Association of Pentraxin 3 with Insulin Resistance and Glucose Response Following Maximal Aerobic Exercise in Obese and Normal-Weight Individuals

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Title: Association of Pentraxin 3 with Insulin Resistance and Glucose Response Following Maximal Aerobic Exercise in Obese and Normal-Weight Individuals

Authors: Aaron L. Slusher\textsuperscript{a,b} and Chun-Jung Huang\textsuperscript{a}

Affiliations: \textsuperscript{a}Exercise Biochemistry Laboratory, Department of Exercise Science and Health Promotion, Florida Atlantic University, Boca Raton, FL, USA, 33431 \textsuperscript{b}Department of Kinesiology and Health Sciences, Virginia Commonwealth University, Richmond, VA, USA, 23284

Corresponding Author: Aaron L. Slusher, M.S.
1020 W. Grace Street
Richmond, Virginia 23284
Phone: 804.828.1948
Fax: 804.828.1946
Email: slusheral@vcu.edu
Abstract: Pentraxin 3 (PTX3), a cardioprotective protein, has recently been shown to be associated with improved insulin resistance (IR) and glucose metabolism. Therefore, the primary purpose of this study was to examine whether or not increased plasma PTX3 following maximal aerobic exercise would differ between obese and normal-weight subjects, and its association with the homeostatic model assessment of insulin resistance (HOMA-IR) and glucose response. Twenty-five untrained obese ($n = 13$ [6 males and 7 females]) and normal-weight ($n = 12$ [5 males and 7 females]) subjects performed an acute bout of maximal aerobic exercise ($V_{O_{2max}}$). At baseline, plasma PTX3 concentrations are decreased in obese compared to normal-weight subjects and are negatively associated with plasma insulin and HOMA-IR values. In response to maximal exercise, plasma PTX3 responses were similar in obese and normal-weight subjects while the intensity of plasma PTX3 response as indicated by area-under-the-curve analysis (AUCi) was not associated with HOMA-IR nor glucose AUCi. However, PTX3 AUCi was positively associated with cardiorespiratory fitness levels (relative $V_{O_{2max}}$). These findings suggest that PTX3 could serve as a biomarker for both metabolic health as well as a measurement to monitor the effectiveness of exercise interventions in obesity.

Keywords: Pentraxin 3; Obesity; Aerobic Exercise; Insulin Resistance, Cardiorespiratory fitness
Introduction

Obesity is characterized as a chronic state of low-grade pro-inflammatory by the enlargement of adipocytes and increased infiltration of circulating monocytes differentiated into resident adipose tissue macrophages (Weisberg et al. 2003; Winkler et al. 2003; Xu et al. 2003). These macrophages have been shown to be the primary source of pro-inflammatory cytokines in circulation (Hamilton et al. 2002; Weisberg et al. 2003). Additionally, macrophage derived pro-inflammatory cytokines directly impair the mechanistic machinery associated with insulin-mediated glucose uptake in both adipose tissue and skeletal muscle. This results in the development of insulin resistance (IR) and the subsequent development of type 2 diabetes mellitus (T2DM) (Plomgaard et al. 2005; Rotter et al. 2003).

