The Decline in Pulsatile GH Secretion throughout Early Adulthood in Mice Is Exacerbated by Dietary-Induced Weight Gain


School of Biomedical Sciences (L.H., F.J.S., H.Y.T., T.Y.X., S.T.N., C.C.), University of Queensland, St. Lucia, Brisbane, Queensland 4072, Australia; and Department of Medicine (J.D.V.), Endocrine Research Unit, Mayo School of Graduate Medical Education, Clinical Translational Science Center, Mayo Clinic, Rochester, Minnesota 55905

The transition between puberty and adulthood is accompanied by a slowing in linear growth. Although GH is a key factor that drives somatic development into adulthood, early adulthood coincides with a reduction in circulating levels of GH. To this extent, a pathological decline in postpubertal GH secretion is detrimental to attainment of peak lean muscle mass and bone mass and promotes adiposity and increases susceptibility to the development of obesity in adulthood. Here we characterized pulsatile GH secretion in C57BL/6J mice at 12 and 16 wk of age. Deconvolution analysis of these measures reveals a reduction in pulsatile GH secretion between 12 and 16 wk of age. Dietary intervention with high-fat feeding at 8 wk of age results in a significant increase in adiposity, the development of glucose intolerance, and hyperinsulinemia. We show the exacerbation of the age-associated decline in pulsatile GH secretion in high-fat-fed mice after 4 wk of dietary intervention (at 12 wk of age), and a further suppression of pulsatile GH secretion by 8 wk of dietary intervention (at 16 wk of age). Suppressed pulsatile secretion of GH did not coincide with an elevation in circulating free fatty acids. Rather, we observed increased hepatic triglyceride content and an eventual decrease in circulating levels of IGF-I. Given the established role of GH in maintaining healthy aging, we anticipate that an advancing of the age-associated decline in pulsatile GH secretion as a consequence of dietary-induced weight gain may have long-term ramifications on adult health. (Endocrinology 153: 4380–4388, 2012)

Age-associated changes in endocrine function result in morphological and functional alterations throughout the body (1, 2). The GH/IGF-I axis plays a vital part in regulating body composition and maintaining physical fitness throughout adult life (3). By promoting lipid mobilization (4, 5) and by increasing protein synthesis (3), GH reduces body fat accumulation and preserves lean mass (6). In addition, GH is an important hormone for the maturation of muscle mass and strength in adolescents and young adults (7). To this extent, GH is a key regulator of somatic maturation in early adulthood (8). Consequently, the GH/IGF-I axis is thought to be one of the most important endocrine pathways that regulates lifespan and health (9).

In humans, spontaneous pulsatile GH secretion remains stable throughout childhood and peaks at puberty (10). This results in an elevation of circulating levels of IGF-I (11) and accounts for rapid somatic growth (12). After pubertal growth, GH secretion declines by approximately 14% per decade (13). This progressive decline occurs after the achievement of adult body height and sexual maturation (10). Interestingly, changes in body composition in aged individuals reflect observations from organic GH-deficient patients (14). Furthermore, adult-onset GH deficiency results in reduced muscle mass and strength, increased total body fat content, and reduced bone density...
The resemblance in changing body composition between adult-onset GH deficiency and aged individuals, together with observations of an age-dependent decline in the activity of the GH/IGF axis (16) suggests that the age-associated decline in GH secretion may contribute to the development of many of the physiological alterations that accompany aging. Second to this, attainment of low peak bone and muscle mass and the predisposition to developing obesity in childhood-onset GH-deficient patients after the cessation of GH treatment highlight the importance of optimal GH secretion throughout early adulthood (17). In this context, the primary role of GH as an anabolic hormone that promotes pubertal linear growth shifts to that of an important metabolic hormone that regulates body composition and adiposity throughout adulthood. It is therefore essential that we identify the factors that may advance the progressive decline in GH secretion throughout aging.

The inverse relationship between adiposity and GH secretion is well documented. In humans, the degree of reduction in both stimulated and spontaneous GH release correlates with the amount of total and visceral adipose mass (18–21). Increased adiposity is associated with a reduction in daily GH secretion rate, the mass of GH released per secretory event, and mean GH serum concentrations (22). Similarly, aging is characterized by a reduction in GH pulse frequency and the amplitude of GH secretion (13). In parallel to the age-dependent fall of GH secretion, a progressive increase in adiposity is observed throughout aging (23). The cause–effect relationship between an increase in adiposity and the reduction of GH secretion remains unclear. Given the role of GH in stimulating lipolysis and preserving protein (3), it is reasonable to conclude that the age-associated decline in GH secretion (irrespective of its cause) may further promote increased adiposity.

