Determination of the Lumped Constant for [^{18}F]Fluorodeoxyglucose in Human Skeletal Muscle

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Quantitative [^{18}F]fluorodeoxyglucose (FDG) PET has considerable potential for the study of the physiology of skeletal muscle glucose metabolism and for the assessment of perturbations associated with insulin resistance in skeletal muscle. This application of FDG PET imaging depends in part on the determination of the analog effects of FDG relative to true glucose with respect to skeletal muscle. Deoxyglucose has a higher affinity for transporters than glucose and a lower affinity for hexokinase. This study was undertaken to assess the lumped constant (LC) for skeletal muscle, determined empirically as the quotient of FDG metabolism to that of [^{3}H]glucose ([^{3}H]G), and to assess whether the LC is affected by insulin, which is the principal hormonal regulator of glucose metabolism in muscle. **Methods:** Seventeen healthy lean volunteers were randomly assigned and were studied at insulin infusion rates of 0, 20, 40 and 120 mU/min/m^2 body surface area. After attaining steady-state euglycemic conditions, injections of FDG and [^{3}H]G were given, and the fractional extraction (E) for each compound across the leg was measured by arterial and venous sampling for 90 min. The LC was calculated as the ratio of the respective fractional extractions ($LC = E_{FDG}/E_{[^3H]G}$). **Results:** During fasting conditions (i.e., absence of insulin infusion), the LC for skeletal muscle was slightly greater than 1. Insulin had a robust effect to increase fractional extractions of both FDG and [^{3}H]G. The effect was symmetrical for the two compounds, and, hence, the LC did not change significantly in response to progressive insulin stimulation. The mean value of the LC across insulin doses for human skeletal muscle was 1.23 ± 0.05. **Conclusion:** Direct comparison of [^{3}H]G and FDG metabolism during insulin-stimulated conditions, across the in vivo tissue bed of skeletal muscle in the leg with both tracers given in an identical manner, yielded an LC value of 1.2, indicating that there was modest preferential uptake of FDG and that insulin did not alter the LC in skeletal muscle.

Key Words: lumped constant; insulin sensitivity; skeletal muscle; PET; deoxyglucose; [^{18}F]fluorodeoxyglucose

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The study of regional metabolism of the glucose analog [^{18}F]fluorodeoxyglucose (FDG) in brain (*1,2*) and heart (*3,4*) is a valuable application of PET. More recently, PET imaging of FDG has been used to study insulin-regulated glucose metabolism within skeletal muscle (*3,5–8*). In healthy individuals, skeletal muscle accounts for a considerable portion of glucose metabolism during insulin-stimulated conditions, whereas in insulin resistance, which is prevalent in disorders such as type 2 diabetes mellitus and obesity, rates of skeletal muscle glucose metabolism are substantially reduced (*9–12*). Accordingly, PET imaging of FDG may have considerable value for noninvasive, region-specific investigation of insulin-stimulated glucose metabolism in skeletal muscle in these disorders. Several important observations concerning glucose and fatty acid substrate competition (*13*), the relation of blood flow to glucose metabolism (*8,14*) and the kinetics of glucose transport and phosphorylation (*5*) have been made from applications of this methodology to skeletal muscle. However, FDG is an analog of glucose. Compared to glucose, FDG has a higher affinity for glucose transporters and a lower affinity for hexokinase (*15,16*). These differences could lead to differences in the uptake and phosphorylation of FDG relative to that of actual glucose. These differences are expressed in the lumped constant (LC), defined as the ratio of FDG metabolism to that of glucose (*17–19*).

In the brain, glucose metabolism is not regulated by insulin (*20*) and rates of FDG uptake do not change in response to insulin (*21*). However, hypoglycemia can dramatically increase the LC in the brain (*22,23*), because limited glucose availability during hypoglycemia makes transport a rate-limiting step. In cardiac muscle, several studies indicate that insulin reduces the LC (*4,24*). These findings have been interpreted to signify that insulin shifts the locus of control of glucose metabolism from transport to phosphorylation (*24*). Russell et al. (*25*) postulate that the effect of insulin on the LC is due to insulin's effect in further reducing the affinity of deoxyglucose relative to glucose for hexokinase. To our knowledge, there are few data concerning the LC in skeletal muscle. Nuutila et al. (*13*) compared rates of FDG utilization in arm muscle with arteriovenous differences of glucose across the forearm during insulin-stimulated conditions and estimated that the LC had

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a value of approximately 1; similar values have been reported in animal studies (*26–28*).

