The Effects of Adiponectin and Exercise Training on Lean Muscle and Body Fat Percent

Dylan Patrick Hendrickson
THE FLORIDA STATE UNIVERSITY
COLLEGE OF ARTS AND SCIENCES

THE EFFECTS OF ADIPOnectIN AND
EXERCISE TRAINING ON LEAN
MUSCLE AND BODY FAT PERCENT

By

DYLAN HENDRICKSON

A Thesis submitted to the Department of
Biological Sciences
in partial fulfillment of the requirements for graduation with
Honors in the Major

Degree Awarded:
[Spring, 2023]
The members of the Defense Committee approve the thesis of Dylan Hendrickson defended on March 7, 2023.

Professor Judy Delp
Thesis Director

Research Facility Deirdre McCarthy
Outside Committee Member

Associate Professor Lisa Lyons
Committee Member

Assistant Professor Roberto Vincis
Committee Member

Signatures are on file with the Honors Program office.
Abstract

This pilot study was conducted to determine the role of adiponectin in exercise training-induced adaptations of body composition. A cre/lox system under control of the tamoxifen promoter was used to acutely delete adiponectin (AdipoKO) in adult male and female mice. Wild type (WT) and acute knockout (AdipoKO) mice were assigned to 8 weeks of treadmill exercise or 8 weeks of sedentary cage confinement. Exercise tolerance was assessed before and after the exercise training or sedentary cage confinement period. Fat and lean mass were determined bi-weekly during the exercise training or sedentary cage confinement period using EchoMRI. In male and female mice, exercise training increased exercise tolerance, in both WT and AdipoKO mice. In sedentary male and female AdipoKO mice, but not in sedentary WT mice, exercise tolerance decreased during eight weeks of cage confinement. Exercise training reduced fat mass in both male and female WT mice, but not in AdipoKO mice. During cage confinement, lean mass decreased in AdipoKO mice, but exercise training mitigated this decline. These results indicate that adiponectin is important for reduction of fat mass by exercise training. These results also suggest that deletion of adiponectin in adult mice reduces lean mass, but this loss of lean mass can be mitigated by exercise training.
**Introduction**

Weight gain is an increasing issue within first world nations, especially among American adults, with obesity prevalence reaching 41.9% in 2020 (Bryan et al., 2021). In the American diet, average daily consumption has increased from 2,025 calories in 1970, to 2,481 calories in 2010, a 23% increase over 40 years (Desilver, 2016). An estimated 12% of total daily caloric intake in the average American is from saturated fat, above the 10% maximum recommended by dietary guidelines (Shan et al., 2019). Weight gain leads to insulin resistance (Taylor, 2013); thus, the obesity epidemic has contributed to the increase of Type II diabetes, which affects 10% of Americans (National Diabetes Statistics Report). Regular exercise is known to stimulate mechanisms that contribute to regulation of body mass. Studies that increase our understanding of the mechanisms by which regular exercise regulates metabolism may contribute to development of therapies that can be used, alone or in conjunction with exercise, to counter obesity.

Increasing evidence indicates that hormones produced in adipose tissue, termed adipokines, influence body weight gain. Additionally, inflammation related to an imbalance in adipokines may contribute to insulin resistance (Kwon et al., 2013). Two adipokines, ghrelin and apelin, decrease in response to regular exercise, even in the absence of an overall change in body weight (Kadoglou et al., 2012). These two adipokine hormones, ghrelin and apelin, are upregulated in patients with Type II diabetes, which also decreases insulin sensitivity (Kadoglou et al., 2010). Obesity also causes leptin resistance in both mice and humans, which can be counteracted with a low-fat diet and exercise when compared to high fat diet or standard chow diet (Kang et al., 2013). Exercise training does more than just decrease leptin; when diabetes was induced in mice by feeding them a high fat diet, exercise training of the diabetic mice lowered triglycerides, lipoprotein cholesterol, and leptin. Exercise training
also increased insulin in the diabetic mice (Ghozhdi et al., 2021). Exercise training also effects levels of
the adipokine, adiponectin, eliciting a 55% increase in healthy elderly adults. The exercise-induced
increase in adiponectin may combat age-related inflammation (Markofski et al., 2013).

