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Insulin sensitivity derived from oral glucose tolerance testing in athletes: Disagreement between available indices

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Abstract
The aims of the present study were to determine whether available ''fasting'' and oral glucose tolerance test-derived insulin sensitivity indices could effectively discriminate between individuals with higher than normal insulin sensitivity, and whether they would all provide similar information in clinical practice. Sprint runners ($n = 8$), endurance runners ($n = 8$) and sedentary controls ($n = 7$) received a 75-g oral glucose tolerance test. All participants were healthy lean males, aged 21 – 29 years. Besides glucose and insulin responses, a total of nine such indices were computed. Fasting as well as post-load glucose concentrations were similar in the three groups, while basal plasma insulin and the insulinaemic response to glucose were both higher in untrained individuals (at $P < 0.05$ and $P < 0.02$, respectively). There were no differences between endurance and sprint runners. The results for insulin sensitivity, however, were quite variable: three indices showed that both groups of athletes were more insulin-sensitive than controls; three indicated that this was the case for endurance runners only; one indicated that this was the case for sprint runners only; and two showed that sprint runners were more insulin-sensitive than either sedentary individuals or endurance runners (all differences were significant at $P < 0.05$). Controlling for total body weight or lean mass did not effectively resolve this disagreement. Apparently, the various insulin sensitivity indices examined provided different quantitative and qualitative information, despite insulin action being greater in both groups of athletes relative to controls, as reflected by their similar glucose tolerance with lower insulin concentrations. We suggest, therefore, that the use and interpretation of such indices among physically active individuals be made with caution.

Keywords: *Athletes, endurance, glucose tolerance, insulin sensitivity, oral glucose tolerance test, sprint*

Introduction

The hyperinsulinaemic – euglycaemic clamp technique (DeFronzo, Tobin, & Andres, 1979) provides a ''gold standard'' for the quantitative assessment of insulin sensitivity in humans *in vivo*. This procedure involves a continuous intravenous infusion of insulin and a variable infusion of glucose to maintain euglycaemia. Under these steady-state conditions, the exogenous rate of glucose infusion equals glucose uptake rate by all tissues of the body, and is therefore a measure of whole-body sensitivity to exogenous insulin (DeFronzo *et al.*, 1979). The above points notwithstanding, this method cannot be readily applied in large-scale investigations or in clinical practice, because intravenous infusion of insulin, frequent blood sampling over 2 – 3 h, and continuous adjustment of glucose infusion are required for each of the paricipants studied. It is therefore a rather cumbersome and labour-intensive procedure, placing considerable demands on expertise and resources.

Many investigators have sought more practical methods to obtain an index of insulin sensitivity. Relevant attempts abound in the literature, and a number of such indices have been proposed. The most straightforward ones may comprise simple (Seltzer, Allen, Herron, & Brennan, 1967) or more complex (Katz *et al.*, 2000; Matthews *et al.*, 1985) mathematical combinations of glucose and insulin concentrations in the fasting state. Most insulin sensitivity indices, however, have been developed on

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the basis of the oral glucose tolerance test, which is the most commonly used technique for evaluating whole-body glucose tolerance *in vivo* (Avignon, Boegner, Mariano-Goulart, Colette, & Monnier, 1999; Gutt *et al.*, 2000; Matsuda & DeFronzo, 1999).

One point of concern is that all these indices have been designed and validated for use in subsets of the population, such as sedentary individuals with normal glucose tolerance, or insulin-resistant individuals, including diabetics and the obese (Avignon *et al.*, 1999; Gutt *et al.*, 2000; Katz *et al.*, 2000; Matsuda & DeFronzo, 1999; Matthews *et al.*, 1985). None of them, however, has been specifically developed for physically active persons. Hence their ability to quantify higher than normal insulin sensitivity values, or to discriminate between athletes and sedentary people in this respect, is unclear. In fact, there is some evidence that some commonly used indices may not accurately reflect changes in insulin sensitivity consequent to endurance exercise training (Duncan, Hutson, & Stacpoole, 2001, 2002).

The present study, therefore, was designed to examine whether available ''fasting'' and oral glucose tolerance test-derived insulin sensitivity indices could effectively distinguish between individuals with higher than normal insulin sensitivity, and whether they would all provide similar information in clinical practice. For this purpose, two groups of athletes (endurance and sprint runners) and a group of sedentary individuals received an oral glucose tolerance test. The glucose load was the same for all participants, rather than administered relative to body weight or lean mass, because all of the insulin sensitivity indices examined are based on the standard 75-g oral glucose tolerance test. Besides fasting and post-load glucose and insulin concentrations, nine of the most commonly used indices have been determined, and the agreement between them has been evaluated.