Pentraxin 3 (PTX3) has been recently identified as an acute-phase reactant primarily expressed from adipose tissue, skeletal muscle, as well as monotypes/resident macrophages in response to pro-inflammatory and metabolic insult (Abderrahim-Ferkoune et al. 2003; Imamura et al. 2007; Miyaki et al. 2014). In animal models, PTX3 has been shown to serve as cardioprotective protein and anti-inflammatory mediator, protecting against the development of atherosclerotic lesions and improving survival from endotoxic shock (Dias et al. 2001; Norata et al. 2009). However, Miyaki et al. (2014) demonstrated that the expression of PTX3 protein in skeletal muscle and adipose tissue was decreased in obese diabetic rodents compared to wild-type controls. Furthermore, the expression of glucose transporter 4 (GLUT4) in skeletal muscle has been shown to be positively associated with increased PTX3 protein expression (Miyaki et al. 2014). This evidence supports observations of decreased circulating PTX3 concentrations in obese populations as well as individuals with metabolic syndrome and T2DM (Chu et al. 2012; Ogawa et al. 2010; Osorio-Conles et al. 2011; Slusher et al. 2015a), indicating that PTX3 may serve as a predictor for IR.
While chronic and acute aerobic exercise have been demonstrated to enhance glucose metabolism and reverse IR (Henriksen 2002), regular participation in endurance exercise may also augment circulating concentrations of PTX3. For example, Miyaki et al. (2011) showed that plasma levels of PTX3 are elevated in endurance trained males compared to sedentary counterparts. In elderly women, plasma PTX3 concentrations were increased following 8 weeks habitual aerobic endurance training at moderate intensities (Miyaki et al. 2012). Furthermore, a single bout of submaximal aerobic exercise has also been found to enhance the expression of PTX3 in plasma (Huang et al. 2014; Slusher et al. 2015a). However, there is limited information regarding the potential effect of PTX3 in the modulation of IR and glucose metabolism in response to exercise in obese individuals. Therefore, the primary purpose of this study was to examine whether or not increased plasma PTX3 following maximal aerobic exercise would differ between obese and normal-weight subjects, and its association with the homeostatic model assessment of insulin resistance (HOMA-IR) and glucose uptake. Although our laboratory has previously demonstrated that the plasma PTX3 response was similar in obese and normal-weight subjects following an acute bout of submaximal aerobic exercise (Slusher et al. 2015a), this exercise-mediated PTX3 response may occur in an intensity-dependent manner (Nakajima et al. 2010). Thus, it was hypothesized that maximal aerobic exercise would reveal an attenuated PTX3 plasma response in obese compared to normal-weight subjects, and this increased PTX3 would be negatively associated with HOMA-IR and positively associated with glucose response following exercise.

**Materials and Methods**

**Subjects**
Twenty-five untrained subjects (13 obese [6 males and 7 females] and 12 normal-weight [5 males and 7 females]) aged 18 to 35 participated in this research investigation. Subjects with a body mass index (BMI) above 30 kg/m$^2$ were classified as obese, and those with a BMI between 18.5 and 24.9 kg/m$^2$ were classified as normal-weight. All subjects completed the informed consent process and a medical history questionnaire prior to data collection. Additionally, to limit the effects of training on physiological response (Haskell et al. 2007), all subjects participated in less than 150 minutes of physical activity as determined by the 7-day physical activity record. The study was approved by the University’s Institutional Review Board.

Subjects were excluded from the study if they presented inflammatory diseases and/or conditions (e.g., cardiovascular disease, chronic kidney or liver disease, diabetes), were under current administration of medication known to affect the results, were users of tobacco products (cigarettes, cigars, chewing tobacco), or consumed an average of ten or more alcoholic beverages per week.

Subjects were instructed to undergo an overnight fast for at least eight hours and to abstain from alcohol, caffeine intake, and intense physical activity for at least 24 hours prior to each laboratory visit. Finally, women who were pregnant or nursing also were excluded from the study because of the potential effects on immune responses (Mor and Cardenas 2010).

**Maximal Exercise Testing Procedures**

Subjects arrived at the laboratory between 7:00 and 9:00 on the morning of the testing session. The testing session consisted of informed consent, familiarization with all instruments and procedures, anthropometric measures, and an assessment of maximal oxygen consumption ($V\text{O}_2\text{max}$) test administered in gradation on a treadmill with the intention of reaching maximal
exertion within 12-15 minutes according to our laboratory’s previously described methods (Slusher et al. 2015b). In brief, a 3 minute warm-up was administered at 3 mph with 0% grade. Speed was increased during the first stage (2 min) to elicit 80% ± 5 beats per minute of the subjects age predicted maximal heart rate and allowed to reach steady-state during stage 2. Beginning at stage 3 (min 4), speed remained constant while grade was increased 2% every 2 min until voluntary exhaustion. VO₂ max was determined using ParvoMedics Metabolic Measurement System (ParvoMedics, Sandy, UT, USA). HR and rating of perceived exertion (RPE) were recorded every exercise stage. Exhaled carbon dioxide (VCO₂) and inhaled oxygen (VO₂) was averaged every 15 seconds to calculate respiratory exchange ratio (RER: VCO₂/VO₂). Criteria for attaining VO₂ max included a plateau in O₂ consumption and two of the following secondary criteria: RER ≥ 1.15, HR within 10 bpm of subject’s age-predicted maximum heart rate (220-age), and an RPE ≥ 19. This criteria was met for all normal-weight and obese subjects, suggesting that VO₂max was attained. Resting and post-exercise HR and blood pressure were assessed by HR monitors (Polar T31, Polar Electro, Kempele, Finland) and sphygmomanometer (752M-Mobile Series, American Diagnostic Corporation, Hauppaige, NY) prior to exercise and during recovery.

