Comparison of glucose tolerance tests to detect the insulin sensitizing effects of a bout of continuous exercise

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Abstract

The aim of the present study was to determine which of the available glucose tolerance tests (oral, OGTT vs. intravenous, IVGTT) could more readily detect the insulin sensitizing effects of a bout of continuous exercise. Ten healthy moderately-fit young men (VO2peak of 45.4±1.8 mL·kg⁻¹·min⁻¹; age 27.5±2.7 yr) underwent four OGTT and four IVGTT on different days following a standardized dinner and overnight fast. One test was performed immediately after 55-min of cycle-ergometer exercise at 60% VO2peak. Insulin sensitivity index was determined during a 50-min IVGTT according to Tura (CISI) and from a 120-min OGTT using the Matsuda composite index (MISI). After exercise, MISI improved 29±10% without reaching statistical significance (P=0.182) due to its low reproducibility (CV 16±3 %; intra-class reliability 0.846). However, CISI significantly improved (50±4%; P<0.001) after exercise showing better reproducibility (CV 13±4 %; intra-class reliability 0.955). Power calculation revealed that 6 participants were required for detecting the effects of exercise on insulin sensitivity when using IVGTT while 54 were needed when using OGTT. The superior response of CISI compared to Matsuda index suggests the preferential use of IVGTT to assess the effects of exercise on insulin sensitivity when using a glucose tolerance test.

Keywords: endurance exercise; glucose tolerance; insulin sensitivity; oral glucose tolerance test; intravenous glucose tolerance test.
Introduction

Exercise is recommended for the treatment and prevention of type 2 diabetes (American-Diabetes-Association. 2011) due to its insulin-sensitizing effects (Roden 2012, Mikines et al. 1988, Hawley 2004). Although the euglycemic hyperinsulinemic clamp (EHC) is the gold standard method to assess insulin sensitivity, it requires costly and complex equipment and trained hospital personnel to obtain accurate measures and avoid complications, (Bloomgarden 2006, Muniyappa et al. 2008). Insulin sensitivity indexes derived from oral and intravenous glucose tolerance tests (i.e., OGTT and IVGTT, respectively) are affordable surrogates of the EHC frequently reported in the literature. However, to our knowledge, data comparing the reliability and response to exercise of these indexes are scarce.

Although M\textsubscript{ISI} based on OGTT shows a fairly good agreement with the EHC ($r=0.73$; (Matsuda and DeFronzo 1999)) its reproducibility measured by the coefficient of variation (CV) has been estimated between 14.0 and 20.4%; (Utzschneider et al. 2007)). Glucose ingestion, besides inducing pancreatic insulin release, stimulates gastrointestinal hormones and affects liver metabolism. Furthermore, the ingested glucose would interact with enteric hormones and neural factors capable of altering glucose absorption and insulin secretion (Kahn 1997). We believe that this may be behind the increased within-subject variability when using the OGTT technique. On the other hand, it is worth to mention that the signals initiated from the gastrointestinal system after an oral load of glucose resemble the ones that an individual faces after a meal, justifying the use of OGTT for an ecological, but less reproducible, assessment of insulin sensitivity.
To avoid the variable interaction between the ingested glucose and gastrointestinal hormones and neural factors (Kahn 1997) the glucose load is often administered through an intravenous catheter using the intravenous glucose tolerance tests (IVGTT). A mathematical model (i.e. minimal model (Bergman et al. 1987)) has been developed to calculate insulin sensitivity from a 180 min IVGTT. When using this model researchers report a high correlation with the EHC ($r=0.89; P<0.05$; (Bergman et al. 1987)) and a CV=14%; (Ferrari et al. 1991)). To reduce testing time and costs, Tura and co-workers (Tura et al. 2010) have recently developed a simpler mathematical model to calculate insulin sensitivity from a 50 min IVGTT (i.e., $C_{ISI}$). They found that $C_{ISI}$ was highly correlated with the EHC ($r=0.91; P<0.05$) and the minimal model ($r=0.92; P<0.05$; (Tura et al. 2010)) when tested in a mixed group of healthy and insulin resistant participants at rest. However, to our knowledge, $C_{ISI}$ response to exercise or its within-subject reproducibility has not been established.

