Altered Growth Hormone, Cortisol, and Leptin Secretion in Healthy Elderly Persons With Sarcopenia and Mixed Body Composition Phenotypes

Debra L. Waters, Clifford R. Qualls, Richard I. Dorin, Johannes D. Veldhuis, and Richard N. Baumgartner

1University of New Mexico, Health Sciences Center, Albuquerque.
2Endocrine Research Unit, Mayo School of Graduate Medical Education, Rochester, Minnesota.

Background. Obese phenotypes and aging are independently associated with hypothalamic–pituitary–adrenocortical (HPA) axis and leptin secretion alterations. However, leptin secretion and HPA axis function in elderly persons with other body composition phenotypes is largely unknown.

Methods. Forty-five healthy elderly participants were classified normal lean (NL), sarcopenic (SS), sarcopenic-obese (SO), or obese (OO) using dual-energy x-ray absorptiometry. Growth hormone (GH), cortisol, and leptin secretion were evaluated during a free-running night, and oral glucocorticoid suppression test (dexamethasone DEX). Diurnal cortisol secretion was assessed by hourly salivary samples with timed meals. Data were analyzed using cluster, deconvolution, and approximate entropy (ApEn) analyses.

Results. GH area, total secretion, and mean concentration during the free-running night was lower in the SO and OO groups versus the SS and NL groups (p < .02, Wilcoxon test). GH mean concentration and total secretion significantly increased in all groups during DEX (overall p < .05) except the SO group, in which ApEn increased (p = .03). Pre- and postbreakfast peak salivary cortisol (p = .004) and area under the curve (p = .03) was greatest in the SS group. Baseline leptin (11:00 PM) was significantly higher in the SO, OO, and SS groups versus the NL group (p = .01). Appendicular skeletal muscle mass was independently and negatively correlated with leptin in all groups, even after adjusting for percentage body fat (p = .001).

Conclusions. In the presence of obesity, GH secretion was depressed with a blunted and disorderly response to oral glucocorticoid suppression in SO participants. Sarcopenic participants had concomitantly elevated leptin and cortisol relative to their low body fat mass. Complex or dysregulated neuroendocrine feedback systems appear to be operating in elderly persons with specific body composition phenotypes.

Key Words: Aging—Sarcopenia—HPA axis—Leptin.

AGING and obesity have been associated with hypothalamic–pituitary–adrenocortical (HPA) axis and leptin secretion alterations (1–5). However, the function of these hormonal axes in other body composition phenotypes is largely unknown. The dysregulation of growth hormone (GH), cortisol, and sex hormone has been postulated in the pathophysiology of sarcopenia, whereas leptin is a more recent candidate hormone (5,6). The health consequences of sarcopenia are documented (7,8), whereas recent evidence suggests that sarcopenic-obesity (the combination of sarcopenia and obesity) increases the risk for functional disability by over 2-fold compared to other body composition phenotypes (9).

To examine the complex interrelationships between select hormones and body composition phenotypes, GH, cortisol, and leptin were examined in three settings: (i) diurnally with timed meals; (ii) a nocturnal free-running series; and (iii) in response to nocturnal oral glucocorticoid (dexamethasone, DEX).

**METHODS**

Forty-five older persons (24 men, 21 women, 77.6 ± 6.5 years) were recruited from the New Mexico Aging Process Study cohort described elsewhere (10). They were not depressed and were free of major medical conditions. None were receiving hormones or medications known to interfere with the study. The University of New Mexico Human Research Review Committee approved the protocol.

Participants were admitted to the General Clinical Research Center (GCRC) at the University of New Mexico for a sleep acclimatization night. Three caffeine-free standardized meals were served the following day at: 7:30 AM, 12:00 PM, and 5:30 PM. Five mg of zolpidem tartrate (Ambien) was offered at 10:00 PM, and lights were out at 11:00 PM. Twenty-minute, 3 mL blood samples for cortisol and GH were collected from 11:00 PM through 7:00 AM. Hourly salivary cortisol samples were obtained from 7:00 AM through 11:00 PM according to the manufacturer protocol with standardized meals at 7:30 AM, 12:00 PM, and 5:30 PM eaten within 20 minutes. Baseline blood samples for cortisol, GH, and leptin were obtained at 11:00 PM followed by 1.0 mg of oral DEX and 20-minute samples from 11:00 PM through 7:00 AM. Participants were discharged at 8:00 AM.