Adiponectin has been reported to have several regulatory roles in skeletal muscle. Adiponectin
phosphorylates AMP-activated protein kinase (AMPK) which is necessary for fatty acid oxidation in
skeletal muscle (Tomas et al., 2002). Adiponectin is also vital in glucose transport within skeletal muscle
(Karbowska et al., 2006). Adiponectin has insulin-sensitizing effects and acute deletion of adiponectin
induced an upregulation of immune markers within subcutaneous white adipose tissue, which suggests
that insulin resistance associated with adiponectin deletion could be due, in part, to activation of an
immune response (Karbowska et al., 2006, Xia et al., 2018). Adiponectin has also been identified as
being involved in inflammation in major muscle groups, like the gastrocnemius muscle in the calf. A
combination of adiponectin gene therapy and exercise training protected gastrocnemius muscle from
inflammation caused by type 2 diabetes (Safwat et al., 2013).

Adiponectin’s role in the metabolic benefits associated with exercise training remains an active
area of research. Ritchie et al. (2014) tested the hypothesis that adiponectin is required for exercise-
mediated improvements in glucose homeostasis. These researchers exercise trained (treadmill training)
wild type and germline adiponectin knockout mice for 8 weeks. These investigators reported that
treadmill exercise training increased glucose and insulin tolerance similarly in wild type and adiponectin
knockout mice (Ritchie et al., 2014). They concluded that adiponectin is not required for exercise
training-induced improvements in glucose metabolism, surmising that compensatory mechanisms are
stimulated by exercise training in the absence of adiponectin. In contrast, the Delp laboratory recently
reported that germline deletion of adiponectin resulted in increased oxidative metabolism in sedentary
adult mice. Although adiponectin was higher in sedentary adiponectin knockout mice, when wild type
and germline adiponectin knockout mice underwent treadmill exercise training, oxidative metabolism
increased in skeletal muscle of wild type, but not adiponectin knockout mice. Enhancement of cardiac and coronary vascular function also occurred in wild type, but not adiponectin knockout mice (Caldwell et al., 2021).

In contrast to the report by Ritchie et al. (2014), in which germline deletion of adiponectin had little effect on exercise training-induced adaptations of glucose metabolism, acute deletion of adiponectin from adipose tissue of adult mice led to development of severe insulin resistance and hyperlipidemia (Xia et al., 2018). Additionally, Xiu et al. reported that 50% of adult mice died within the first five days of acute adiponectin deletion, due to a lack of insulin (Xia et al., 2018).

Thus, both exercise training and acute deletion of adiponectin have been shown to alter glucose homeostasis and to affect lean and fat mass. Both exercise training and adiponectin have also been shown to have anti-inflammatory effects (Gleeson et al., 2011; Ouchi et al., 2007); however, the role that adiponectin plays in exercise training-induced adaptations of lean and fat mass remains unclear. This project addressed the overall hypothesis that adiponectin is necessary for exercise training-induced adaptations of lean and fat mass to occur. We used a mouse model of acute deletion of adiponectin to test the following specific hypotheses: 1) Exercise training-induced reduction of fat mass is impaired in mice in which adiponectin is acutely deleted. 2) Exercise training-induced stabilization/increase of lean mass is impaired in mice in which adiponectin is acutely deleted.
**Methods**

**Table 1. Circulating Adiponectin in Genotypes**

<table>
<thead>
<tr>
<th>Group (n)</th>
<th>Adipo Lox+/+ (3)</th>
<th>Cre+/+ (3)</th>
<th>Cre+/+ post-TAM (4)</th>
<th>Adipo Crelox+/+ post-TAM (3)</th>
<th>Adipo Crelox+/+ post-TAM (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adiponectin (µg/ml)</td>
<td>6.58±2.44</td>
<td>6.81±1.96</td>
<td>6.76±1.27</td>
<td>2.49±0.01</td>
<td>4.49±0.44</td>
</tr>
</tbody>
</table>