This study was undertaken to measure the effect of insulin on the LC for FDG within human skeletal muscle. The LC was determined at four rates of insulin infusion: 0, 20, 40 and 120 mU/min/m^2 body surface area. The last rate achieved insulin concentrations substantially above the physiologic range, and the two middle rates achieved insulin levels consistent with those attained during prandial conditions, thus within the physiologic range. To determine the LC, we directly compared the arteriovenous fractional extraction of FDG across the leg with that of [^{3}H]glucose ([^{3}H]G).

MATERIALS AND METHODS

Participants

Seventeen lean, healthy and glucose-tolerant participants (14 men, 3 women) were recruited by advertisement and were randomly assigned to euglycemic insulin infusion studies (4 participants per group) at rates of 0, 20, 40 and 120 mU/min/m^2. Characteristics of study participants are shown in Table 1. The mean age of the participants was 35 ± 2 y, and mean body mass index was 24.6 ± 0.6 kg/m^2. Fasting plasma insulin was 35 ± 7 pmol/L. These characteristics did not differ significantly across groups. Before participating in this study, each volunteer had a medical examination. Participants were of stable weight, were in good general health and had normal values for hematologic, renal, thyroid and hepatic function. The investigation was approved by the University of Pittsburgh Institutional Review Board and all volunteers gave informed written consent.

Study Design

Participants were admitted to the University of Pittsburgh General Clinical Research Center on the evening before the studies to standardize activity and the length of fast. Participants had been instructed to ingest a diet containing at least 200 g carbohydrate for at least 3 d before the study and to refrain from exercise on the day before the study. On the evening of admission, participants received a dinner of standardized composition (10 kcal/kg; 50% carbohydrate, 30% fat and 20% protein) and then fasted overnight and until completion of the study.

Arteriovenous balance studies of FDG uptake were performed at the University of Pittsburgh PET Center. On the morning of a study, at approximately 7 AM, an intravenous catheter was placed in an antecubital vein for infusion of insulin and glucose and for later injection of FDG and [^{3}H]G. For blood sampling, catheters were placed in a radial artery and in a femoral vein. After basal measurements of arterial insulin and arterial and femoral venous glucose, insulin infusions (or saline for 0 dose of insulin) were begun at 0 (saline), 20, 40 or 120 mU/min/m^2 and were continued for 270 min. During insulin infusions, arterial glucose was measured at 5-min intervals with a YSI Glucose Analyzer (Yellow Springs Instruments, Yellow Springs, OH), and an adjustable infusion of 20% dextrose was given to maintain euglycemia. Euglycemic insulin infusions were maintained for 3 h before injection of FDG, so that steady-state metabolic conditions were attained. Blood flow to the leg was measured using venous occlusion strain-gauge plethysmography. Injections of 148 MBq FDG, synthesized using a modification of the Hamacher method (*29*), and 0.75 MBq [2-^{3}H]G (high-performance liquid chromatography purified; New England Nuclear, Boston, MA), dissolved in 5 mL normal saline, were then administered through an antecubital venous catheter. The label is lost as ^3H_2O at the hexose isomerase step, which immediately follows glucose phosphorylation, making it unlikely that subsequent steps of metabolism would influence the uptake of [2-^{3}H]G (*30*). Sampling of arterial and femoral venous blood for plasma FDG and [2-^{3}H]G radioactivity was obtained at 6-s intervals for 2 min, 20-s intervals for 1 min, 30-s intervals for 1 min and at 5, 7, 10, 15, 20 and 30 min, then every 15 min until 90-min postinjection of FDG and [2-^{3}H]G. Exact timing of each sample was recorded. Blood was centrifuged, and radioactivity in 0.1 mL plasma was counted using a Packard Canbarra well counter (Packard Instrument Co., Downers Grove, IL). For determination of [2-^{3}H]G, these plasma samples were stored, frozen at −80°C, deproteinized, evaporated to dryness to remove tritiated water, reconstituted (scintillation liquid) and counted with liquid scintillation, as previously described (*31*). Representative curves of FDG and [2-^{3}H]G plasma radioactivity in the artery and femoral veins are shown in Figure 1. Plasma insulin was measured by radioimmunoassay.

TABLE 1
Clinical Characteristics

Insulin infusion rate*	Sex		Age (y)	Body mass index (kg/m^2)
	Male	Female		
0	3	1	35 ± 2	25.3 ± 1.1
20	4	0	32 ± 3	23.2 ± 0.8
40	4	1	38 ± 2	24.6 ± 0.8
120	4	0	37 ± 2	25.4 ± 0.7

*Units are mU/min/m^2 body surface area.
Values are mean ± SEM.