**Definition of Sarcopenia and Sarcopenic-Obesity**

Body composition was measured by a Lunar DPX dual-energy x-ray absorptiometer (GE/Lunar Radiation Corp., Madison, WI). Appendicular skeletal muscle mass (ASM)
was calculated, and participants were classified as normal lean (NL), sarcopenic (SS), sarcopenic-obese (SO), or obese (OO), using cut points defined previously (7, 10). Groups were balanced for age and sex.

Assays
Cortisol, GH, and leptin blood samples were allowed to clot at room temperature, centrifuged, and frozen at $-70\degree$C for subsequent analysis. GH was assayed using ultrasensitive chemiluminescence (Immulite; Diagnostic Products Corp., Los Angeles, CA), serum cortisol by ultrasensitive chemiluminescence (Immulite), and leptin by radioimmunoassay (Linco Research, St. Louis, MO). Sensitivity and intra-assay precision was 0.026 μg/L and 5.3% for GH, 0.2 μg/dL, and 8.8% for cortisol, and 8.8% for leptin. Salivary cortisol was assayed using solid-phase radioimmunoassay (Coat-a-Count; Diagnostic Products Corp.) and insulin-like growth factor-1 (IGF-1) by radioimmunoassay acid-ethanol extraction (Nichols Institute Diagnostics, San Juan Capistrano, CA). Sensitivity and intra-assay precision was 0.2 μg/dL and 4.8% for salivary cortisol and 60 μg/L and 2.4% for leptin.

Deconvolution Analysis
Free-running cortisol and GH secretory profiles were assessed using deconvolution analysis as previously described (11). Basal secretion rates for cortisol were assumed to approach zero (12), and total GH basal secretion was calculated by multiplying the basal secretion rate per minute by sampling duration (480 minutes). This product was added to the pulsatile production rate to calculate total GH secretion. Ten percent of GH values fell below the assay limit of detection and were assigned a value of 0.025 μg/L.

Cluster Analysis
A waveform-independent deconvolution analysis (PULSE) was used to calculate leptin secretion (11), based on the one component half-life of 24.9 minutes (13).

### Table 1. Participant Demographics by Group

<table>
<thead>
<tr>
<th>Body Composition Classification</th>
<th>Normal Lean</th>
<th>Sarcopenic</th>
<th>Sarcopenic-Obese</th>
<th>Obese</th>
<th>Kruskal–Wallis Test</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td>(n = 8)</td>
<td>(n = 5)</td>
<td>(n = 6)</td>
<td>(n = 5)</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>76.8 ± 5.3</td>
<td>83.8 ± 4.5</td>
<td>77.8 ± 8.8</td>
<td>80.4 ± 10.1</td>
<td>NS</td>
</tr>
<tr>
<td>Height, cm</td>
<td>173.8 ± 8.3</td>
<td>171.8 ± 8.7</td>
<td>175.5 ± 2.9</td>
<td>174.6 ± 10.1</td>
<td>NS</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>74.2 ± 9.1</td>
<td>64.3 ± 5.5</td>
<td>80.5 ± 4.5</td>
<td>91.0 ± 14.2</td>
<td>.005</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.5 ± 1.2</td>
<td>21.8 ± 1.3</td>
<td>26.1 ± 1.4</td>
<td>29.8 ± 3.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Percent body fat %</td>
<td>23.1 ± 5.5</td>
<td>24.3 ± 3.2</td>
<td>34.8 ± 3.5</td>
<td>33.4 ± 2.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Lean body mass, kg</td>
<td>54.3 ± 6.7</td>
<td>46.3 ± 4.1</td>
<td>49.3 ± 3.4</td>
<td>56.4 ± 8.6</td>
<td>.06</td>
</tr>
<tr>
<td>ASM index</td>
<td>8.1 ± 0.7</td>
<td>6.7 ± 0.4</td>
<td>6.8 ± 0.4</td>
<td>8.2 ± 0.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td>(n = 7)</td>
<td>(n = 3)</td>
<td>(n = 6)</td>
<td>(n = 5)</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>75.4 ± 4.5</td>
<td>75.7 ± 6.4</td>
<td>77.8 ± 3.9</td>
<td>74.0 ± 6.5</td>
<td>NS</td>
</tr>
<tr>
<td>Height, cm</td>
<td>165.5 ± 5.6</td>
<td>163.8 ± 3.7</td>
<td>155.9 ± 7.5</td>
<td>161.8 ± 6.1</td>
<td>NS</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>64.9 ± 5.2</td>
<td>56.0 ± 5.1</td>
<td>65.2 ± 12.5</td>
<td>71.7 ± 6.8</td>
<td>NS</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>23.7 ± 1.6</td>
<td>21.0 ± 1.3</td>
<td>26.6 ± 3.4</td>
<td>27.4 ± 2.1</td>
<td>.007</td>
</tr>
<tr>
<td>Percent body fat, %</td>
<td>36.3 ± 2.3</td>
<td>35.7 ± 3.6</td>
<td>44.1 ± 3.6</td>
<td>44.6 ± 2.6</td>
<td>.002</td>
</tr>
<tr>
<td>Lean body mass, kg</td>
<td>38.8 ± 2.9</td>
<td>33.6 ± 1.9</td>
<td>31.3 ± 3.3</td>
<td>37.2 ± 3.9</td>
<td>.01</td>
</tr>
<tr>
<td>ASM index</td>
<td>5.9 ± 0.3</td>
<td>5.1 ± 0.3</td>
<td>5.0 ± 0.2</td>
<td>6.1 ± 0.5</td>
<td>.002</td>
</tr>
</tbody>
</table>