*Figure 1. Cre+/+ mice were mated with AdipoLox+/+ mice, producing heterozygous Adipo Crelox+/+ mice that were mated to produce Adipo CreLox+/+ mice. Adipo CreLox+/+ mice have normal levels of circulating adiponectin until fed tamoxifen.*

**Mouse model of adiponectin deletion:** Acute deletion of adiponectin was achieved by using a CreLox mouse model (Figure 1) in which the activation of Cre recombinase is under the control of a tamoxifen-binding promoter region. In such a genetic model, the activation of a specific enzyme, cre recombinase, recombines a pair of short target sequences called the lox sequences. The lox sequences flank the sequence for the adiponectin gene, and when Cre recombinase is activated, the adiponectin gene is deleted from the genome. Because the Cre recombinase is under the control of the tamoxifen-binding promoter, deletion of the adiponectin gene can be achieved by feeding the mice chow that contains tamoxifen. AdipoKO mice received chow containing tamoxifen (Harlan TD.130859; 0.4g TAM/kg food) for 1wk before beginning 8wk of exercise training or sedentary cage confinement. We chose a global inducible knockout of adiponectin because we wanted to study the overall contribution of adiponectin to the whole body response to exercise training, rather than focusing on a specific tissue knockout.

Table 1 shows that circulating adiponectin is reduced by 40% in heterozygous mice (Adipo CreLox+/+) and by 70% in double knockout mice (Adipo CreLox+/+). This was determined by an ELISA test of blood serum samples.
Exercise training: Exercise trained (WT and AdipoKO) double knockout CreLox\(^{+/+}\) mice ran 5 days a week. Intensity of exercising was increased until a speed of 20m/min up a 10° was maintained for 20 minutes. Duration of exercise was increased from week 1 to week 4 by 10 minutes each week until mice were running at 20m/min up a 10° incline for 60 minutes. This intensity and duration were then maintained between week 4 through week 8. Mice were housed in a 12:12 reverse light:dark cycle, and training occurred in the dark with red light illumination. Food and water was provided ad libitum. Sedentary controls (WT and AdipoKO) were cage confined under similar conditions for the duration of exercise training.

Assessment of body mass: Lean body mass and fat mass were assessed in WT and AdipoKO mice at weeks 1, 3, 5, and 7 of exercise training or sedentary cage confinement. Total body mass was collected by weighing the mice on a scale. Fat mass, lean mass, and water mass were assessed with Echo MRI. Total compression to prevent excessive movement in the echo MRI for each mouse was found using the equation:

\[
\frac{\text{Body Weight}}{23.8*2.5+.1}
\]

Total compression is the amount of room each individual mouse had in the echo MRI chamber, which was measured in cm. The number 23.8 represents a practice mouse and 2.5 represents compression to 2.5 cm. This practice mouse, weighing 23.8 grams, was compressed to 2.5 cm, which resulted in a body mass percentage of 93%. This is the percentage the manufacturer states should be obtained for precise results. The .1 is a handicap to ensure no mouse is compressed too intensely. To assess the accuracy and reproducibility of the scans, total body mass percentage was calculated for each mouse after each scan, using the equation:

\[
\frac{(\text{Body Fat} + \text{Lean Muscle} + \text{Free Water})}{\text{Body Weight}}*100
\]
Assessment of exercise tolerance: Exercise tolerance testing was conducted on all mice before and after the 8-week period of exercise training or sedentary cage confinement. Exercise tolerance testing consisted of running at 12cm/s for 3 minutes, followed by 2cm/s increases in speed every 2 minutes until mouse reaches exhaustion. Time at which the mouse did not move off on the lower end of the treadmill for more than 5 seconds was recorded. All mice were familiarized to the treadmill by walking on it for 10 minutes a day for 3 days at a speed of 8cm/s.

