity and lipid ingestion in suppressing the growth hormone response to exercise in children

GH increased significantly in all groups at the end of the exercise challenge. In CTL children, ingestion of a high-fat meal caused a small, nonsignificant blunting of the GH response. In Ob children, the GH response to exercise was lower than in CTL fasting conditions. The GH response in Ob was then further reduced after ingestion of a high-fat meal. Data are means ± SE. $*P < 0.01$, Ob fasting vs. Ob high-fat ingestion exercise change; $\dagger P < 0.001$, Ob vs. CTL high-fat ingestion exercise change.

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