Observations from human studies provide information to address the effects of increased aging and adiposity on the GH secretion; however, attempts to define the mechanisms through which this may occur increasingly rely on observations from animal-based experiments. Although the effects of adiposity on GH secretion are well characterized (24–26), studies did not longitudinally assess the impact of progressive dietary-induced weight gain on pulsatile GH secretion. Consequently, it remains unclear whether dietary-induced weight gain impairs GH secretion during early adulthood.

We describe a decline in pulsatile GH secretion during early adulthood in mice. Moreover, we illustrate that increased adiposity, due to dietary-induced weight gain via high-fat feeding, occurs concurrently with significantly impaired pulsatile GH secretion. Suppressed pulsatile secretion of GH in high-fat-fed mice did not coincide with an elevation in circulating free fatty acids (FFA). Rather, we observed early fatty infiltration of the liver, reminiscent of GH deficiency (27, 28), and the eventual decline in circulating levels of IGF-I. We conclude that dietary-induced weight gain advances the natural decline in GH secretion observed in early adulthood and anticipate that these changes may impact somatic development throughout adulthood.

Materials and Methods

Animals

Wild-type C57BL/6J male mice were obtained from the University of Queensland Biological Resources and group housed (n = 2) in a 12-h light, 12-h dark cycle (lights on at 0600 h). Room temperature was maintained at 22 ± 2 C. Animals had free access to water and food for the duration of all experiments, unless otherwise specified. All experimental procedures were approved by the University of Queensland Animal Ethics Committee.

Dietary intervention strategy

Mice maintained on a standard diet (SD) received regular mouse chow (4.6% fat, meat-free rat and mouse diet; Specialty Feeds, Glen Forrest, Western Australia, Australia). For high-fat feeding, mice were maintained on a commercial high-fat diet (HFD, SF04-001; 22.6% protein, 23.5% fat; Specialty Feeds) starting at 8 wk of age.

Characterizing pulsatile GH secretion in mice

For measures of pulsatile GH secretion, blood samples were collected and processed as previously described (29). Starting at 0700 h, 36 sequential tail-tip blood samples (4 µl) were collected from each mouse at 10-min intervals. Samples were immediately placed on dry ice and transferred to −80 C for storage for future analysis.

Assessment of age-associated changes in pulsatile GH secretion

At 11 wk of age, mice were relocated to a quiet room, individually housed, and allowed 1 wk to acclimate to the new housing conditions. Animals remained in this room for the duration of the experiment. For repeat assessment of GH secretion, blood samples were collected from the same mouse at 12 and 16 wk of age. After collection of blood samples at 12 wk of age, mice were returned to their home cage and allowed to recover for 4 wk before repeat blood collection at 16 wk of age. The age-associated decline in pulsatile GH secretion was assessed in mice maintained on a SD or HFD. After collection of blood samples at 16 wk of age, mice were returned to their home cage and given 2 d to recover before assessment of metabolic profile.

Assessment of the dietary-induced changes in pulsatile GH secretion

Starting at 8 wk of age, mice were maintained on a SD or HFD as described above. At 11 wk of age, mice were relocated to a...
quiet procedure room and prepared for collection of blood for pulsatile GH analysis as detailed above. After 4 wk of dietary intervention (at 12 wk of age), blood samples were collected from SD or HFD mice. After collection of blood samples, mice were returned to their home cage and given 2 d to recover before assessment of metabolic profile.

Characterizing the metabolic profile of mice

After 4 and 8 wk of dietary intervention, mice underwent a glucose tolerance test (GTT). Immediately preceding the onset of the GTT, a single 20-μl tail-tip blood sample was collected using a heparinized pipette tip (100 IU/ml), and plasma was separated for the assessment of fasting FFA. After the GTT, mice were given free access to food and allowed 2 d to recover from fasting before collection of blood and tissue for further analysis. At the time of killing (between 0900 and 1000 h), mice were anesthetized with a single ip injection of sodium pentobarbitone (32.5 mg/ml, 1PO643-1; Virbac Animal Health, Milperra, New South Wales, Australia). Terminal blood samples were collected using a heparinized syringe (100 IU/ml). Plasma was collected, placed on dry ice, and stored at −80 C for future analysis. To determine the adiposity of mice, gonadal fat pads were isolated by dissection, and the fat pad mass was determined. Measures of adiposity were limited to gonadal fat pad mass, because this is recommended as a simple and accurate estimate of body fat in mice (30). Isolation of gonadal fat mass allows accurate estimates of adiposity in nonobese mice. This is not possible by conventional dual energy x-ray absorptiometry analysis (31).