Data Analysis: Body fat, lean mass, and free water percentage were found using the equation:

\[
\frac{\text{(Total Gram of Body Fat or Lean Muscle or Free Water)}}{\text{Total Body Mass in Grams}} \times 100
\]

Change in lean mass or body fat were calculated using the equation:

\[
\frac{\text{(Value for % fat or muscle (at Week 7 scan) – Value for % fat or muscle (at Week 1 scan))}}{\text{Value for % fat or muscle (at Week 1 scan)}} \times 100
\]

Statistical analyses were run separately in males and females as male and female body fat and lean muscle distribution differ (Chang et al., 2018; O’Reilly et al., 2021). For statistical purposes, the change in time to exhaustion (post-training exhaustion time – pretraining exhaustion time) was calculated for each mouse and a two-way ANOVA was run to assess the effects of genotype and exercise training status. The changes in lean mass and fat mass were also compared by two-way ANOVA to assess the effects of genotype and exercise training status. Changes in lean mass (%) and fat mass (%) measured over time (pre, weeks 1, 3, 5, 7) were compared by three-way ANOVA with two between factors (genotype and exercise training status) and one within factor (time). Significance was set at \( \alpha \leq 0.05 \). Data are presented as means ± SEM.

Results
**Age and Body Weight.** At the time of sacrifice, the ages of both male and female mice ranged from 6-11 months. The average age of male WTEX was 6.6 months, the average of male KOEX was 5.7 months, the average age of male WTSED mice was 7 months, and the average age of male KOSED mice was 5.9 months. The average of female WTEX was 7.5 months, the average of female KOEX was 9 months, with 2 mice being 10.5 months at time of sacrifice. The average age of female WTSED mice was 9.7 months, and the average of female KOSED mice was 7 months. The older mice found in KOEX and WTSED would influence the results and are expanded upon in the limitations. The average age at sacrifice was 7.2 months. Total body mass was higher in males as compared to females, but was not different between exercise trained and sedentary mice in either males (Table 2) or females (Table 3), regardless of genotype. In males, at the time of sacrifice, the absolute mass of the gastrocnemius muscle and the normalized mass of the gastrocnemius muscle (normalized to body weight) was similar between groups and was not changed by exercise training in either WT mice or AdipoKO mice. Similarly, in females, at the time of sacrifice, the absolute mass of the gastrocnemius muscle and the normalized mass of the gastrocnemius muscle (normalized to body weight) was similar between groups and was not changed by exercise training in either WT mice or AdipoKO mice.

**Table 2. Average weights with SD of male mice across time**

<table>
<thead>
<tr>
<th>Cohorts</th>
<th>Before Experiment (g)</th>
<th>Week 1 (g)</th>
<th>Week 3 (g)</th>
<th>Week 5 (g)</th>
<th>Week 7 (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WTSED (n=5)</td>
<td>27.4±2.2</td>
<td>27.7±2.0</td>
<td>27.7±1.93</td>
<td>28±2.2</td>
<td>28±2.5</td>
</tr>
<tr>
<td>SEDKO (n=10)</td>
<td>26.9±2.0</td>
<td>26.8±2.0</td>
<td>28.2±1.7</td>
<td>28.2±1.4</td>
<td>28.4±1.6</td>
</tr>
<tr>
<td>KOEX (n=6)</td>
<td>27.7±2.1</td>
<td>28.2±2.1</td>
<td>27.9±1.6</td>
<td>28.5±1.6</td>
<td>28.6±1.9</td>
</tr>
<tr>
<td>WTEX(n=5)</td>
<td>28.5±1.9</td>
<td>28±1.5</td>
<td>28.5±1.5</td>
<td>29.6±1.5</td>
<td>29.4±1.7</td>
</tr>
</tbody>
</table>