Without knowing the response to exercise of each insulin sensitivity index, researchers often default to use the simpler OGTT technique perhaps limiting the statistical significance of their findings. The purpose of this study was to compare the insulin sensitivity response to exercise from glucose tolerance tests with different routes of glucose administration (i.e., $M_{ISI}$ from OGTT vs. $C_{ISI}$ from IVGTT). We compared the response to exercise of each of these indices as well as their reproducibility. We hypothesized that insulin sensitivity measures derived from IVGTT would be more reproducible and responsive to the effects of exercise than when derived from OGTT.
Materials and methods

Participants

Ten young, healthy and physically active males with a mean ± SEM age of 27.5 ± 2.7 years, and a BMI 24.6 ± 0.9 kg·m⁻² were recruited from the University’s student and workers population after medical clearance. After detailed information about the benefits and risks involved with their participation in the study, all gave their written consent which was approved by the local Hospital’s Ethics Committee and conformed to the latest revision of the Declaration of Helsinki.

Preliminary testing

A week before participation in the study, under medical supervision, participants underwent a maximal graded exercise test until volitional exhaustion according to the ACSM's guidelines for exercise testing and prescription (American·College·of·Sports·Medicine 2006), starting at 100 W and increasing 25 W·min⁻¹ in an electrically braked cycle-ergometer (Ergoselect 200, Ergoline, Germany). During the exercise test, O₂ consumption was measured by indirect calorimetry (Quark b², Cosmed, Italy) and peak oxygen consumption and cycling peak power output was assessed. Continuous, standard 12-lead ECG (Quark T12, Cosmed, Italy) was performed to ensure a normal cardiovascular response to exercise.

Experimental design

All participants underwent eight experimental trials, four OGTT and four IVGTT, with a separation of at least 72 hours among them. One of the OGTT (i.e., \( \text{OG}_{\text{Ex}} \)) and one of the IVGTT (i.e., \( \text{IV}_{\text{Ex}} \)) were performed after a standardized bout of...
cycling exercise. Trial order was fully randomized, starting the morning (0800-1000 hours) after an overnight 10-h fast that followed a standardized dinner which was provided by the investigators and was composed by a frozen lasagna, two apples and an isotonic beverage (703 Kcal, 50% from carbohydrate, 38% from fat, 3% saturated fatty acids, and 12% from protein. Fiber content: 8.4 g). During the 24-hours prior to each trial, participants were instructed to ingest at least 7 g of carbohydrate per kg of body weight to ensure full glycogen storage. This amount of ingested carbohydrates should avoid the confounding effect of reduced muscle glycogen levels on insulin sensitivity as previously described (Ivy et al. 1985). In addition, all participants were asked to refrain from vigorous exercise 48-hours prior to each trial and to ingest 500 mL of bottled water upon awakening to promote euhydration.

**Experimental trials**

Upon the participant’s arrival to the laboratory, nude body weight (Hawk, Mettler Toledo, USA) and urine specific gravity ($U_{SG}$; Uricon-NE, Atago, Japan) were measured to assess hydration status. Following this, the participants lay in a stretcher and a 20G intravenous catheter (BD Insyte, Becton-Dickinson, Spain) was inserted in an antecubital vein and a Luer-lock three-way stopcock attached (Vitroway, Vitromed Healthcare, India). After 15 minutes of rest in supine position, 5 ml of blood were withdrawn to obtain a baseline fasting sample. Five minutes later, the participants underwent the glucose tolerance test (either OGTT or IVGTT) or started the aerobic exercise bout according to their assigned trial. The glucose tolerance tests were performed approximately 20 minutes after exercise. We chose not to delay the glucose tolerance tests beyond 20 min of supine rest because prior data using hyperinsulinemic euglycemic clamp demonstrated no difference in insulin sensitivity when assessed either 30 or 180 minutes after an exercise bout similar in
intensity and duration to the exercise presently used (Howlett et al. 2008) in subjects of similar characteristics (i.e., untrained young men).