Methods

Participants

A total of 23 male volunteers aged 21 – 29 years were recruited. They consisted of endurance-trained runners (n = 8), sprint-trained runners (n = 8) and untrained individuals who served as controls (n = 7). All athletes competed at national and/or international level and had been training for at least the last 5 years before the studies were performed. The untrained participants were individuals of normal weight who did not engage in any consistent form of physical activity and had been sedentary for at least the previous 2 years. They all underwent an initial screening, including comprehensive medical history, physical examination, and standard blood chemistry and urine tests. They were in good health, did not smoke, and none of them were using any medication known to affect glucose metabolism. The study protocol was approved by the Human Subjects Committee of the University of Athens, Greece. The purpose, nature and possible risks associated with the experimental procedures were thoroughly explained to all participants, and written consent was obtained.

Body composition assessment

The participants were weighed on a medical beam scale (SECA, Hamburg, Germany), without shoes and in light clothing or underwear. Body weight was recorded to the nearest 0.1 kg. Standing height was measured without shoes to the nearest 0.5 cm using a portable wall-mounted stadiometer (SECA, Hamburg, Germany), using the stretch stature method. Body mass index (BMI, $kg \cdot m^{-2}$) was calculated as weight (kg) divided by height (m) squared. Soft tissue composition of the total body (fat and fat-free mass) was determined by dual-energy X-ray absorptiometry, using a DPX1 scanner (Lunar Corp., Madison, WI, USA) and Lunar software 1.3z. Scans were performed after 3 h abstinence from food and drink, with the participants lying comfortably wearing their clothes, but without shoes or any metal object.

Physical performance assessment

Anaerobic capacity was evaluated on the basis of peak power and mean power produced by the limb muscles during a 30 s Wingate test, on a mechanically braked cycle ergometer (Monark 864, Sweden). The resistance load was the same for all participants ($75\ g \cdot kg^{-1}$), and number of pedal revolutions was counted electronically (Biopac System TSD 120, USA). The test started after a 10 min warm-up.

Maximal oxygen consumption ($\dot{V}O_{2max}$) was determined during an incremental exercise test on a motor-driven treadmill (Runrace HC 1200, Technogym, Italy). For endurance runners, the treadmill speed was constant ($10\ km \cdot h^{-1}$) and the grade was increased by 2% every minute. For sprint runners and controls, the treadmill speed started at $5\ km \cdot h^{-1}$ and was increased by $1\ km \cdot h^{-1}$ each minute for the first 6 min; thereafter, the speed was kept constant and the grade was increased by 2% every minute. Mixed expiratory flow and gases were sampled for O_2 and CO_2 analysis (Medgraphics, CPX/D, USA). Maximal oxygen consumption was recorded when levelling off occurred.

Oral glucose tolerance test

The participants received a 75 g oral glucose tolerance test at approximately 08.00 h in the morning. They were studied after an overnight fast ($>$ 12 h) and having followed a standardized diet (250 – 300 $g \cdot day^{-1}$ carbohydrates) for the previous 4 days. They were also instructed to refrain from alcohol and caffeine consumption for 24 h, as well as from any form of physical activity in the 2 days before the studies were carried out. Compliance of athletes to exercise abstinence was confirmed by their coaches. A teflon indwelling catheter was inserted into an antecubital vein, and a baseline blood sample was obtained after 15 min of rest (t = 0 min). Then, each participant was given 75 g of anhydrous glucose (Sigma Diagnostics, St. Louis, MO, USA) dissolved in 400 ml water, and drank it within 5 min. Venous blood (6 ml) was drawn at 30 min intervals after the glucose load over a 2 h period (i.e. at 30, 60, 90 and 120 min of the oral glucose tolerance test). Plasma glucose was measured by the glucose oxidase method on an automated analyser (Falcor 300, Alcyon, France). Aliquots of plasma were frozen at $-30^{\circ}C$ until measurement of insulin by radioimmunoassay was done. The five samples for each participant were analysed in a single insulin assay to eliminate inter-assay variation.