**Table 3. Average weights with SD of female mice**

<table>
<thead>
<tr>
<th>Cohorts</th>
<th>Before Experiment (g)</th>
<th>Week 1 (g)</th>
<th>Week 3 (g)</th>
<th>Week 5 (g)</th>
<th>Week 7 (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WTSED</td>
<td>25.1±1.1</td>
<td>24.8±.9</td>
<td>25.2±1.0</td>
<td>25.1±1.2</td>
<td>25.9±1.4</td>
</tr>
<tr>
<td>SEDKO</td>
<td>22.1±1.2</td>
<td>21.3±.8</td>
<td>22.3±.9</td>
<td>22.7±.8</td>
<td>22.5±.6</td>
</tr>
<tr>
<td>KOEX</td>
<td>22.2±.6</td>
<td>21.4±.6</td>
<td>21.3±.7</td>
<td>22.1±1.0</td>
<td>22.2±.6</td>
</tr>
<tr>
<td>WTEX</td>
<td>21.8±2.5</td>
<td>21.1±2.1</td>
<td>21±2.5</td>
<td>20.8±2.2</td>
<td>21.6±2.8</td>
</tr>
</tbody>
</table>
**Exercise Tolerance.** Exercise tolerance was assessed in both male and female mice. In males, exercise training increased the time to exhaustion by 13.13 minutes in WT mice and by 11.22 minutes in AdipoKO mice (Figure 2). Thus, after completion of eight weeks of exercise training, there was no difference in exercise tolerance between WT and AdipoKO mice. In male WT mice that remained sedentary for eight weeks, time to exhaustion was increased by only 1.17 minutes. In contrast, in male AdipoKO mice that remained sedentary for eight weeks, time to exhaustion decreased by 3.63 minutes (Figure 2). Thus, after the eight-week training period, exercise tolerance was significantly higher (P=.0001) in exercise trained male mice as compared to sedentary male mice, regardless of genotype (Figure 2). After the eight-week period of sedentary cage confinement, exercise tolerance was reduced in male AdipoKO mice as compared to male WT mice (Figure 2). In females, exercise training increased the time to
exhaustion by 5.75 minutes in WT and AdipoKO mice, respectively (Figure 3). These values represent only 2 mice in the WT group, but overall, exercise training increased exercise tolerance, regardless of genotype. As in male mice, after completion of eight weeks of exercise training, there was no difference in exercise tolerance between WT and AdipoKO mice. In contrast to results in male mice, exercise tolerance decreased over the eight weeks of sedentary cage confinement in both female WT and female AdipoKO mice. Time to exhaustion decreased by -5.69 minutes in WT mice and by -4.9 minutes in AdipoKO mice (Figure 3).

**Body Fat.** Exercise training reduced body fat in WT male mice, whereas eight weeks of cage confinement increased body fat in WT male mice (Figure 4). At week 7, body fat percentage was significantly higher in WTSED mice as compared to WTEX mice. In contrast, body fat increased in both male KOEX mice and male KOSED mice.
To better determine how body fat changed across the time of the exercise/cage confinement period, we calculated the change in percent body fat from pre-study to week 7. Body fat percentage decreased only in WTEX male mice from pre-study to week 7 (Figure 6). In all other male groups (WTSED, KOEX, KOSED) body fat increased from pre-study to week 7. In female WT mice, body fat percentage was lower in WTEX as compared to WTSED by week 1 of exercise training, and body fat percentage remained lower in exercise trained mice across the training/cage confinement period (Figure 7). In female KO mice, body fat percentage was lower pre-study in KOSED mice as compared to KOEX mice, and it remained lower throughout the study (Figure 8). This difference might be attributable to a slight age difference in these two female cohorts, since the average age of the KOEX mice was 2 months greater than the average age of the KOSED mice. To better determine how body fat changed across the time of the exercise/cage confinement period, we calculated the change in percent body fat from pre-study
to week 7. In WTEX female mice, body fat decreased from pre-study to week 7, whereas in WTSED mice, body fat increased from pre-study to week 7 (Figure 9). In both KOEX and KOSED female mice, body fat decreased slightly from pre-study to week 7 (Figure 9).