Both exercise trials (i.e., OGEx and IVEx) were followed by 20 min of resting supine after which a new baseline blood sample was withdrawn before starting the glucose tolerance test. Exercise duration and intensity resembled the ones used by Mikines et al., (Mikines et al. 1988) in a study in which they showed improved insulin sensitivity in participants of similar characteristics (male, young, and healthy). In addition, the chosen exercise bout followed the recommendations of the last American College of Sports Medicine and American Diabetes Association joint statement of exercise for type 2 diabetes treatment and prevention (Colberg et al. 2010). Specifically, exercise commenced with a warm-up (5 min, 100 W) followed by 45-min at 65% VO2peak and a 5 min cool-down (75 W). The average workload for the 55 min of exercise was 60% VO2peak.

**Glucose and insulin analysis**

Samples were mixed in tubes with 3K-EDTA (Vacuette®, Greiner Bio-One GmbH, Austria) and centrifuged at 4000 rpm during 10 min at 4°C (MPW-350R, Med. Instruments, Poland) to obtain plasma that was stored at -80°C. Glucose was measured with an enzymatic glucose oxidize assay (Enzymatic Glucose Reagent, Thermoscientific, USA). Insulin concentration was analyzed by chemiluminescence (Architect System Insulin, Abbott Diagnostics Division, Germany).

**OGTT and IVGTT procedures and insulin sensitivity indexes calculation**

After collection of the basal blood sample, OGTT started with the ingestion of 75 g of anhydrous glucose (Guinama Laboratorio, Spain) diluted into 250 mL of water. Immediately after all fluid was ingested, a timer was started and 5 mL blood
samples were obtained after 30, 60, 90 and 120-min of glucose ingestion. For IVGTT we delivered a glucose load of 0.5 g · kg\(^{-1}\) body mass with a maximal dose of 35 g. We used a 30% glucose solution (Glucosada 30%, Grifols, Spain) manually infused at an even pace during 3-min using two 60 mL syringes (BD Plastipak, Spain). Immediately after delivering the glucose load, the stopcock, catheter and vein were rapidly flushed with 10 ml of 0.9% saline solution. Following, every ten minutes (i.e., 10, 20, 30, 40, and 50-min) a 5 mL blood sample was obtained and the catheter flushed with 5 mL of 0.9% saline. For IVGTT procedure we strictly complied with the recommendations of the Islet Cell Antibody Register User’s Group (ICARUS; (Bingley et al. 1992)) in all aspects, including the use of a single catheter for glucose infusion and sample collection.

Basal glucose and insulin concentrations were used to calculate HOMA2-IR index (Levy et al. 1998) using a specific software (HOMA calculator, Version 2.2.2 Diabetes Trial Unit, University of Oxford, available at www.dtu.ox.ac.uk/homacalculator).

Data from the OGTT technique was used to calculate \(M_{\text{ISI}}\) (Matsuda and DeFronzo 1999) as follows:

\[
M_{\text{ISI}} = \frac{10000}{\sqrt{[\text{FPI} \, \mu\text{IU} \cdot \text{mL}^{-1} \cdot \text{FPG} \, \text{mg} \cdot \text{dL}^{-1}] \cdot (\text{PG}_\text{MEAN} \cdot \text{PI}_\text{MEAN})}}
\]

where, FPI is the fasting plasma insulin, FPG is the fasting plasma glucose, and \(\text{PG}_\text{MEAN}\) and \(\text{PI}_\text{MEAN}\) are respectively the mean of the glucose and insulin concentration of all the samples collected during the 120 min OGTT, and 10000 is the constant to obtain numbers ranging between 1 and 12.

Data from the IVGTT technique was used to calculate \(C_{\text{ISI}}\) (Tura et al. 2010) as follows:
where $\alpha$ is a scaling factor (0.604), $K_G$ is the rate of glucose disappearance (slope of log glucose), $\Delta AUC_{INS}$ is the area under the curve of insulin concentration above basal value and $T$ is the time interval between 10 and 50 min (i.e. 40 min) when glucose and insulin data are computed.