Measurement of FDG Uptake with PET

Participants were positioned in the PET scanner during the last 90 min of the insulin infusion so that the midthigh corresponded to the midpoint axial field of view. Before each emission scan, 20-min transmission scanning was performed using rotating rods of ^{68}Ge/^{68}Ga to correct the emission data for photon attenuation. An intravenous injection of 148 MBq FDG, synthesized using a modification of the Hamacher method (*29*), was injected, and 90-min dynamic PET was simultaneously initiated (19 frames: 4 scans at 30 s each, 4 scans at 2 min each, 6 scans at 5 min each and 5 scans at 10 min each). The PET scans were acquired in two-dimensional and three-dimensional imaging modes using a Siemens CTI 951 R/31 (n = 10) scanner and an ECAT ART scanner (Siemens, Chicago, IL) (n = 8), respectively. The imaging characteristics of the two scanners were comparable. The Siemens 951R/31 scanner acquired 31 imaging planes simultaneously (two-dimensional in-plane resolution 6.0 mm full width at half maximum (FWHM) [ramp filter]; axial slice width 3.4 mm), whereas 47 imaging planes were acquired using the ECAT ART scanner (three-dimensional in-plane resolution 6.0 mm FWHM [ramp filter]; axial slice width 3.4 mm). The scatter fraction was low for the two-dimensional Siemens CTI 951 (13%) (*32*) and no scatter correction was performed after conventional methods. The three-dimensional ART had a scatter fraction that was approximately 37% (*33*); these emission data were corrected for scattered photons using a model-based correction method (*34*). After correc-