**Biochemical Analyses**

A 10 ml blood sample was drawn from each subject’s anticubital vein prior to, immediately post, and at 1 hour into recovery (R1h) using a 21G butterfly needle into a tube containing K₂ ethylenediaminetetraacetic acid (K₂EDTA) (BD Vacutainer, Franklin Lakes, NJ). Blood samples were immediately centrifuged at 3000 RPM for 20 minutes at room temperature. Plasma was collected and immediately stored at -80°C in cryogenic tubes in 500µL aliquots for
analysis of PTX3 (R&D Systems, Minneapolis, MN), insulin (ALPCO, Salem, NH, USA), and glucose (Cayman Chemical Company, Ann Arbor, MI, USA) using enzyme-linked immunosorbent assay (ELISA) according to manufacture instructions.

Insulin resistance (IR) was determined by HOMA-IR, calculated from plasma insulin and glucose values according to Matthews et al. (1985):

$$\text{HOMA-IR} = \frac{\text{Fasting insulin} (\mu U/ml) \times \text{fasting glucose} (\text{mg/dL})}{405}.$$ 

**Statistical Analyses**

Data analysis was performed using the SPSS version 23.0. Subject sample size was determined to be adequate using power analysis, which permitted at least 80% power with an alpha of 0.05 to detect an effect size between 0.5 and 1.0. Independent t-tests were conducted to compare baseline levels on all variables between obese and normal-weight subjects. A two group (obese and normal-weight) by three time point (pre, post, R1) repeated measures analysis of variance (ANOVA) was utilized to examine the effect of acute aerobic exercise on PTX3, insulin, and glucose. If the Mauchly's test indicated violation of the sphericity assumption, the degrees of freedom were corrected by using Greenhouse-Geisser estimates. To assess the intensity of the exercise-induced PTX3, insulin, and glucose responses relative to baseline as well as compare these responses between obese and normal-weight subjects, area-under-the-curve “with respect to increase” (AUCi) was calculated according to Pruessner et al. (2003). Finally, Pearson’s correlation was utilized to examine the relationship of PTX3 with anthropometric and cardiovascular measures, and indices of IR at baseline and in response to exercise (AUCi). All data is presented as means ± S.E.M. with statistical significance being defined as a $P$-value ≤ 0.05.
Results

Participant Anthropometric, Cardiovascular, and Metabolic Measures

Baseline anthropometric characteristics and cardiovascular measures between obese and normal-weight subjects are reported in table 1. Obese subjects presented with greater body weight ($t [23] = 6.19, p < 0.001$), BMI ($t [15.59] = 11.53, p < 0.001$), waist and hip circumferences ($t [23] = 8.09; t [17.20] = 8.14, p < 0.001$, respectively), waist-to-hip ratio ($t [23] = 3.83, p = 0.001$), both resting systolic and diastolic blood pressures ($t [23] = 4.11; t [23] = 4.57, p < 0.001$, respectively) as well as HOMA-IR values ($t [18.38] = 4.90, p < .001$) compared to normal-weight subjects. However, cardiorespiratory fitness levels (relative VO$_{2\max}$) were significantly lower in obese compared to normal-weight subjects ($t [19.18] = -5.52, p < 0.001$).

In addition, body weight ($t [23] = 2.82, p = 0.010$), height ($t [23] = 6.96, p < 0.001$), waist circumference ($t [23] = 2.20, p = 0.038$), and waist-to-hip ratio ($t [23] = 3.348, p = 0.002$) were lower, while resting heart rates ($t [23] = -2.74p = 0.012$) were greater in women compared to men.

Comparison of Plasma PTX3, Indices of IR, and Glucose Response at Baseline and in Response to Exercise

At baseline, PTX3 plasma concentrations were significant lower ($t [23] = -2.20, p = 0.038$) while both plasma insulin and glucose concentrations were elevated in obese compared to normal-weight subjects ($t [23] = 4.24; t [23] = 5.06, p < 0.001$, respectively) (Table 2). Moreover, plasma PTX3 levels were negatively associated with insulin ($r = -0.503, p = 0.010$; Figure 1A), HOMA-IR ($r = -0.521, p = 0.008$; Figure 1B), resting heart rate ($r = -0.399, p = 0.010$).
and both resting SBP and DBP (r = -0.397, p = 0.050; r = -0.667, p < 0.001, respectively), and positively associated with relative VO$_{2\text{max}}$ (r = 0.424, p = 0.035; Figure 2A).