**Statistics**

We used Shapiro-Wilk to test the normal distribution of data. In the three resting trials, absolute reliability was calculated using coefficient of variation (CV) and relative reliability using intraclass reliability (ICR) (Vincent 1999). Student's T-test identified insulin sensitivity differences between rest (one of the trials randomly chosen) and post-exercise. Nutritional and hydration status stability among trials was evaluated using repeated measures ANOVA comparing pre-trial body weight, $U_{SG}$, fasting plasma glucose, insulin and HOMA2-IR among trials. Correlations between $M_{ISI}$ and $C_{ISI}$ in all variables were sought using Pearson coefficient. Limits of agreement (LOA) were calculated according to Bland and Altman (Bland and Altman 1986) Sample size estimates for each index were calculated based on the standard deviations of the differences ($t$ test) between rest and post-exercise values using an $\alpha$-level of 0.05 and a 90% power (Utzschneider et al. 2007). Results are reported as means $\pm$ SEM. Significance value was set at $P < 0.05$. All the tests were performed with SPSS for windows (Version 19, SPSS Inc., USA).
Results

Participant characteristics and pre-trial hydration and nutritional status

Participants VO_{2peak} was 45 ± 2 ml·kg^{-1}·min^{-1} and they reached a peak pedaling power of 300 ± 18 W before exhaustion. Body weight and urinary specific gravity values were not different before any of the eight trials evidencing a similar pre-test hydration status (Table 1). HOMA2-IR index was not different among any trial (Table 1), suggesting compliance with the prescribed diet and exercise refraining.

Reproducibility and response to exercise of insulin sensitivity indices

At rest, the within subject reproducibility of insulin sensitivity measured in three different days, was superior when using C_{ISI} from IVGTT than when using M_{ISI} from OGTT, showing lower coefficient of variation and a higher intraclass reliability (Table 2). HOMA2-IR from fasting glucose and insulin concentrations obtained at rest before the OGTTs had a coefficient of variation of 15.9% and an intraclass reliability of 0.827. HOMA2-IR before the IVGTTs had a coefficient of variation of 18.6% and an intraclass reliability of 0.793.

After moderate exercise (55 min at 60% VO_{2peak}), OGTT derived M_{ISI} rose 29% from rest due to a 17% reduction in the product of the mean glucose and insulin concentration, and a 11% reduction in the product of fasting plasma glucose and insulin concentration (Table 3). However, that improvement in M_{ISI} did not reach statistical significance (Figure 1A; P = 0.141), likely due to the inconsistent inter-subject response to exercise since four out of the ten participants did not show improvement in M_{ISI} (individual responses are dotted lines in Figure 1A). Post-exercise C_{ISI} increased significantly by 50% (Figure 1B; P<0.001) mainly by a 27%
reduction in the area under the curve of plasma insulin above basal value ($P = 0.034$, Table 3). The individual response showed that all ten participants improved their post-exercise $C_{ISI}$ (individual responses are dotted lines in Figure 1B). After exercise HOMA2-IR did not show significant differences from pre-exercise values despite a 15% improvement ($0.78 \pm 0.07$ to $0.67 \pm 0.12$ from pre to post exercise, $P=0.479$).

**Correlations between techniques**

During resting conditions $M_{ISI}$ and $C_{ISI}$ showed a high and significant correlation ($r = 0.828; P = 0.003; 95\% \text{ LOA} = 4.1$ to $-3.9$). However, the correlation between $M_{ISI}$ and $C_{ISI}$ scores after exercise was not significant ($r = 0.547; P = 0.102; 95\% \text{ LOA} = 10.2$ to $-6.2$). In addition, the changes in the insulin sensitivity from rest to exercise obtained from both indices ($M_{ISI}$ and $C_{ISI}$) were calculated from one randomly chosen resting condition trial ($OG_{REST}$ and $IV_{REST}$) and the exercise trial ($OG_{EX}$ and $IV_{EX}$). Correlation of those changes with exercise in each of the techniques ($OG$ and $IV$) did not show statistical significance ($r = 0.337; P = 0.341; 95\% \text{ LOA} = 9.4$ to $-6.1$).