Determination of insulin sensitivity

The Quantitative Insulin Sensitivity Check Index (QUICKI) developed by Katz *et al.* (2000) was calculated as: QUICKI = 1 / ($\log I_0 + \log G_0$), where G_0 ($mg \cdot dl^{-1}$) and I_0 ($\mu U \cdot ml^{-1}$) are the plasma glucose and insulin concentrations in the fasting state. Avignon *et al.* (1999) proposed three insulin sensitivity indices, including:

- one in the basal state: Sib = 10^8 / ($I_0 \times G_0 \times V_D$);
- one at the second hour of the oral glucose tolerance test: Si2h = 10^8 / ($I_2 \times G_2 \times V_D$); and
- one averaging Sib and Si2h after balancing Sib by a weighting coefficient: SiM = ($R \times$ Sib + Si2h) / 2;

where R = mean Si2h / mean Sib, G_0 ($mg \cdot dl^{-1}$) and I_0 ($\mu U \cdot ml^{-1}$) are the plasma glucose and insulin concentrations in the fasting state, G_2 ($mg \cdot dl^{-1}$) and I_2 ($\mu U \cdot ml^{-1}$) are the plasma glucose and insulin concentrations at 120 min of the oral glucose tolerance test, and V_D is an estimate of the apparent glucose distribution volume derived from single-compartmental modelling (V_D = 150 $ml \cdot kg^{-1}$ body weight).

The insulin sensitivity index developed by Matsuda and DeFronzo (1999) was determined by the equation: ISI = 10000 / square root of ($G_0 \times I_0 \times G \times I$), where G_0 ($mg \cdot dl^{-1}$) and I_0 ($\mu U \cdot ml^{-1}$) are the plasma glucose and insulin concentrations in the fasting state, and G ($mg \cdot dl^{-1}$) and I ($\mu U \cdot ml^{-1}$) are the mean plasma glucose and insulin concentrations during the oral glucose tolerance test.

Gutt *et al.* (2000) have developed an insulin sensitivity index based on fasting and 2 h post-load glucose and insulin values, that is ultimately derived from the formula: $ISI_{0,120} = m / (G \times \log I)$, where G ($mg \cdot dl^{-1}$) and I ($\mu U \cdot ml^{-1}$) are the mean glucose and insulin concentrations during the oral glucose tolerance test, and m represents an estimate of glucose uptake rate by the peripheral tissues. The above-mentioned six indices are positively related to insulin sensitivity.

Furthermore, the simplified formula of homeostatic model assessment (HOMA), introduced by Matthews *et al.* (1985), was used to calculate the HOMA value, which is inversely related to insulin sensitivity: HOMA = $I_0 \times G_0$ / 22.5, where G_0 ($mmol \cdot l^{-1}$) and I_0 ($\mu U \cdot ml^{-1}$) are the plasma glucose and insulin concentrations in the fasting state.

Finally, the product of the areas under the glucose and insulin response curves ($AUC_G \times AUC_I$), proposed by Levine and Haft (1970), as well as the ratio of insulin to glucose in the fasting state (I_0/G_0), referred to as the insulinogenic index by Seltzer *et al.* (1967), were also calculated. Like HOMA, these indices are inversely related to insulin sensitivity.

Statistical analysis

The results are presented as the mean $\pm$ standard error of the mean ($s_{\bar{x}}$) unless otherwise stated. Differences between the three groups were examined by one-way analysis of variance (ANOVA), followed by Tukey's Honestly Significant Difference (HSD) test for pairwise comparisons. Adjustment for the effect of other variables was made by analysis of covariance (ANCOVA). Glucose and insulin responses to the oral glucose tolerance test were examined by ANOVA for repeated measurements. When significant interactions between time and group emerged, *post-hoc* comparison of means was carried out by Tukey's HSD test. Relationships between selected variables were analysed by Pearson's correlation coefficients (r). Statistical significance was set at $P < 0.05$. All analyses were performed using SPSS 10.0.5 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Body composition and performance

There were several significant differences between the three groups in terms of body composition and physical performance characteristics (Table I). For instance, the untrained participants and sprint runners were heavier and had a higher body mass index than endurance runners. In absolute terms, both groups of athletes had less fat mass than the controls, while sprint runners had more lean mass than the other two groups. In relative terms, however, both endurance and sprint athletes had lower percent fat and higher percent lean mass than the untrained group. Differences in aerobic and anaerobic performance were as one would generally expect between the three groups (Table I). Relative peak power was higher in sprint runners than in endurance runners or controls, while both groups of athletes had greater mean power than sedentary individuals. A similar result was obtained for absolute $\dot{V}O_{2max}$, though relative $\dot{V}O_{2max}$ was higher in endurance runners than in sprint runners and controls.