**Notes:** Mean ± standard deviation.

BMI = body mass index; ASM index = appendicular skeletal muscle mass from DXA/height$^2$; NS = not statistically significant.

Approximate Entropy
Approximate entropy (ApEn) as described previously was used to analyze the orderliness/disorderliness of hormone profiles (14).

### Statistical Analyses
Statistical analyses were performed using the SAS statistical package (version 8; SAS Institute, Cary, NC). The distributions for leptin and cortisol were positively skewed and transformed using natural logarithms. Correlations were examined using Pearson correlation matrices within body composition grouping. Analyses to determine the independent association of each variable with body composition classification included multivariate analysis, linear regression, stepwise variable selection, Kruskal–Wallis test, and Student’s $t$ test.

### RESULTS

#### Descriptive Characteristics

Descriptive characteristics are presented in Table 1. Differences in body composition parameters were as per study design.

### Free-Running Night GH

Total secretion for GH was significantly different between the groups (Kruskal–Wallis, $p = .02$) and was due to the presence or absence of obesity (Wilcoxon rank sum test, $p = .002$, Figure 1). Mean concentration and area were lowest in the SO and OO groups (Table 2).

### Cortisol

There were no differences in cortisol secretion associated with body composition classification or sex.

**ApEn**

Neither cortisol nor GH displayed ApEn differences by group.
Salivary Cortisol and Timed Meals

Meal 1 cortisol area under the curve (AUC) was greater than that of meal 3 (p = .005) across all groups with no group differences. The SS group had higher peak salivary cortisol concentrations following breakfast (meal 1) compared to the OO, NL, and SO groups (23.5 [13.2–33.6], 14.6 [10.8–18.5], 13.8 [11.0–16.6], 12.4 [9.9–14.9] nmol/L, respectively; p = .004). Peak concentrations were not different between groups for meals 2 or 3. Cortisol AUC (7:00 AM through 11:00 PM) was higher in the SS group versus the SO, OO, and NL groups, respectively (p = .03, Figure 2).

Oral Dexamethasone Suppression (DEX)

Cortisol.—There were no group differences in 7:00 AM (post DEX) cortisol concentrations (NL = 2.98 [0.59–5.4]; SO = 1.79 [0.28–3.30]; SS = 1.79 [0.94–2.40]; OO = 1.33 [0.90–1.77] nmol/L; p = .50).

Growth hormone.—Group differences in GH total secretion (NL = 29.0 [20.0–38.1], SO = 22.4 [13.2–31.5], SO = 15.3 [12.0–18.7], OO = 18.1 [12.5–23.7] µg/L, Kruskal–Wallis, p = .02) and mean concentration (NL = 1.3 [0.9–1.7], SS = 1.0 [0.6–1.4], SO = 0.6 [0.5–0.8], OO = 0.8 [0.5–1.0] µg/L; Kruskal–Wallis, p = .02) were observed, and related to obesity (post hoc analysis, p < .005). In a paired analysis comparing DEX administration versus free-running night, in the NL and OO, area (p = .01, p = .005), total secretion (p = .04, p = .001), and mean concentration (p = .01, p = .002) increased respectively. In SS, area (p = .006), mean concentration (p = .008), and mean interval (p = .01) increased, and number of peaks decreased (p = .03, Wilcoxon signed rank test). No GH deconvolution parameters were significantly changed in SO; however, ApEn significantly increased (p = .03).