Glucose tolerance test

Starting at 1800 h, mice were fasted overnight (12 h) with free access to water. At 0600 h, mice were injected with glucose (ip, 1.0 g/kg body weight). A tail-tip blood sample was collected immediately before the injection and at 15, 30, 45, 60, 90, and 120 min after the injection. Blood glucose concentration in tail-tip blood samples was determined using the Accu-Chek Performa blood glucose meter (Roche Diagnostics, Indianapolis, IN). A change in blood glucose concentration in response to the glucose injection was compared relative to starting blood glucose levels for each mouse.

Hormone and metabolite analysis

Circulating levels of leptin, insulin, and IGF-I were determined by commercial ELISA kits [EZML-82K mouse leptin and EZRMI-13K rat/mouse insulin (Millipore, Billerica, MA) and SMG100 mouse/rat IGF-I (R&D Systems, Minneapolis, MN)]. Circulating levels of FFA, glucose, and triglycerides were determined by colorimetric assay kits [FFA kit, 279-75401, NEFA C assay (Wako, Osaka, Japan); 10009582 glucose assay kit and 10010303 triglyceride assay kit (Cayman, Ann Arbor, MI)]. To determine hepatic triglyceride content, liver samples were digested by saponification in ethanolic KOH and neutralized with MgCl₂ as described previously (32). Glycerol content was determined using a glycerol standard (G7793; Sigma, St. Louis, MO) and free glycerol reagent (F6428; Sigma). Analysis for GH was performed using an in-house GH ELISA as characterized previously (29). The within- and between-assay coefficients of variation for all ELISA ranged from 2.89–11.01%, respectively.

Data and statistical analysis

Data are presented as mean ± SEM. Age-associated differences between groups were analyzed by paired t test. Diet-associated differences between groups were identified by two-tailed Student’s t test. All measures (excluding deconvolution analysis) were performed using GraphPad Prism version 5.0c (GraphPad, Inc., San Diego, CA). The threshold level for statistical significance was set at *P* < 0.05. The quantitative features underlying GH secretion and clearance associated with the observed GH concentration profiles were determined by deconvolution analysis following parameters established previously (22, 33).

Results

Pulsatile GH declines significantly between 12 and 16 wk of age

Representative secretory profiles and output figures illustrating the onset of pulsatile GH secretion in mice maintained on a SD at 12 and 16 wk of age are illustrated in Fig. 1. A and B. Peaks in GH secretion occurred at regular in-
tervals and were dispersed by periods of low basal levels of secretion. There was no apparent age-associated difference in the secretory pattern; however, peak levels of GH secretion were clearly lower by 16 wk of age. Deconvolution analysis of pulsatile measures of GH confirmed a significant decline in GH secretion between 12 and 16 wk of age. This is characterized by a reduction in both total (Fig. 1C) and pulsatile (Fig. 1D) GH secretion rate and the mass of GH secreted per burst (Fig. 1E). Basal GH secretion rate declined; however, this did not reach statistical significance. Paired comparisons of GH secretory parameters after deconvolution analysis are summarized in Table 1.

Characterization of diet-induced weight gain model

Phenotypic differences in body weight and fat mass are summarized in Fig. 2 and Table 2. Weight gain in HFD mice started to deviate from SD mice as early as 2 wk of dietary intervention and reached statistical significance by 3 wk of dietary intervention (Fig. 2A). Increased body weight in HFD mice was associated with a significant increase in gonadal fat mass at 12 and 16 wk of age (Table 2). Data confirm that our dietary-induced weight gain strategy promotes significant weight gain and increased adiposity, as is seen using similar dietary intervention strategies (34).