In response to exercise, repeated measures ANOVA analysis demonstrated a significant increase in plasma PTX3 ($F\[2, 46\] = 19.52, p < .001) and insulin ($F\[1.22, 28.03\] = 25.82, p < 0.001) concentrations across time in both groups, whereas the plasma glucose response ($F\[1.53, 35.08\] = 6.90, p = 0.006) was significantly attenuated in obese subjects compared to normal-weight subjects. In addition, plasma PTX3 concentrations were significantly elevated immediately following exercise compared to baseline, and returned to baseline at R1. These results suggest that the utilized time points were appropriate to assess exercise induced changes in plasma PTX3 concentrations. The intensity of plasma PTX3 response (AUCi) following maximal aerobic exercise was not associated with anthropometric measures or HOMA-IR at baseline nor with insulin AUCi and glucose AUCi. However, although no associations were observed between PTX3 AUCi and absolute VO$_{2\text{max}}$ (r = 0.355, p = 0.082), PTX3 AUCi was positively associated with relative VO$_{2\text{max}}$ (r = 0.417, p = 0.038; Figure 2B). While no gender differences were observed in baseline levels of plasma PTX3 and other outcome variables at baseline or in response to exercise, the PTX3 response immediately following exercise was greater in male compared to female subjects ($F\[2, 46\] = 4.83, p = 0.013). However, given that males tended to have greater VO$_{2\text{max}}$ (41.98 ± 12.63 vs. 35.59 ± 35.59, p = 0.161), this gender difference in PTX3 no longer existed after controlling for VO$_{2\text{max}}$ ($F\[2, 44\] = 3.02, p = 0.059).

**Discussion**

The main findings from this research investigation reveal that plasma PTX3 concentrations at baseline are lower in obese compared to normal-weight subjects and negatively
associated insulin and HOMA-IR. Following acute exercise, plasma PTX3 responses were
similar in obese and normal-weight subjects and this exercise-mediated PTX3 response (AUCi)
was positively associated with cardiorespiratory fitness levels (relative VO$_{2\text{max}}$). However, PTX3
AUCi was neither associated with HOMA-IR nor glucose AUCi following exercise.

While previous research has investigated the role of PTX3 as a cardioprotective
modulator (Dias et al. 2001; Norata et al. 2009), this study demonstrated that obese subjects
presented with a lower resting plasma PTX3 concentration compared to normal-weight
counterparts. In addition, resting plasma PTX3 concentrations were negatively associated with
fasting insulin levels and HOMA-IR. However, the lack of association between PTX3 AUCi
with HOMA-IR or glucose AUCi in response to acute maximal exercise suggests that the
facilitation of glucose uptake during acute aerobic exercise occurs independent of PTX3
mediated signaling. Although to our knowledge no other studies have investigated the
relationship of PTX3 with glucose and indices of IR in response to acute exercise, Chu et al.
(2012) recently demonstrated that increased plasma PTX3 concentrations following physical
activity intervention were associated with decreased fasting insulin and HOMA-IR values in
obese subjects. These findings indicate that elevated plasma PTX3 concentrations in healthy
subjects may serve as a potential biomarker for metabolic health, and that increased PTX3
concentrations in response to aerobic exercise training may attenuate the severity of IR during