Fasting glucose and insulin

Basal glucose concentrations were similar between endurance runners, sprint runners and sedentary individuals (4.8 ± 0.1, 4.6 ± 0.2 and 4.8 ± 0.1 $mmol \cdot l^{-1}$, respectively; $F = 0.8$, $P = 0.464$). On the other hand, fasting insulin concentrations differed ($F = 6.6$, $P = 0.006$). Basal plasma insulin was higher ($P < 0.05$) in the untrained group (6.9 ± 0.7 $\mu U \cdot ml^{-1}$) than in the endurance (4.1 ± 0.4 $\mu U \cdot ml^{-1}$) and sprint (4.8 ± 0.5 $\mu U \cdot ml^{-1}$) trained athletes.

Glycaemic and insulinaemic responses

Glucose and insulin responses to the oral glucose tolerance test are shown in Figure 1, while summary measures are given in Table II. All groups had adequate and similar glycaemic responses to the glucose load, as reflected by the almost superimposable plasma curves (Figure 1a). There was a main effect of time ($F = 23.5$, $P < 0.001$), but no interaction between time and group. The effect of group was not significant ($F = 1.0$, $P = 0.376$). Thus, average glucose concentrations during the oral glucose tolerance test were similar between endurance runners, sprint runners and sedentary individuals (5.6 ± 0.3, 5.1 ± 0.2 and 5.5 ± 0.4 $mmol \cdot l^{-1}$, respectively). Similarly, there were no significant group differences in total, incremental or fasting (i.e. total minus incremental) glucose AUC (Table II).

In contrast, untrained individuals had generally higher insulin concentrations after the glucose load (Figure 1b). There was a main effect of time ($F = 35.1$, $P < 0.001$), as well as an interaction between time and group ($P < 0.02$). The time course of plasma insulin was similar, but the effect of group was significant ($F = 7.9$, $P = 0.003$). Thus, sedentary individuals had a greater insulinaemic response ($P < 0.02$) than the two groups of athletes, with average insulin concentrations being higher in the controls (47.4 ± 6.7 $\mu U \cdot ml^{-1}$) than in the endurance (26.5 ± 3.5 $\mu U \cdot ml^{-1}$) or sprint (23.4 ± 3.2 $\mu U \cdot ml^{-1}$) runners. Accordingly, the untrained group had higher total ($P < 0.02$), incremental ($P < 0.03$) and fasting (at $P < 0.05$) insulin AUCs than the endurance or sprint runners (Table II).

Insulin sensitivity

The results for insulin sensitivity surrogate measures are given in Table III. Differences between groups varied, depending on the particular index used. For instance, SiM showed that endurance and sprint athletes had similarly higher insulin sensitivity compared with untrained individuals ($F = 9.0$, $P = 0.002$). Similarly, the untrained group had higher values for HOMA ($F = 6.1$, $P = 0.009$) and $AUC_G \times AUC_I$ ($F = 5.6$, $P = 0.012$) than both groups of runners. These two indices are inversely related to insulin sensitivity, meaning that sedentary individuals were more insulin-resistant than either endurance or sprint athletes. On the other hand, QUICKI ($F = 5.2$, $P = 0.016$), Sib ($F = 6.6$, $P = 0.006$) and I_0/G_0 ($F = 6.5$, $P = 0.007$) suggested that only endurance runners had greater insulin sensitivity (QUICKI and Sib) or lower insulin resistance (I_0/G_0) than untrained individuals. There were no significant differences, however, between sprint runners and the untrained group. The reverse was true when ISI was considered ($F = 4.7$, $P = 0.021$), with only sprint athletes having greater insulin sensitivity than sedentary individuals. Finally, Si2h ($F = 8.1$, $P = 0.003$) and $ISI_{0,120}$ ($F = 11.7$, $P < 0.001$) indicated that sprint runners had higher insulin sensitivity than either endurance runners or untrained individuals. Evidently, therefore, these nine insulin sensitivity indices were not directly interchangeable, since they provided quite different information.

This is also apparent from the correlation matrix shown in Table IV. ''Fasting'' indices (QUICKI, Sib, HOMA, I_0/G_0) correlated well with each other, while the same was observed among those indices utilizing glucose and insulin concentrations both before and during the oral glucose tolerance test (SiM, ISI, $ISI_{0,120}$, $AUC_G \times AUC_I$). The strength

Table 1. Body composition and physical performance characteristics (mean ± $s_{\bar{x}}$)