Changes in circulating levels of leptin, insulin, fed and fasting glucose and FFA, and triglycerides after 4 and 8 wk of dietary intervention are summarized in Table 2. Circulating levels of leptin increase in proportion to adiposity (35–37) and thus reflect an overall increase in whole body fat mass. Circulating levels of leptin in HFD mice were elevated by 4 wk of dietary intervention. We observed a significant increase in insulin by 4 wk of dietary intervention; however, this did not reach statistical significance at 8 wk of dietary intervention. In human obesity, elevated circulating levels of FFA may contribute to the suppression of pulsatile GH secretion (38, 39). Thus, we determined FFA levels in HFD mice. Circulating FFA levels between HFD and SD mice after 4 and 8 wk of dietary intervention under both fed and fasting conditions remained unchanged. In addition to this, circulating levels of triglycerides remained unchanged (Table 2). Compared with the SD group, circulating levels of fed and fasting glucose in HFD animals after 4 and 8 wk of dietary intervention remained unchanged. Irrespective of this, mice main-
tained on the HFD were glucose intolerant (as assessed by GTT) at 4 and 8 wk of dietary intervention (Fig. 2, B and C).

**Dietary intervention with high-fat feeding results in a suppression of pulsatile GH secretion**

Representative GH secretion profiles and output figures illustrating the onset of GH pulses in mice fed either the SD (Fig. 3A) or HFD (Fig. 3B) after 4 wk of dietary intervention (at 12 wk of age) are illustrated in Fig. 3. Deconvolution analysis confirms a significant reduction in total, pulsatile, and basal GH secretion in response to HFD (data summarized in Table 3). We observed an overall reduction in the mass of GH secreted per burst; however, this did not reach statistical significance. Parameters of pulsatile GH measurement after 4 wk of high-fat feeding (12 wk of age, Table 3) resemble that of SD mice at 16 wk of age (Table 1).

**High-fat feeding results in further suppression of the age-associated decline in pulsatile GH secretion**

Representative secretory profiles and output figures illustrating the onset of pulsatile GH secretion at 12 and 16 wk of age in mice maintained on the HFD are illustrated in Fig. 3, C and D. Deconvolution analysis of pulsatile measures of GH secretion confirmed a further and significant decline in GH secretion between 12 and 16 wk of age. This is characterized by a reduction in both total (Fig. 3D) and pulsatile (Fig. 3E) GH secretion rate. Basal GH secretion rate and the mass of GH secreted per burst declined (Table 4 and Fig. 3F); however, this did not reach statistical significance. Paired comparisons of GH secretory parameters after deconvolution analysis of mice maintained on a HFD are summarized in Table 4. Collectively, data demonstrate a further age- and diet-associated decline in pulsatile GH secretion.

**Dietary intervention with high-fat feeding results in hepatic triglyceride accumulation and a reduction of circulating levels of IGF-I**

In contrast to circulating levels of FFA and triglycerides (Table 2), we observed a significant increase in triglyceride accumulation in the livers of HFD mice after 4 and 8 wk of dietary intervention (Fig. 4A). Observations are consistent with hepatic fatty infiltration in GH-deficient individuals (27, 28). Circulating levels of IGF-I were significantly reduced in HFD mice after 8 wk of dietary intervention (Fig. 4B). Observations suggest that impaired hepatic IGF-I production occurs in response to a reduction of circulating levels of GH and possibly after impaired liver function. This was not directly assessed and thus warrants further investigation.

**Discussion**

To further investigate the decline in GH secretion after sexual maturation and to assess the impact of dietary-induced weight gain on GH secretion, we examined pulsatile GH secretion in mice during early adulthood under basal conditions and after dietary-induced weight gain. We document a rapid decline in pulsatile GH secretion in mice between 12 and 16 wk of age. Second to this, we demonstrate that high-fat feeding contributing to increased adiposity results in a reduction in pulsatile GH secretion after 4 wk of high-fat feeding. A further reduction in pulsatile GH secretion was observed after 8 wk of high-fat feeding. Impaired pulsatile GH secretion occurred alongside hepatic lipid accumulation and impaired circulating levels of IGF-I. Observations confirm that diet-induced weight gain exacerbates the age-associated decline in pulsatile GH secretion in the mouse.