**Sample size calculation**

Sample size estimates (Utzschneider et al. 2007) revealed that to find the effect of exercise on insulin sensitivity, 54 participants would be required when using $M_{ISI}$ ($SD = 4.1$) while only 6 participants when using $C_{ISI}$ ($SD = 2.1$).
Discussion

It is well established that exercise stimulates insulin-dependent and insulin-independent glucose uptake in human skeletal muscle (Hayashi et al. 1997). The OGTT and the IVGTT are two dynamic methods to assess insulin sensitivity when the euglycemic hyperinsulinemic clamp technique is not affordable. These surrogate insulin sensitivity indexes from glucose tolerance tests are indistinctly reported in the scientific literature without much regard to questions of reproducibility or responsiveness. We tested the reliability of Matsuda index (M_{ISI}, derived from OGTT) and Tura’s insulin sensitivity index (C_{ISI}, derived from IVGTT) at rest during standardized conditions. In addition, we investigated which index more readily detects the insulin sensitizing effects of a single bout of prolonged (55 min) moderately-intense exercise (60% VO_{2peak}). Unlike most of the literature in this area, we tested reliability and response in the same participants using a cross-over repeated measures experimental design.

A major finding of this study is that C_{ISI} derived from IVGTT showed the highest reproducibility (Table 2). Due to this higher reproducibility and consistency (i.e., every subject improved) only with C_{ISI} we detected the improvements in insulin sensitivity with exercise (P < 0.001; Figure 1B). In contrast, M_{ISI} was not responsive enough to significantly detect the effects of exercise on insulin sensitivity (Figure 1A). Testing another 44 similar participants would be needed to ascertain the effects of exercise using M_{ISI}. The extra cost and effort of testing that amount of participants may not be justified in many studies and out of the scope of many research laboratories with restricted budgets. On the other hand, C_{ISI} is calculated after a 50 min IVGTT whereas M_{ISI} requires a 120 min OGTT. The reduced time of study is another advantage when using C_{ISI} instead of M_{ISI}. Thus, our data support
the preferential use of the IVGTT technique in comparison to OGTT when
evaluating the effects of and exercise bout (or exercise program) on insulin
sensitivity.

While most studies show a positive effect of exercise on insulin sensitivity
when assessed by OGTT (Balducci et al. 2010, Dumortier et al. 2003, Jenkins and
Hagberg 2011, Kishimoto et al. 2002, Venables and Jeukendrup 2008), some report
no effects. Hansen et al., (Hansen et al. 2009) found in obese type 2 diabetes patients
that two exercise training programs of different intensities improved glycated
hemoglobin (HbA\(_1C\)) and whole body oxidative capacity while insulin area under the
curve measured during OGTT remained unchanged. Mitchell et al. (Mitchell et al.
2011) measured insulin sensitivity using OGTT in obese participants after aerobic
exercise finding no improvements. Niakaris and coworkers (Niakaris et al. 2005)
recommended caution on the interpretation of OGTT-derived insulin sensitivity
results since they seem to be population dependent. Our data suggest that the
discrepancies about the effects of exercise on OGTT derived insulin sensitivity
calculations originate from the low reproducibility of this technique. In addition, the
response was inconsistent since 4 out of the 10 participants did not improve \(M_{\text{ISI}}\)
after exercise.

\(M_{\text{ISI}}\) does not only reflect peripheral insulin sensitivity but also hepatic insulin
sensitivity (Matsuda and DeFronzo 1999). Since exercise is mostly known to affect
peripheral insulin sensitivity, it is possible that Matsuda index was not that sensitive
to the effects of exercise because a portion of the calculation is devoted to hepatic
insulin sensitivity. The fasting glucose and insulin concentration portion of the \(M_{\text{ISI}}\)
formulae (see materials and methods) reflects hepatic insulin sensitivity. When we
remove that portion of the formula and only the glucose and insulin concentrations
during the OGTT are compared, no significant differences are found between the
exercise and rest trials ($P=0.136$, Table 3). We interpret this to indicate that the lack
of improvement in $\text{M}_{\text{ISI}}$ after exercise is also due to a variable response in peripheral
insulin sensitivity.