	Endurance (n = 8)	Sprint (n = 8)	Control (n = 7)
Age (years)	24.0 ± 1.1	23.8 ± 0.6	23.0 ± 0.4
Body mass (kg)	60.9 ± 0.9⋆†	78.9 ± 2.4	75.0 ± 3.6
Height (m)	1.71 ± 0.01†	1.80 ± 0.02	1.76 ± 0.03
BMI ($kg \cdot m^{-2}$)	20.8 ± 0.3⋆†	24.4 ± 0.4	24.3 ± 0.8
Fat mass (kg)	4.9 ± 0.8⋆	6.2 ± 0.6⋆	16.1 ± 2.7
Fat mass (%)	8.0 ± 1.3⋆	7.7 ± 0.5⋆	20.9 ± 2.8
Fat-free mass (kg)	56.0 ± 1.1†	72.7 ± 2.0⋆	58.9 ± 2.3
Fat-free mass (%)	92.0 ± 1.3⋆	92.3 ± 0.5⋆	79.1 ± 2.8
Peak power ($W \cdot kg^{-1}$)	11.4 ± 0.2†	13.5 ± 0.2⋆	11.8 ± 0.5
Mean power ($W \cdot kg^{-1}$)	8.6 ± 0.2⋆	9.2 ± 0.1⋆	7.6 ± 0.3
$\dot{V}O_{2max}$ ($l \cdot min^{-1}$)	4.41 ± 0.06⋆	4.02 ± 0.15⋆	3.33 ± 0.20
$\dot{V}O_{2max}$ ($ml \cdot kg^{-1} \cdot min^{-1}$)	72.6 ± 1.7⋆†	51.0 ± 1.0	44.8 ± 2.5

Note: BMI = body mass index; $\dot{V}O_{2max}$ = maximal oxygen consumption.
⋆ $P < 0.05$ vs. control. † $P < 0.05$ vs. sprint.

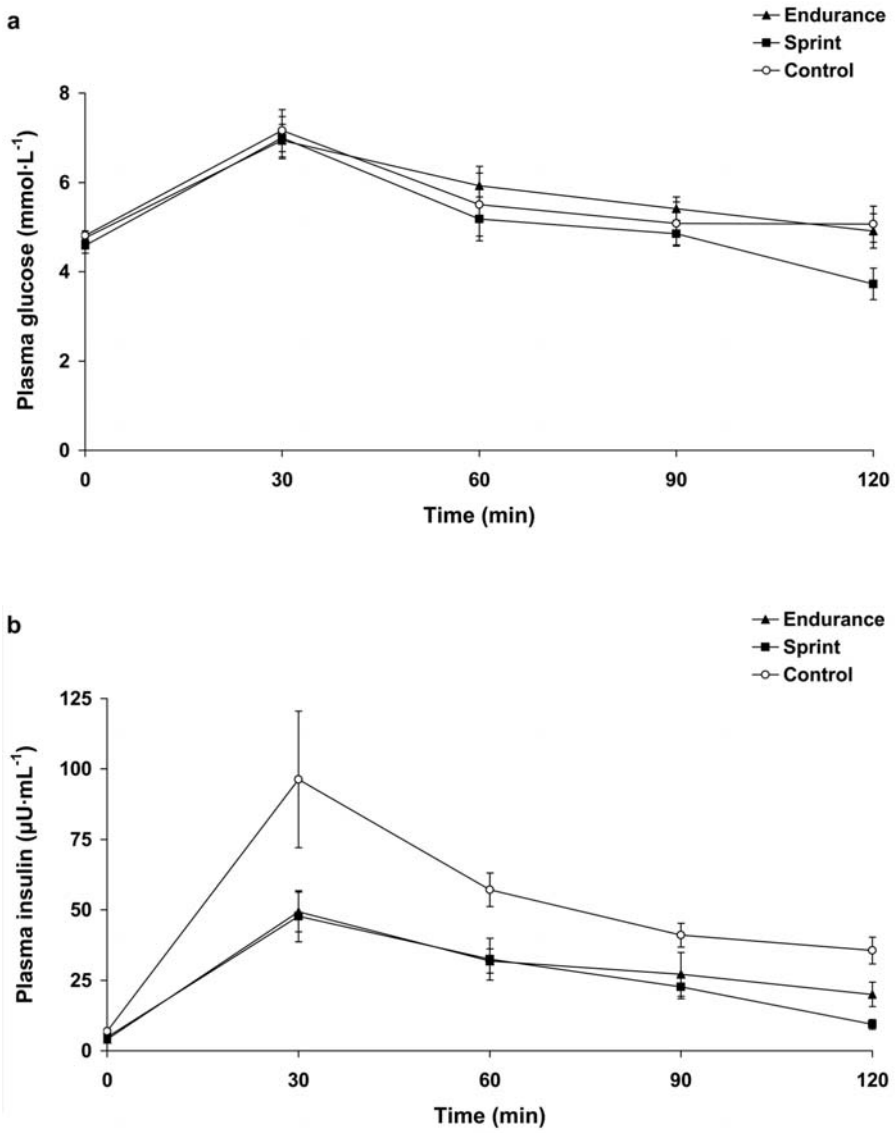

Figure 1. Glucose (a) and insulin (b) concentrations during the oral glucose tolerance test for endurance athletes (n = 8), sprint athletes (n = 8) and controls (n = 7) (mean ± $s_{\bar{x}}$) Untrained individuals had a greater insulinaemic response than the two groups of athletes ($P < 0.02$).