The reduction in pulsatile GH secretion at 16 wk of age corresponds well with the timing of age-associated

---

**TABLE 2.** Body weight, gonadal fat pad weight, and circulating levels of leptin, insulin, and metabolites in plasma from mice maintained on SD or HFD for 4 wk (12 wk of age) or 8 wk (16 wk of age)

<table>
<thead>
<tr>
<th></th>
<th>4 wk of dietary intervention (12 wk of age)</th>
<th>8 wk of dietary intervention (16 wk of age)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SD</td>
<td>HFD</td>
</tr>
<tr>
<td>Body weight (g)</td>
<td>26.7 ± 0.41</td>
<td>30.6 ± 1.34</td>
</tr>
<tr>
<td>Gonadal fat pad weight (g)</td>
<td>0.40 ± 0.05</td>
<td>1.21 ± 0.15</td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>5.24 ± 0.88</td>
<td>22.1 ± 1.95</td>
</tr>
<tr>
<td>Insulin (ng/ml)</td>
<td>0.74 ± 0.20</td>
<td>1.82 ± 0.35</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>228 ± 9.77</td>
<td>222 ± 20.00</td>
</tr>
<tr>
<td>Fasting glucose (mg/dl)</td>
<td>96.9 ± 3.06</td>
<td>108 ± 6.41</td>
</tr>
<tr>
<td>FFA (mEq/liter)</td>
<td>0.33 ± 0.04</td>
<td>0.26 ± 0.02</td>
</tr>
<tr>
<td>Fasting FFA (mEq/liter)</td>
<td>1.04 ± 0.10</td>
<td>0.97 ± 0.07</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>42.8 ± 6.47</td>
<td>35.4 ± 3.34</td>
</tr>
</tbody>
</table>

Plasma samples were collected between 0900 and 1000 h. Fasting glucose and FFA levels were determined after a 12-h overnight fast. Data are presented as mean ± SEM; n = 6–8 per group.
changes in the circuitry of the pituitary gland (40) and may occur as a consequence of morphological changes in the integration of the somatotroph network. Indeed, Bonnefont et al. (40) describe a progressive increase in the clustering of the proportion of somatotrophs at puberty (from 4–10 wk of age) and a later reduction in clustering (at approximately 16 wk of age) to levels similar to that observed before pubertal onset. Given that somatotroph function is under direct hypothalamic control, it is unlikely that altered integration of the somatotroph network will solely account for reduced GH secretion at this time. For example, the number of GHRH neurons in mice decreases significantly between 8 and 16 wk of age (41), and this correlates well with the observed reduction in pulsatile GH secretion in mice during early adulthood. The loss of GHRH neurons by 16 wk of age may account for the reversal in synchrony of the somatotroph network (40) and our observed reduction in pulsatile GH secretion.

TABLE 3. Deconvolution analysis of GH in whole-blood tail-tip samples collected from mice maintained on SD or HFD for 4 wk (12 wk of age)

<table>
<thead>
<tr>
<th></th>
<th>SD</th>
<th>HFD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total GH secretion rate</td>
<td>873 ± 160</td>
<td>442 ± 36.3</td>
<td>0.015</td>
</tr>
<tr>
<td>(ng/ml per 6 h)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulsatile GH secretion</td>
<td>732 ± 140</td>
<td>414 ± 38.8</td>
<td>0.040</td>
</tr>
<tr>
<td>rate (ng/ml per 6 h)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal secretion rate</td>
<td>141 ± 32.4</td>
<td>26.7 ± 6.02</td>
<td>0.002</td>
</tr>
<tr>
<td>(ng/ml per 6 h)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mass of GH secreted/burst</td>
<td>183 ± 32.6</td>
<td>123 ± 16.2</td>
<td>0.115</td>
</tr>
<tr>
<td>(MPP, ng/ml)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of secretory</td>
<td>4.00 ± 0.33</td>
<td>3.67 ± 0.33</td>
<td>0.482</td>
</tr>
<tr>
<td>bursts/6 h</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Samples were collected at 10-min intervals between 0700 and 1300 h. Data are presented as mean ± SEM; n = 12 per group. MPP, Mass released per pulse.
In humans, increased adiposity is matched with decreased pulsatile GH secretion (13). The degree of reduction in both stimulated and spontaneous GH release correlates with the amount of total and visceral adipose mass (18–21). Likewise, obesity is characterized by GH deficiency (13). We anticipate that a similar relationship would occur in mice after dietary-induced weight gain. Starting at 8 wk of age, 4 wk of high-fat feeding resulted in a significant decline in total, pulsatile, and basal GH secretion rate (Table 3), whereas 8 wk of high-fat feeding resulted in a further decline in pulsatile GH secretion in mice. Measures of pulsatile GH secretion in 12-wk-old mice after 4 wk of high-fat feeding are comparable to measures of pulsatile GH secretion in SD mice at 16 wk of age (Tables 1 and 3). Thus, although the age-associated decline in GH secretion is still evident in HFD animals, it appears that dietary-induced weight gain advanced the normal decline in pulsatile GH secretion observed throughout early adulthood. Given the role of GH in somatic development throughout early adulthood (8), the impact of reduced GH secretion after diet-induced weight gain in early adulthood warrants further investigation.