It is well established that one bout of aerobic exercise improves glycemic
control and insulin sensitivity (Kennedy et al. 1999, Perseghin et al. 1996). In a
recent study healthy non-obese young men were tested twenty minutes after a bout of
30 min of continuous pedaling at 50% of their $\text{VO}_{2\text{max}}$. The authors reported a 45%
 improvement in insulin sensitivity when using frequently sampled IV glucose
tolerance tests (Hayashi et al. 2005). We used a similar energy demanding bout of
exercise (i.e., 55 min of exercise at 60% $\text{VO}_{2\text{peak}}$) and insulin sensitivity improved
50% with $\text{C}_{\text{ISI}}$ ($P<0.001$; Figure 2(b)). Our results using the 50-min IVGTT
technique described by Tura, agree in the magnitude of insulin sensitivity
improvement with previous studies (Hayashi et al. 2005).

Our study design has several limitations that are worth to discuss. We are
favoring the use of IVGTT instead of OGTT. However, it is necessary to note that
OGTT better resembles the physiological challenge that an individual faces after a
meal justifying the use of OGTT especially in large epidemiological studies.
Secondly, we used healthy participants with high baseline insulin sensitivity values
very similar to the ones found by Tura et al. in a similar population (7.5 vs. 5.55 ±
0.25 x10^{-4} \text{ min}^{-1} \text{ [μU•mL]^{-1}}$) (Tura et al. 2010). However, there is an inverse
relationship between baseline insulin sensitivity and insulin sensitivity improvements
with exercise (Magkos et al. 2008). So it is possible that if a group of overweight or
insulin resistant participants were to perform this study, the increase in insulin
sensitivity with exercise would have been more robust and statistically significant
even when using M\textsubscript{ISI}.

Finally, the glucose tolerance tests in resting condition took place 1 hour before
the tests after exercise (i.e., 8 am vs. 9 am). Although circadian rhythm could affect
insulin sensitivity between morning and afternoon trials (Boden et al. 1996), it is
unlikely that circadian rhythm could be a factor when trials are spaced only by one
hour (8 am vs. 9 am). In addition, this difference in the time at the start of the tests
should have not clouded the results of our main aim which was the comparison of
two insulin sensitivity indices with different modes of glucose load delivery (i.e.,
M\textsubscript{ISI} vs. C\textsubscript{ISI}), considering that the difference in time between the rest and post
exercise tests was the same for M\textsubscript{ISI} and C\textsubscript{ISI}.

The homeostasis model assessment of insulin resistance (HOMA2-IR) (Levy et
al. 1998) stands out as the more cost and time efficient insulin sensitivity index, since
it requires just fasting glucose and insulin concentrations. However, HOMA2-IR
was unable to detect the insulin sensitivity changes induced by the 55 min bout of
exercise and it was less reproducible than C\textsubscript{ISI}. Thus, according to our data,
HOMA2-IR is not a recommendable technique to measure the insulin sensitizing
effects of a bout of exercise. In fact, other authors have argued that HOMA-IR is not
indicated to assess insulin sensitivity under non-steady state conditions (Wallace et
al. 2004) like the transitional improvements induced by exercise.

In conclusion, exercise prescription to improve carbohydrate metabolism
requires from a reliable and responsive test to gauge the effect of exercise on insulin
sensitivity. We compared two glucose tolerance tests that could be used for insulin
sensitivity assessment out of hospital boundaries. We found improved
responsiveness and reproducibility when the glucose load is delivered through an
intravenous catheter (C_{ISI}, IVGTT-derived) in comparison to oral ingestion (M_{ISI},
OGTT-derived). Using 10 untrained non-diabetic participants, only the insulin
sensitivity index based on IVGTT was fit to detect the acute effects of a bout of
prolonged aerobic exercise. In most exercise science research environments, where
the use of a euglycemic hyperinsulinemnic clamp is not possible and sample size is
limited, C_{ISI} based on 50 min IVGTT is a superior index to gauge the acute effects of
exercise.