**Lean Muscle.** In male WT mice, lean muscle mass increased slightly in both exercise trained (WTEX) and sedentary mice (WTSED). From pre-study until week 7, the lean mass (%) did not differ between WTSED and WTEX mice (Figure 10). In contrast, % lean mass decreased in male knockout mice that remained sedentary (KOSED, Figure 11), and at week 5, lean mass was lower in KOSED as compared to KOEX (Figure 11). In female mice, lean mass (%) did not change significantly in either WTEX or WTSED mice. However, because lean mass tended to increase in WTEX

![Figure 9. Change in body fat percentage in WT Exercise Trained, WT Sedentary, KO Exercise Trained, and KO Sedentary female mice. #P<0.05, WTEX vs. WTSED, *P≤0.05 KOSED vs. WTSED](image)

![Figure 10. In males, lean mass increased slightly in WTEX mice and WTSED mice. The increase was similar in WTEX and WTSED mice.](image)

![Figure 11. Lean mass was stable in male KOEX mice, but decreased in male KOSED mice. At week 5, lean mass was significantly lower in KOSED mice as compared to KOEX mice. *P<0.05, KOEX vs. KOSED.](image)
mice, and decrease in WTSED mice, at weeks 5 and 7 there was a tendency for lean mass to be higher in WTEX mice (week 5, P=.061, WTEX vs WTSED; week 7, P=.06, WTEX vs WTSED) (Figure 12). In female AdipoKO mice, % lean muscle was significantly higher pre-study (Figure 13), and remained higher throughout the training/cage confinement period.

Figure 12. In female mice, exercise training did not increase lean muscle mass in WTEX mice. Cage confinement tended to decrease lean muscle in WTSED mice. As a result, lean mass tended to be lower in WTSED mice as compared to WTEX mice at week 5 (P=.061) and week 7 (P=.06).

Figure 13. Lean muscle mass was stable in KOEX. Lean muscle mass decreased in KOSED during the sedentary cage period. *P<0.05, KOEX vs. KOSED.
Several key findings have emerged from this study. First, exercise training induced an increase in exercise tolerance in both male and female mice, even in the absence of adiponectin. In male and female AdipoKO mice, but not in WT mice, exercise tolerance decreased during eight weeks of cage confinement. Second, exercise training reduced fat mass in both male and female WT mice, but not in AdipoKO mice. Third, a decline in lean mass in muscle of AdipoKO mice might be mitigated by exercise training. Altogether, the data gathered in this study suggest that adiponectin is important for reduction of fat mass by exercise training; however, the presence of compensatory physiological mechanisms provides a means by which exercise training can improve exercise tolerance in the absence of adiponectin.

Exercise training stimulated an increase in exercise tolerance in both WT and AdipoKO mice of both sexes, suggesting that compensatory mechanisms contribute to exercise training-induced increases in exercise capacity when adiponectin becomes unavailable. Exercise training did not reduce body fat in male or female KOEX mice. Male KOEX mice increased body fat at a rate similar to male KOSED mice (Figure 5), suggesting that loss of adiponectin, at least in males, will increase body fat regardless of training regimen. Administering adiponectin does prevent weight gain in obese mice (Liu et al., 2016) but can reverse insulin resistance in the liver and muscle (Li et al., 2020). Our data indicate that exercise training can compensate for a loss of adiponectin. In contrast, other hormones or molecules cannot compensate for the negative impact of fatty acid oxidation that occurs with removal of adiponectin (Karbowska et al., 2006).