of association between the ''fasting'' and ''post-load'' indices, however, varied. Overall, SiM, ISI and $AUC_G \times AUC_I$ showed a good correlation with ''fasting'' indices, but Si2h and $ISI_{0,120}$ did not. In general, the poorest agreement was obtained for Si2h, which incorporates only the 2 h post-load values. At the other end, SiM correlated well with the remaining eight indices, ISI and $AUC_G \times AUC_I$ correlated with seven, QUICKI, Sib and HOMA with six, and $ISI_{0,120}$ with four.

Taking into account the group differences in body weight and composition (Table I), the same glucose load (75 g) would invariably translate into a different load per kilogram total body weight or per kilogram fat-free mass for each group. In particular, relative to total body weight, the glucose load was higher in endurance athletes than in sprint athletes or controls (1.23 ± 0.05, 0.96 ± 0.09 and 1.01 ± 0.12 g·kg^{-1}, respectively; $F = 21.6$, $P < 0.001$); in contrast, relative to lean mass, it was lower in sprint runners than in endurance runners or controls (1.04 ± 0.09, 1.34 ± 0.07 and 1.28 ± 0.12 g·kg^{-1}, respectively; $F = 23.8$, $P < 0.001$). Because these differences could potentially be responsible for the differences observed in insulin sensitivity indices, the latter were re-examined by ANCOVA, after controlling for either total weight or lean mass.

When adjustments were made for total body weight, there were no group differences in Sib ($P = 0.091$), whereas the remaining indices were uniformly in agreement in that sprint runners had higher insulin sensitivity or lower insulin resistance compared with sedentary individuals ($P < 0.05$). None of these eight indices revealed any significant differences between sprint and endurance athletes, or between endurance athletes and controls ($P > 0.05$). On the other hand, when adjusting for lean mass, there were no group differences in Si2h ($P = 0.102$), while six indices showed that endurance runners were more insulin-sensitive (QUICKI, Sib and ISI) or less insulin-resistant (HOMA, $AUC_G \times AUC_I$ and I_0/G_0) than untrained individuals ($P < 0.05$). Again, none of these six indices revealed any significant differences between endurance and sprint runners, or between sprint runners and controls ($P > 0.05$). One index ($ISI_{0,120}$) still indicated that sprint athletes had greater insulin sensitivity than sedentary individuals, with no significant differences between the two groups of athletes or between endurance athletes and controls.

Table 2. Glycaemic and insulinaemic responses to the oral glucose tolerance test (mean $\pm s_{\bar{x}}$)

	Endurance	Sprint	Control
Glucose			
Total AUC (mmol·h·l^{-1})	11.6 ± 0.6	10.6 ± 0.5	11.3 ± 0.8
Fasting AUC (mmol·h·l^{-1})	9.5 ± 0.2	9.2 ± 0.3	9.6 ± 0.2
Incremental AUC (mmol·h·l^{-1})	2.0 ± 0.6	1.4 ± 0.5	1.7 ± 0.7
Insulin			
Total AUC (μU·h·ml^{-1})	60.1 ± 8.0*	55.9 ± 8.0*	107.8 ± 16.3
Fasting AUC (μU·h·ml^{-1})	8.2 ± 0.8*	9.6 ± 1.1*	13.7 ± 1.5
Incremental AUC (μU·h·ml^{-1})	52.0 ± 7.9*	46.3 ± 7.3*	94.1 ± 14.9

Note: AUC = area under the curve.
* $P < 0.05$ vs. control.