Previous investigations identified the development of leptin resistance (42), hyperinsulinemia (43), and an elevation of circulating levels of FFA (38, 44) as potential causes of suppressed GH secretion after dietary-induced weight gain. Although elevated levels of circulating FFA have been found to reduce GH secretion in rats (45), and long-term (1.5 yr) high-fat feeding results in an increase in circulating levels of FFA in mice (46), the suppression of pulsatile GH secretion after 4 and 8 wk of high-fat feeding in this study did not coincide with an elevation in circulating measures of FFA. Consequently, our data suggest that an elevation in circulating levels of FFA do not underlie the decrease in pulsatile GH secretion seen at this time. This is in line with previous findings that propose a reduction in peak levels of plasma GH coincident with normal circulating measures of FFA after 16 wk of high-fat feeding in mice (43).

GH is thought to promote the uptake and storage of triglycerides in the liver (47). However, GH deficiency is more often associated with fatty infiltration of the liver (27, 28). As seen in humans, hepatic lipid infiltration occurred alongside reduced GH secretion in HFD mice. This occurred by 4 wk of dietary intervention. The increase in hepatic triglycerides coincident with normal levels of plasma FFA in HFD mice may occur as a consequence of increased hepatic lipid supply (48, 49). However, hepatic lipid accumulation has been observed to increase in the absence of GH-dependent signal transducer and activator of transcription 5 (GH/STAT5) signaling (50). Consequently, we anticipate that the reduction in peak GH secretion after high-fat feeding contributes to an elevation in hepatic triglyceride content in our HFD mice.

Peak levels of GH promote the production and release of IGF-I from the liver, and thus circulating measures of IGF-I may be indicative of peak pulsatile levels of GH (51). The decline in pulsatile GH secretion by 16 wk of age in SD mice did not contribute to a reduction in circulating levels of IGF-I. Rather, a decline in circulating levels of IGF-I was seen only after 8 wk of high-fat feeding. Therefore, it appears that the dietary-induced loss in pulsatile GH secretion, coupled with the age-associated decline in pulsatile GH secretion in HFD mice results in a pathological re-
duction in IGF-I secretion. This is in line with the reduction of IGF-I that is often observed in obese patients (52).

Assessment of GH secretion in mice during early adulthood demonstrates a significant reduction in pulsatile GH secretion between 12 and 16 wk of age. Furthermore, dietary-induced weight gain significantly advances this age-associated decline in GH secretion and results in a reduction in circulating levels of IGF-I. Given the role of GH/IGF-I in maintaining healthy aging, exacerbation of the age-associated decline in pulsatile GH secretion in response to high-fat feeding may have significant ramifications on adult health. These long-term consequences are yet to be determined.

**Acknowledgments**

We gratefully acknowledge the assistance and support from staff and animal technicians at the Australian Institute for Bioengineering and Nanotechnology (University of Queensland Biological Resources) and the assistance from Joan W. Leong, Ying Wan, and Kevin Lee.

Address all correspondence and requests for reprints to: Prof. Chen Chen or Dr. Frederik Steyn, School of Biomedical Sciences, University of Queensland, St. Lucia, Queensland 4072, Australia. E-mail: chen.chen@uq.edu.au or f.steyn@uq.edu.au.

This work was supported by the Australian National Health and Medical Research Council and The University of Queensland. L.H. is a recipient of an overseas postgraduate research scholarship from China Scholarship Council and subsidy scholarship from the University of Queensland.

Disclosure Summary: The authors have nothing to disclose.

**References**

like growth factor-I concentrations. Growth Horm IGF Res 8:397–401
52. Gómez JM, Maravall FJ, Gómez N, Navarro MA, Casamitjana R, Soler J 2004 The IGF-I system component concentrations that decrease with ageing are lower in obesity in relationship to body mass index and body fat. Growth Horm IGF Res 14:91–96