Our recent study has demonstrated that obese and normal-weight subjects exhibited
similar increases in plasma PTX3 concentrations in response to an acute bout of submaximal
aerobic exercise (Slusher et al. 2015a). While PTX3 response to acute exercise has been shown
to be elicited in a manner dependent upon exercise intensity (Nakajima et al. 2010), obesity did
not appear to impact the magnitude of the plasma PTX3 response following maximal aerobic exercise compared to normal-weight individuals in this study. However, PTX3 AUCi was positively associated with cardiorespiratory fitness levels (relative VO_{2max}). Although these findings are supported by our laboratory’s previous research (Slusher et al. 2015a), Miyaki et al. (2011; 2012) demonstrated that current endurance training status as well as exercise training-induced improvements in cardiorespiratory fitness were also accompanied by elevated resting plasma PTX3 concentrations and improved indices of cardiovascular health (vascular compliance and cholesterol profiles). Miyaki and colleagues (2013) further associated lower plasma PTX3 concentrations with poor vascular health and metabolic profiles in obese populations. It noteworthy to mention that none of these studies investigating the relationship between plasma PTX3 and aerobic exercise training included both male and female subjects together. Therefore, the impact of gender on plasma PTX3 concentrations in response to acute exercise remains uncertain. In addition, cardiorespiratory fitness has been shown to be a strong indicator of both cardiovascular and metabolic health (Hassinen et al. 2008; Kodama et al. 2009; LaMonte et al. 2005), and other studies have shown that improvements in cardiorespiratory fitness following exercise intervention were associated with positive changes in other CVD and metabolic biomarkers in obese populations (Campbell et al. 2009, 2010). Therefore, these findings suggest that intervention methods which elevate plasma PTX3, such as acute aerobic exercise and interventions aimed at enhancing VO_{2max}, may provide therapeutic benefits and augment the cardioprotective and potential metabolic effects of PTX3. Furthermore, the monitoring of PTX3 concentrations in plasma may serve as a surrogate marker toward the effectiveness of exercise interventions aimed at ameliorating CVD in obese individuals.
It is worth noting that the relationship between plasma PTX3 and cardiorespiratory fitness levels was only apparent with relative VO$_{2\text{max}}$ and not absolute VO$_{2\text{max}}$. While a limitation, this finding also highlights the impact that body weight has on the association between circulating PTX3 concentrations and cardiorespiratory fitness. Therefore, changes in body weight, body composition (ie. body fat percent), and regional distribution of body fat should be considered in future investigations.

In summary, although PTX3 may serve as a biomarker for metabolic health, additional research is warranted to elucidate potential mechanistic actions by which PTX3 may therapeutically regulate glucose metabolism following physical activity. However, the positive association of PTX3 with VO$_{2\text{max}}$ indicates that alterations in plasma PTX3 concentrations in response to physical activity intervention may serve as a method of monitoring cardiorespiratory fitness gains and cardioprotective adaptations in obese populations.

Acknowledgements

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Conflicts of Interest

The authors have not conflicts of interest to declare.

References


Kodama, S., Saito, K., Tanaka, S., Maki, M., Yachi, Y., Asumi, M., et al. 2009. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and

https://mc06.manuscriptcentral.com/cjpp-pubs


### Table 1. Participant anthropometric and cardiovascular measures, and HOMA-IR index

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal-weight (n = 12: 5M/7F)</th>
<th>Obese (n = 13: 6M/7F)</th>
<th>P value</th>
</tr>
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<tr>
<td>Age (y)</td>
<td>23.08 ± 0.638</td>
<td>22.62 ± 1.15</td>
<td>0.730</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>63.19 ± 3.51</td>
<td>99.73 ± 4.65</td>
<td>*&lt; 0.001</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.69 ± 0.03</td>
<td>1.68 ± 0.02</td>
<td>0.707</td>
</tr>
<tr>
<td>BMI</td>
<td>21.86 ± 0.43</td>
<td>35.35 ± 1.09</td>
<td>*&lt; 0.001</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>71.38 ± 1.98</td>
<td>98.92 ± 2.71</td>
<td>*&lt; 0.001</td>
</tr>
<tr>
<td>Hip (cm)</td>
<td>94.96 ± 1.19</td>
<td>117.3 ± 2.47</td>
<td>*&lt; 0.001</td>
</tr>
<tr>
<td>W:H</td>
<td>0.75 ± 0.01</td>
<td>0.84 ± 0.02</td>
<td>0.001</td>
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<tr>
<td>Absolute VO$_{2\text{max}}$ (L min$^{-1}$)</td>
<td>3.00 ± 0.29</td>
<td>3.09 ± 0.22</td>
<td>0.802</td>
</tr>
<tr>
<td>Relative VO$_{2\text{max}}$ (mL kg$^{-1}$ min$^{-1}$)</td>
<td>46.53 ± 2.37</td>
<td>30.9 ± 1.55</td>
<td>*&lt; 0.001</td>
</tr>
<tr>
<td>Resting HR (bpm)</td>
<td>66.83 ± 2.77</td>
<td>72.23 ± 2.56</td>
<td>0.165</td>
</tr>
<tr>
<td>Resting SBP (mmHg)</td>
<td>106.60 ± 3.55</td>
<td>124.62 ± 2.86</td>
<td>*&lt; 0.001</td>
</tr>
<tr>
<td>Resting DBP (mmHg)</td>
<td>65.83 ± 2.99</td>
<td>82.77 ± 2.25</td>
<td>*&lt; 0.001</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>1.02 ± 0.25</td>
<td>3.56 ± 0.46</td>
<td>*&lt; 0.001</td>
</tr>
</tbody>
</table>