Table 3. Oral glucose tolerance test-derived insulin sensitivity indices (mean $\pm s_{\bar{x}}$)

	Endurance	Sprint	Control
QUICKI	0.397 ± 0.008*	0.390 ± 0.009	0.363 ± 0.005
Sib	34.3 ± 4.5*	23.9 ± 3.1	16.4 ± 2.1
Si2h	8.8 ± 1.7†	18.3 ± 3.8*	3.6 ± 1.0
SiM	16.1 ± 1.8*	17.3 ± 2.1*	7.4 ± 1.1
ISI	11.3 ± 1.3	12.5 ± 1.9*	6.5 ± 0.7
$ISI_{0,120}$	0.729 ± 0.070†	1.103 ± 0.106*	0.556 ± 0.053
HOMA	0.872 ± 0.095*	0.986 ± 0.132*	1.457 ± 0.142
$AUC_G \times AUC_I$	708 ± 122*	598 ± 93*	1202 ± 181
I_0/G_0	0.849 ± 0.064*	1.039 ± 0.100	1.438 ± 0.174

Note: See Methods section for details on calculations and units of measurement. The first six indices are positively related to insulin sensitivity, while the last three exhibit a negative relationship.
* $P < 0.05$ vs. control. † $P < 0.05$ vs. sprint.

Table 4. Correlation matrix between the various oral glucose tolerance test-derived insulin sensitivity indices

	QUICKI	Sib	Si2h	SiM	ISI	$ISI_{0,120}$	HOMA	$AUC_G \times AUC_I$
Sib	0.933**							
Si2h	0.258	0.097						
SiM	0.771**	0.696**	0.782**					
ISI	0.864**	0.712**	0.356	0.702**				
$ISI_{0,120}$	0.390	0.191	0.952**	0.806**	0.537**			
HOMA	−0.960**	−0.863**	−0.299	−0.757**	−0.817**	−0.389		
$AUC_G \times AUC_I$	−0.649**	−0.481*	−0.409	−0.596**	−0.805**	−0.509*	0.726**	
I_0/G_0	−0.835**	−0.781**	−0.221	−0.648**	−0.660**	−0.251	0.917**	0.741**

Note: Pearson correlation coefficients (r) are shown for $n = 23$.
* $P < 0.05$. ** $P < 0.01$.

Finally, SiM favoured both groups of athletes relative to untrained individuals ($P < 0.025$). Apparently, therefore, controlling for total body weight or lean mass had a diametrically opposite effect on the results, but neither adjustment quite effectively resolved the disagreement between available indices.

Discussion

The present study used a cross-sectional design to determine whether available ''fasting'' and oral glucose tolerance test-derived insulin sensitivity indices could effectively reflect the differences in glucose tolerance and insulin sensitivity between endurance runners, sprint runners and sedentary individuals. These two groups of athletes were selected as the training mode of endurance runners mainly involves aerobic exercise, while that of sprint runners mainly involves anaerobic or strength exercise. In this respect, our results add to the current literature on the comparative effects of aerobic and anaerobic exercise on glucose tolerance and insulin sensitivity.

There is a wealth of evidence showing that regular endurance exercise increases insulin sensitivity and improves glucose homeostasis (Borghouts & Keizer, 2000; Henriksen, 2002), and a number of putative cellular mechanisms underlying these effects have been highlighted (Goodyear & Kahn, 1998; Wojtaszewski *et al.*, 2003). Cross-sectional studies have shown that endurance athletes have lower basal insulin concentrations (Lohmann, Liebold, Heilmann, Senger, & Pohl, 1978), and significantly diminished insulin responses either to an oral glucose load (Bjorntorp *et al.*, 1972) or to glucose infusion (King *et al.*, 1987; Lohmann *et al.*, 1978). Similarly, in the present investigation, fasting insulin and the insulinaemic response to oral glucose were approximately 30–40% lower in endurance runners than in sedentary controls. That is, endurance runners were able to maintain normal glucose tolerance with lower insulin levels, indicative of greater insulin action.

The oral glucose tolerance test results for our sprint runners were qualitatively and quantitatively similar to those for the endurance-trained runners, demonstrating a similarly enhanced insulin action compared with sedentary individuals. The results of previous research on the effects of anaerobic or strength training on insulin sensitivity, however, have been rather equivocal. Early studies using the euglycaemic clamp technique reported that glucose disposal was virtually identical in weightlifters and endurance runners when calculated per kilogram of total body weight, and approximately 40–45% higher than in controls; when calculated per kilogram of lean mass, however, only the runners had a higher than normal rate of glucose metabolism (Yki-Jarvinen & Koivisto, 1983). In a recent study, Takala, Nuutila, Knuuti, Luotolahti and Yki-Jarvinen (1999) reported no differences in whole-body and skeletal muscle glucose uptake between weightlifters and sedentary individuals. Both at the level of the whole body and skeletal muscle, endurance-trained athletes had more than twofold higher glucose uptake rates (Takala *et al.*, 1999).