Leptin.—Women had a greater average nadir (18.8 [15.0–22.5] vs 7.1 [5.2–9.0] ng/mL, p < .001), mean (20.8 [16.7–24.9] vs 7.4 [5.6–9.2] ng/mL, p < .001), peak height (23.4 [19.1–27.7] vs 9.3 [6.9–11.7] ng/mL, p < .0001), and area (331.4 [253.8–409.0] vs 164.3 [62.9–265.7] ng/mL, p = .004) compared to men.

Controlling for sex, mean concentration (NL = 8.9 [5.4–12.5], SS = 12.8 [5.1–20.5], SO = 18.4 [10.4–26.5], OO = 17.3 [10.7–23.7] ng/mL, p = .004), average nadir (NL = 9.2 [4.8–12.0], SS = 12.0 [4.4–19.5], SO = 16.6 [9.5–23.8], OO = 16.2 [10.4–22.0] ng/mL, p = .003), and peak height (NL = 11.4 [6.9–16.0], SS = 14.8 [6.0–23.5], SO = 21.0 [12.2–29.7], OO = 19.4 [12.7–26.0] ng/mL, p = .007) were greater in the SO and OO groups compared to the NL and SS groups. Total area was greater in the SO, SS, and OO groups compared to the NL group (361.4 [210.4–512.3], 312.7 [39.3–586.1], 216.2 [96.3–336.1] vs 147.6 [76.8–218.4] ng/mL, p = .02).

Classical Parameters

Leptin concentration at 11 PM (pre-DEX) was significantly greater in the SO, OO, and SS groups compared to the NL group (p = .01). At 7:00 AM (post-DEX), fasting leptin levels were significantly greater in the SO and OO groups compared to the SS and NL groups (p = .007).

The SS group had significantly higher log leptin levels at 11:00 PM compared to the other groups when percent fat was fixed at 30 (p = .002, Figure 3). Multivariate regression verified percent fat was a positive predictor, and ASM a negative predictor of log leptin (regression equation = 1.355 + .061 × percent fat – 0.137 × ASM). When treated as continuous variables, leptin was positively correlated with percent fat (regression, p < .001, r² = .78) with no additional sex influence (p = .30). Adjusting for percent fat, ASM had an independent and negative correlation with leptin levels (multiple regression, p = .001). Linear regression demonstrated a significant negative correlation between ASM and log 11 PM leptin (p < .001, r² = 0.50, Figure 4).

Table 2. Growth Hormone Deconvolution Analyses by Group–Free-Running Night

<table>
<thead>
<tr>
<th>Deconvolution Parameters</th>
<th>Normal Lean (N = 15)</th>
<th>Sarcopenic (N = 7)</th>
<th>Sarcopenic-Obese (N = 12)</th>
<th>Obese (N = 10)</th>
<th>Kruskal–Wallis Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Half-duration</td>
<td>20.4 (17.2–23.7)</td>
<td>16.5 (12.4–20.6)</td>
<td>17.7 (13.7–21.7)</td>
<td>17.2 (11.2–23.1)</td>
<td>NS</td>
</tr>
<tr>
<td>No. of peaks</td>
<td>7.0 (5.9–8.1)</td>
<td>8.0 (5.3–10.7)</td>
<td>5.7* (4.2–7.1)</td>
<td>7.0 (5.6–8.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Mean interval</td>
<td>69.4 (53.4–85.4)</td>
<td>58.7 (38.5–78.9)</td>
<td>78.5 (62.5–94.8)</td>
<td>51.0 (40.8–61.2)</td>
<td>.02</td>
</tr>
<tr>
<td>Area, µg/L</td>
<td>2.9 (2.1–3.8)</td>
<td>2.3 (1.0–3.6)</td>
<td>2.7* (0.5–4.7)</td>
<td>1.1* (0.6–1.7)</td>
<td>.07</td>
</tr>
<tr>
<td>Total secretion, mg/L</td>
<td>19.4 (13.5–25.2)</td>
<td>17.0 (7.1–26.9)</td>
<td>11.1* (3.4–18.8)</td>
<td>8.2* (3.1–13.4)</td>
<td>.02</td>
</tr>
<tr>
<td>Mean concentration, µg/L</td>
<td>0.9 (0.6–1.2)</td>
<td>0.8 (0.4–1.2)</td>
<td>0.5* (0.2–0.8)</td>
<td>0.4* (0.3–0.5)</td>
<td>.04</td>
</tr>
</tbody>
</table>