Note: The * indicates a significant difference between normal-weight and obese groups at baseline (p < 0.05). Data are presented as means ± SEM. BMI, body mass index; DBP, diastolic blood pressure; HOMA-IR, homeostatic model assessment of insulin resistance; HR, Heart Rate; SBP, systolic blood pressure; W:H, waist-to-hip ratio; VO$_{2\text{max}}$, maximal oxygen uptake.
Table 2. Assessment of plasma PTX3, insulin, and glucose concentrations at baseline and in response to acute exercise in normal-weight and obese subjects

<table>
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<tr>
<th>Variable</th>
<th>Pre-Exercise</th>
<th>Post-Exercise</th>
<th>Recovery 1 hour</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTX3 (pg/mL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal-Weight</td>
<td>476.95 ± 62.77*</td>
<td>640.90 ± 94.57</td>
<td>497.93 ± 75.19</td>
<td>time &lt; 0.001</td>
</tr>
<tr>
<td>Obese</td>
<td>292.89 ± 55.66</td>
<td>411.70 ± 68.78</td>
<td>321.09 ± 62.85</td>
<td>group = NS</td>
</tr>
<tr>
<td>Insulin (µIU/ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal-Weight</td>
<td>5.18 ± 1.16*</td>
<td>14.94 ± 1.95</td>
<td>6.17 ± 1.72</td>
<td>time &lt; 0.001</td>
</tr>
<tr>
<td>Obese</td>
<td>14.80 ± 1.90</td>
<td>30.04 ± 4.06</td>
<td>11.53 ± 1.53</td>
<td>group = NS</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal-Weight</td>
<td>78.20 ± 3.22*</td>
<td>125.34 ± 6.02</td>
<td>78.39 ± 7.44</td>
<td>time &lt; 0.001</td>
</tr>
<tr>
<td>Obese</td>
<td>97.43 ± 2.12</td>
<td>119.15 ± 5.69</td>
<td>95.09 ± 2.00</td>
<td>group = 0.006</td>
</tr>
</tbody>
</table>

Note: There was a significant change across time for all variables in both the normal-weight and obese groups. The * indicates a significant difference between normal-weight and obese groups at baseline (p < 0.05). Data are presented as means ± SEM.
**Figure Legends**

**Figure 1.** Associations of PTX3 concentrations at baseline with fasting insulin and HOMA-IR in normal-weight (closed circle) and obese (open square) subjects. Baseline PTX3 concentrations were negatively associated with both fasting insulin concentrations (panel A) and HOMA-IR values (panel B) ($p \leq 0.05$).

**Figure 2.** Relationships between cardiorespiratory fitness ($V_{O_{2}max}$) with baseline PTX3 concentrations and PTX3 area-under-the-curve “with respect to increase” (AUCi) as result of maximal aerobic exercise in normal-weight (closed circle) and obese (open square) subjects. $V_{O_{2}max}$ was positively associated with baseline PTX3 concentrations (panel A) and PTX3 in response to exercise (panel B) ($p \leq 0.05$).
Figure 1. Associations of PTX3 concentrations at baseline with fasting insulin and HOMA-IR in normal-weight (●) and obese (□) subjects. Baseline PTX3 concentrations were negatively associated with both fasting insulin concentrations (panel A) and HOMA-IR values (panel B) ($p \leq 0.05$).
Figure 2. Relationships between cardiorespiratory fitness (VO$_{2\text{max}}$) with baseline PTX3 concentrations and PTX3 area-under-the-curve “with respect to increase” (AUC$_{i}$) as result of maximal aerobic exercise in normal-weight (○) and obese (□) subjects. VO$_{2\text{max}}$ was positively associated with baseline PTX3 concentrations (panel A) and PTX3 in response to exercise (panel B) ($p \leq 0.05$).