On the other hand, in cross-sectional studies using the intravenous glucose tolerance test, strength-trained athletes have been reported to have higher insulin sensitivity and similar (Gippini *et al.*, 2002) or greater (Fujitani *et al.*, 1998) glucose effectiveness compared with untrained individuals. Furthermore, longitudinal studies involving training interventions have provided considerable evidence that resistance exercise increases whole-body insulin sensitivity in healthy young women (Poehlman, Dvorak, DeNino, Brochu, & Ades, 2000) and men (Holten *et al.*, 2004), in middle-aged (Miller *et al.*, 1994) and older (Zachwieja, Toffolo, Cobelli, Bier, & Yarasheski, 1996) men, as well as in obese (Ryan, Pratley, Goldberg, & Elahi, 1996), diabetic (Eriksson *et al.*, 1998; Fenicchia *et al.*, 2004; Ishii, Yamakita, Sato, Tanaka, & Fujii, 1998) and hypertensive (Reynolds, Supiano, & Dengel, 2004) patients. The increased

insulin sensitivity following strength training has been attributed either to a reduction in fat mass (Gippini *et al.*, 2002) or to an augmentation of lean muscle mass (Poehlman *et al.*, 2000), although substantial improvements after resistance training can be brought about with no accompanying changes in body composition (Ishii *et al.*, 1998; Ryan *et al.*, 1996).

A recent study shed some light on the putative cellular mechanisms underpinning the effects of resistance exercise on skeletal muscle glucose homeostasis. Unilateral strength training was shown to result in increased insulin-mediated glucose uptake, increased protein content of GLUT4, insulin receptor, protein kinase B and glycogen synthase, and increased glycogen synthase total activity in the trained leg of healthy young adult men and type II diabetics (Holten *et al.*, 2004). This led the authors to conclude that adaptation to resistance exercise is attributable to local contraction-mediated mechanisms involving key proteins in the insulin signalling cascade, rather than to body composition changes (Holten *et al.*, 2004). Regardless of the underlying mechanism(s), there seems to be good evidence that at least some types of anaerobic exercise may improve insulin sensitivity. The results of the present study are in accord with this notion.

Since fasting as well as post-load glucose concentrations were similar in endurance runners, sprint runners and controls, while fasting insulin and the insulinaemic response to oral glucose were both higher in untrained individuals (with no differences between endurance and sprint runners), one would expect all insulin sensitivity indices to provide similar information, and show that both groups of athletes had equally higher insulin sensitivity or lower insulin resistance relative to controls. However, this was not the case. In fact, only the ''fasting'' HOMA and the ''post-load'' SiM and $AUC_G \times AUC_I$ indices agreed in that both endurance and sprint runners had similarly greater insulin sensitivity compared with untrained individuals. Other indices showed that only endurance (QUICKI, Sib and I_0/G_0) or only sprint (ISI) athletes were more insulin-sensitive than sedentary individuals, while a couple of them (Si2h and $ISI_{0,120}$) demonstrated a difference between the two groups of athletes as well, with sprint runners having greater insulin sensitivity not only relative to controls but also relative to endurance runners. It is useful to note that the values obtained for our untrained group were in the range reported previously for healthy, non-obese and non-diabetic persons (Avignon *et al.*, 1999; Gutt *et al.*, 2000; Katz *et al.*, 2000; Matsuda & DeFronzo, 1999; Matthews *et al.*, 1985).

Therefore, the insulin sensitivity indices studied showed a variable efficiency in discriminating between athletes and untrained individuals, as well as between endurance and sprint runners, if indeed the latter two groups differed from each other. This would certainly be of clinical relevance when attempting to form conclusions or when comparing the results from different studies, based on information solely provided by these surrogate measures of insulin sensitivity. To examine whether this disagreement could possibly result from differences in body weight or composition between the participants, the analysis was repeated after controlling for total body weight or lean mass. This procedure reduced but did not remove the observed differences, and certainly did not lead to uniform agreement between the various indices. Needless to say, these indices were originally developed irrespective of differences in body weight or composition, and are targeted for use among individuals with a wide range of body weights and degrees of fatness/leanness. Most probably, therefore, the ability of each index to correctly identify existing differences, or to incorrectly reveal non-existing ones, is inherent to its calculation process.

Because this study did not employ a reference method against which these indices could be evaluated, we cannot point out which index more closely reflected ''true'' differences between groups, nor can we conclude which is the more suitable when it comes to comparing individuals of different background training and fitness status. Nevertheless, our results do suggest that not all indices are directly interchangeable, as they do not provide the same quantitative and qualitative information. Caution in the use and interpretation of such surrogate measures of insulin sensitivity among physically active persons, therefore, is warranted.

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