Notes: Data are expressed as mean (95% confidence interval).

*p = .002 Wilcoxon test, Obese less than Nonobese group.

NS = not statistically significant.

Figure 1. Significant group difference for total growth hormone (GH) secretion on the free-running night (Kruskal–Wallis, p = .02). Difference was due to the presence or absence of obesity (Wilcoxon rank sum test, *p = .002).

SS = sarcopenic; SO = sarcopenic-obese; OO = obese; NL = normal lean.
ApEn.—Post-DEX leptin ApEn was significantly higher in the OO (.74, .57–.91), SO (.72, .60–.85, and NL groups (.71, .61–.80) compared to the SS group (.50, .39–.62) (p = .04). There were no ApEn group differences for GH during DEX.

IGF-1.—There were no 7:00 AM group differences following the free-running blood draw night. Repeated measures analysis revealed that 7:00 AM IGF-1 was greater in all groups following DEX compared to the free-running night (p = .008).

Metabolic Parameters
A post hoc analysis demonstrated that total triglyceride levels were greater in the OO and SO groups compared to the SS and NL groups (p = .02). However, these levels were at or below the 1.69 mmol/L cutoff for hypertriglyceridemia. Systolic blood pressure was significantly higher in the

DISCUSSION
The primary findings of this investigation were: (i) a depressed GH secretion in the presence of obesity both with and without sarcopenia; (ii) a blunted and disordered GH response to dexamethasone in sarcopenic-obesity; (iii) a concurrently elevated leptin and cortisol in sarcopenia; and (iv) a negative relationship between ASM and log leptin.

Our data corroborate reports of decreased overall GH secretion in the presence of obesity (15). Factors contributing to this decrease are alterations in somatostatin, GH-releasing hormone (GHRH), or ghrelin secretion (15–17). Our hypothesis that sarcopenic-obesity may display greater derangements in the somatotropic axis than obesity was supported by a trend toward a lower number of GH peaks and longer mean interval than the obese group (p = ns) on the free-running night. We also confirmed reports that DEX administration increases overall GH secretion in nonobese persons (18). However, DEX-stimulated GH secretion increased in the obese group and was blunted and more chaotic in the sarcopenic-obese group. The mechanism by which glucocorticoids stimulate GH secretion is uncertain, as their effects on GH regulation are pleiotropic. Glucocorticoids regulate GH and IGF-1 signaling and expression, and also regulate somatostatin- and GHRH-receptor gene expression (19). GH pulsatility is regulated by somatostatin, GHRH, and systemic GH autofeedback, and the muting of autofeedback restraint can increase serial irregularity of GH secretory patterns (5,20). These regulatory mechanisms suggest that GH secretion in the sarcopenic-obese group was blunted with muted negative feedback restraint resulting in more a chaotic pattern of GH secretion.

Taken together, these findings highlight abnormalities in the regulation of GH secretion that distinguish sarcopenic-obese persons from those with simple obesity. Whether the observed abnormalities are secondary to changes in body composition or play a causal role in the development of sarcopenic-obesity remains uncertain. If a causal role was
established, then sarcopenic-obese persons might represent a subgroup of the elderly population in whom GH replacement may have a clinical role, especially in view of the high degree of disability associated with this phenotype.