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(DEP2011-28615). The authors report no conflicts of interest.
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Table 1. Baseline hydration and glucose metabolism before glucose load delivery and before exercise. Values are means ± SEM for 8 trials in each participant (n=10). *P* values from repeated measures ANOVA among all 8 trials. Urine specific gravity (U\textsubscript{SG}), fasting plasma glucose (FPG), and fasting plasma insulin (FPI).

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th><em>P</em> value</th>
</tr>
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<tbody>
<tr>
<td>Body Weight (kg)</td>
<td>78.9 ± 0.2</td>
<td>0.420</td>
</tr>
<tr>
<td>U\textsubscript{SG}</td>
<td>1.016 ± 0.002</td>
<td>0.416</td>
</tr>
<tr>
<td>FPG (mM·L\textsuperscript{-1})</td>
<td>5.0 ± 0.1</td>
<td>0.088</td>
</tr>
<tr>
<td>FPI (µIU·mL\textsuperscript{-1})</td>
<td>6.2 ± 0.3</td>
<td>0.111</td>
</tr>
<tr>
<td>HOMA2-IR</td>
<td>0.79 ± 0.06</td>
<td>0.101</td>
</tr>
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</table>
Table 2. Within-subject reproducibility of the three resting trials when using insulin sensitivity indices derived from oral (OGTT) or intravenous (IVGTT) glucose tolerance test. Values are means ± SEM.

<table>
<thead>
<tr>
<th></th>
<th>OGTT Matsuda Index $M_{ISI}$</th>
<th>IVGTT $C_{ISI}$</th>
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<tbody>
<tr>
<td>Rest 1</td>
<td>7.5 ± 0.7</td>
<td>7.4 ± 1.0</td>
</tr>
<tr>
<td>Rest 2</td>
<td>6.8 ± 0.8</td>
<td>7.5 ± 1.0</td>
</tr>
<tr>
<td>Rest 3</td>
<td>7.0 ± 0.7</td>
<td>7.6 ± 1.0</td>
</tr>
<tr>
<td>Coefficient of variation (%)</td>
<td>16.4 ± 2.5</td>
<td>13.4 ± 3.8</td>
</tr>
<tr>
<td>Intraclass reliability (ICR)</td>
<td>0.846</td>
<td>0.955</td>
</tr>
</tbody>
</table>
Table 3. Components of the $M_{SI}$ from oral (OGTT) and $C_{SI}$ from intravenous (IVGTT) during rest and after exercise. Values are means ± SEM. Fasting plasma insulin (FPI), fasting plasma glucose (FPG), mean plasma glucose ($PG_{MEAN}$) and insulin ($PI_{MEAN}$) during OGTT. Rate of glucose disappearance ($K_{G}$) and area under the curve of insulin concentration ($\Delta AUC_{INS}$).

<table>
<thead>
<tr>
<th>$M_{SI}$</th>
<th>Rest</th>
<th>Exercise</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPI ($\mu$IU·L$^{-1}$) · FPG (mg·dL$^{-1}$)</td>
<td>537 ± 43</td>
<td>455 ± 38</td>
<td>0.320</td>
</tr>
<tr>
<td>$PG_{MEAN}$ (mg·dL$^{-1}$) · $PI_{MEAN}$ (µUI·mL$^{-1}$)</td>
<td>4755 ± 525</td>
<td>3848 ± 475</td>
<td>0.136</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>$C_{SI}$</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>$K_{G}$ (%·min$^{-1}$)</td>
<td>2.9 ± 0.3</td>
<td>3.1 ± 0.2</td>
<td>0.138</td>
</tr>
<tr>
<td>$\Delta AUC_{INS}$ (µIU·mL$^{-1}$)</td>
<td>1437 ± 347</td>
<td>1042 ± 233</td>
<td>0.034</td>
</tr>
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</table>
Figure captions

Figure 1. (A) Matsuda index (M_{ISI}) from 2 h OGTT during resting (OG_{REST}) and after exercise (OG_{EX}). (B) Tura’s insulin sensitivity index (C_{ISI}) from 50 min IVGTT during resting (IV_{REST}) and after exercise (IV_{EX}). Individual responses shown as dotted lines. Values are means ± SEM. * Different from rest (P < 0.05).
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