Although our finding that lean muscle was lower in KOSED male mice as compared to KOEX male mice (Figure 11) may be due to variability within the data, these results suggest that adiponectin may be important to maintenance of lean muscle. Adiponectin in skeletal muscle depends on diet and exercise
training (Marteniz-Huenchullan et al., 2018). One report in the literature states that adiponectin is adequate, but not needed, for energy production in skeletal muscle, since with V̇O₂ and time to exhaustion were not altered in adiponectin knockout mice (Ritchie et al., 2014). Similarly, we found that exercise training increased time to exhaustion similarly in WT and AdipoKO mice. However, time to exhaustion decreased in male sedentary AdipoKO mice, but not male sedentary WT mice (Figure 2), suggesting that acute deletion of adiponectin, in the absence of exercise training, negatively impacts the cardiovascular system or oxidative metabolism in muscle. We did not find the same effect of acute adiponectin deletion in female KOSED mice; time to exhaustion decreased similarly in female SEDWT and SEDKO mice (Figure 3). The lack of difference in our female sedentary mice could be due to differences in the average age of the female mice within WTSED being older (age = 9.67 months) when compared to average age in KOSED mice (age = 7 months). In future studies, we will carefully match all groups for age. The difference in time to exhaustion between male SED groups is likely related to the loss of adiponectin. Removal of adiponectin could affect several pathways that are utilized during hypertrophy and atrophy in skeletal muscle. Insulin-like growth factor-1 (IGF-1)/ATK pathway stimulates muscle production via protein synthesis, which does this through the inhibition of FoxO transcription factors that induce atrophy of skeletal muscle (Hitachi et al., 2014). FoxO transcription factors, alongside insulin, inversely regulate adiponectin receptors AdipoR1 and AdipoR2 and adiponectin sensitivity (Tsuchida et al., 2004). Removal of adiponectin could lead to increased activation of this pathway, resulting in activation of FoxO transcription factors and muscle atrophy in sedentary AdipoKO mice. It is also possible exercise training sufficiently compensates for this loss of adiponectin, as time to exhaustion increased in both KOEX male and female mice.

It has been theorized that adiponectin can be used as a pharmaceutical drug to treat obesity, type II diabetes, endothelial disorders (Achari et al., 2017), and cardiovascular disorders (Zhao et al., 2021). The scope for treatment would be narrow, focusing on patients who have dysfunctional adipose
tissue that doesn’t produce enough adiponectin (Manna et al., 2015). Future anti-obesity drugs now focus on mimicking the effects of bariatric surgery, which has seen successful procedures on patients who kept a weight loss of at least 10% of initial body weight (Müller et al., 2022). Adiponectin as a drug itself would be able to mimic this, as bariatric surgery tends to increase adiponectin in obese patients (Valenzano et al., 2020).

Due to the narrow scope of this study, there were limitations as to what we could accomplish. One major limitation was the variability in measurements obtained with EchoMRI. In male mice, body fat and lean muscle do not follow conventional trends. Body fat increased in male WTEX mice until week 7. Lean muscle declined in just one week (between pre study and week 1) in male KOEX mice. Another issue of variability was the high lean muscle and low body fat % of female KOSED, which caused results to be skewed and, while statistically significant, may not be biologically significant. This variability is most likely due to the lower total body % than what the manufacturer states should be obtained with an echo MRI, which is 93%. Inconsistent total body % would lead to variability in both fat and muscle. While this was identified during the study it was decided to continue scans as we did before to ensure consistency. Another limitation was the number of mice per cohort. Low n values in each cohort reduce the power of statistical analyses.

In future studies should increase the cohort size, ensure a total body mass % of at least 90% to ensure accuracy of the data and carefully match the ages of the mice between cohorts. Future studies should run hormonal tests to identify if there are any hormones that are upregulated after deletion of adiponectin. For the SED group there should be tests run to identify if FoxO transcription factors are upregulated. Additional tests should be run on lipid regulatory pathways to identify any difference between WT and AdipoKO mice.
Bibliography


https://doi.org/10.1161/circresaha.120.314458