We found no differences in free-running serum cortisol associated with body composition classifications. This finding agrees with an investigation in which free cortisol levels were independent of body composition and leptin levels but were related to increased cortisol clearance, which was not measured in this study (4). We anticipated that salivary cortisol concentrations would be greater in the sarcopenic-obese and obese groups than in the normal or sarcopenic groups. Accordingly, it was unexpected to find significantly elevated salivary cortisol at 7:00 AM and 11:00 PM in the sarcopenic group. The higher 7:00 AM cortisol resulted in a significantly greater AUC and absolute peak salivary concentration following meal 1 in the SS group compared to the other groups. This finding contrasts with studies where higher salivary cortisol levels were associated with abdominal fat (21), but may corroborate studies (22,23) that report differences in salivary cortisol in twins and obese subgroups in the morning only. Variation in HPA axis activity between individuals is a function of many influences including individual feedback sensitivity, circadian rhythm, episodic secretion, and genetics. A strong genetic influence on the HPA axis has been proposed (24) with elevated morning cortisol concentrations being highly heritable, and low day and evening concentrations demonstrating low heritability (25). Whether elderly persons with sarcopenia are predisposed to intrinsically elevated cortisol needs prospective longitudinal studies to clarify the temporal relationship between these hormones and the development of sarcopenia.

In agreement with our earlier finding of hyperleptinemia in elderly people with sarcopenia relative to their low levels of body fat, predexamethasone leptin concentrations were comparable in the sarcopenic-obese, obese, and sarcopenic groups (7,26). Leptin and cortisol normally display an inverse circadian rhythm, and supraphysiological doses of glucocorticoids are reported to increase leptin in some studies (27,28). Our findings support high correlations between leptin concentration and total fat, whereas leptin pulsatility appeared weakly related to fat (29). It was unanticipated that, after adjusting for percent fat, we found ASM to have an independent and negative correlation with leptin levels. Reports of increased serum leptin in pro-inflammatory states during active weight loss (30) raised the question of weight stability in our participants. A retrospective analysis of our longitudinal body composition data (not shown) demonstrated that all participants had stable body weight in the year prior to this study. A recent report of increased cytokine-related-protein and interleukin-6 levels in sarcopenic-obese elderly persons (31) could indicate that sarcopenic-obesity and sarcopenia are driven by distinct mechanisms. The mechanism in sarcopenic-obesity may be more influenced by cytokines (31), and in sarcopenia by a combination (and possibly interaction) of high cortisol and leptin levels. Sex hormones, which were not measured in this study, may also be playing a role as previously reported (2,32).

Although our participants did not have metabolic syndrome, systolic blood pressure was significantly higher in the sarcopenic, obese, and sarcopenic-obese groups and was within the range of mild hypertension. The relationship of blood pressure with cortisol is known; however, leptin is also speculated to play a role in hypertension (33,34). Leptin and the renin–angiotensin system can influence the sympathetic nervous system, water and electrolyte metabolism, and vascular remodeling, which are involved in the regulation of arterial blood pressure. Thus, the unique hormonal profile in our sarcopenic group may place them at a heightened risk for developing essential hypertension despite normal or low body fat.

Conclusion
This investigation found decreased GH secretion in the presence of obesity, which increased in response to glucocorticoid suppression in all body composition groups but the sarcopenic-obese. ASM was independently and negatively correlated with leptin even after adjusting for percent body fat. Moreover, frankly sarcopenic elderly persons had concomitantly elevated leptin and cortisol levels relative to their body fat mass, suggesting that leptin may be weakly related to actual fat mass in this body composition phenotype. These data suggest that complex or dysregulated neuroendocrine feedback systems may be operating in specific body composition phenotypes which warrants further investigations to clarify these relationships.

ACKNOWLEDGMENTS
This study was supported by DHSS/NIH/R01 AG 10149 and DHSS/NIH/NCCR/GCRC 5MO1 RR00997.

We thank the members of the New Mexico Aging Process Study, the staff at the Aging and Genetic Epidemiology Program, and the General Clinical Research Center at the University of New Mexico for their valued contributions.

Debra L. Waters is currently with the University of Otago, Dunedin, New Zealand.

Richard N. Baumgartner is currently with the University of Louisville, Kentucky.

CORRESPONDENCE
Address correspondence to Debra L. Waters, PhD, University of Otago, Dunedin School of Medicine, Department of Preventive and Social Medicine, P.O. Box 913, Dunedin, New Zealand 9059. E-mail: debra.waters@otago.ac.nz

REFERENCES
4. Purnell JQ, Brandon DD, Isabelle LM, Loriaux DL, Samuels MH. Association of 24-hour cortisol production rates, cortisol-binding globulin, and plasma-free cortisol levels with body composition, leptin