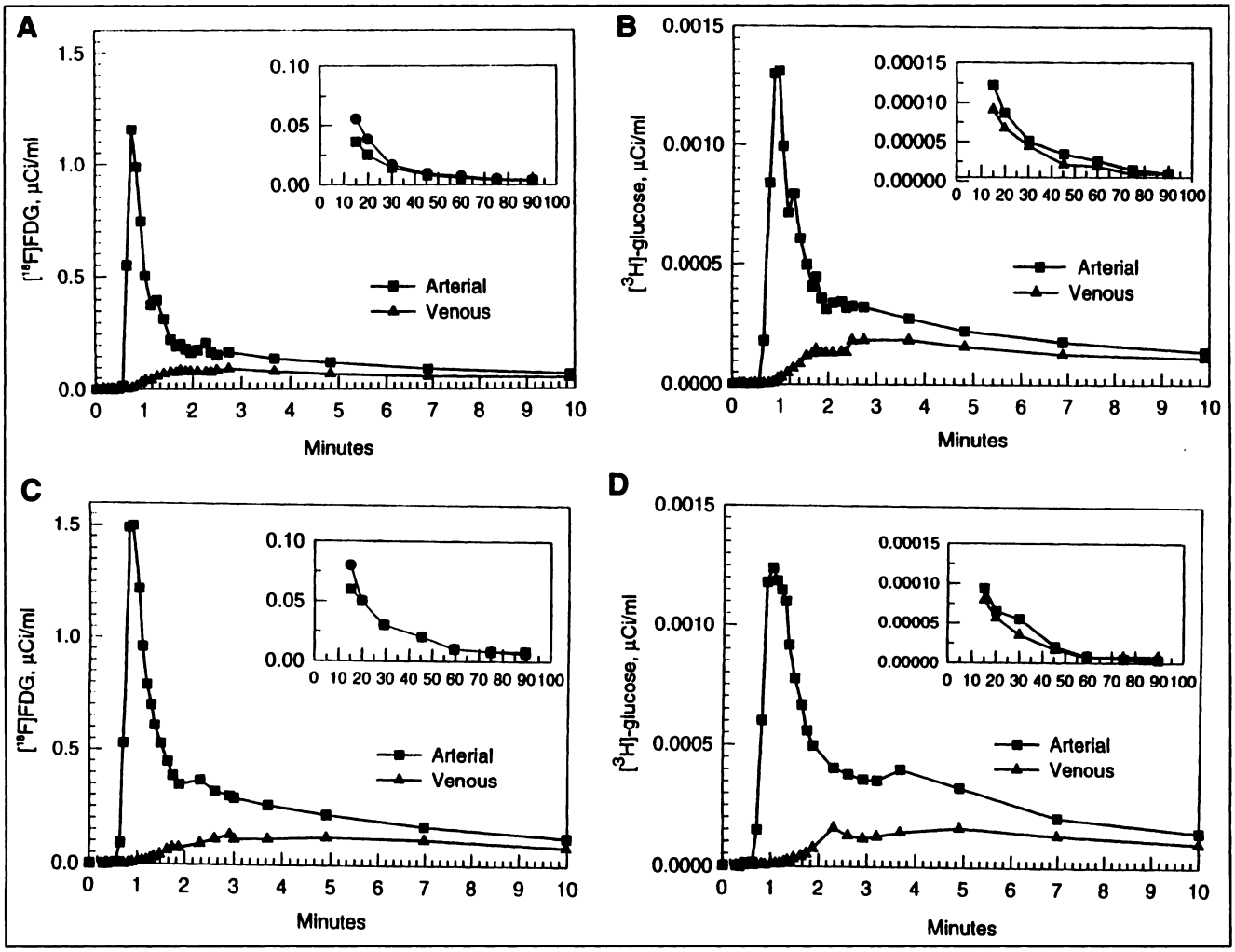

FIGURE 1. Representative arterial and femoral venous plasma time-activity curves for [^{18}F]fluorodexoyglucose (FDG) and [^{3}H]G. FDG at insulin infusion of 20 mU/min/m^2 (A), [^{3}H]G at insulin infusion of 20 mU/min/m^2 (B), FDG at insulin infusion of 120 mU/min/m^2 (C) and [^{3}H]G at insulin infusion of 20 mU/min/m^2 (D). Data from later time points are shown in inset graph.

tion of the PET data for radioactive decay, the tissue time-activity data were converted to units of radioactivity concentration (μCi/mL) using an empiric phantom-based calibration factor (μCi/mL/PET counts per pixel). Sampling of arterial blood for plasma FDG radioactivity began simultaneously with PET scanning as previously described (*5*). Graphical analysis, using the arterial data as an input function, was applied to the emission data using tissue FDG activity from 30 through 90 min postinjection to determine overall FDG uptake (K) (*35*).

Calculations

The non–steady-state fractional extractions of FDG and [^{3}H]G were determined based on the respective arterial (C_A) and femoral venous (C_V) plasma radioactivity concentration differences over the study period (*36*). The fractional extractions (E) were calculated over the study duration (T), such that:

$$E_{FDG} \text{ or } E_{[^3H]G} = \sum_{i=1}^{T} (C_A - C_V) \Big/ \sum_{i=1}^{T} C_A.$$

The LC was determined as the ratio between E_{FDG} and $E_{[^3H]G}$. During steady-state conditions, the rate of glucose uptake across the leg was calculated as the product of arteriovenous differences for glucose and blood flow according to the Fick principle. The mean of five determinations of blood flow and the mean of eight determinations of arteriovenous differences for glucose were used in the calculation. The LC was used to extrapolate the metabolic rate of glucose uptake (MRGlc) in skeletal muscle from FDG uptake, using the formula: MRGlc = (arterial glucose × K)/LC.

Statistics

Data are expressed as mean ± SEM. Analysis of variance (ANOVA) was used to examine the effects of insulin dose on the various metabolic parameters (e.g., leg glucose uptake). Correlations and linear regression were used to examine associations between variables. $P < 0.05$ was considered significant.

RESULTS

Arteriovenous Insulin-Stimulated Glucose Uptake Across the Leg

Fasting rates of glucose uptake across the leg (LGU) were similar across groups (overall mean value of 0.04 ± 0.01 mg/min/100 mL leg tissue), whereas rates of LGU during

insulin infusions differed across groups ($P < 0.001$) in relation to increasing rates of insulin infusion as shown in Table 2. Euglycemia was maintained during insulin infusions, and, as per study design, steady-state levels of plasma insulin differed significantly, as also shown in Table 2. The rate of steady-state systemic glucose infusion needed to maintain euglycemia also differed across groups, in relation to insulin infusion rates ($P < 0.01$), and were correlated with respective values for LGU ($r = 0.68$, $P < 0.01$).

Determination of Lumped Constant

Table 3 shows the fractional extractions of glucose, FDG and [^{3}H]G across the leg during a 90-min period of steady-state insulin-stimulated metabolism. The arteriovenous fractional extraction of glucose increased in response to insulin dose ($P < 0.001$). A similar effect of insulin to increased fractional extraction of FDG ($P = 0.004$) and [^{3}H]G ($P = 0.02$) was observed. Data on the fractional extraction of [^{3}H]G from 1 individual appeared to represent an outlier value and, excluding this data point, the statistical significance of the effect of insulin to increase the fractional extraction of [^{3}H]G was $P = 0.001$. The correlation between the fractional extractions of glucose and FDG was 0.89 ($P < 0.001$), and the correlation between the fractional extractions of glucose and [^{3}H]G was 0.88 ($P < 0.001$), even including data from the potential outlier with low fractional extraction of [^{3}H]G.

Values for the LC, calculated from the relation of the fractional extraction of FDG across the leg to that of [^{3}H]G, are shown in Table 3. The mean for all values, across the four rates of insulin infusion, was 1.38 ± 0.16. If the data of the 1 participant described earlier, who manifested an apparent outlier value of 4.2 for the LC, is excluded, the mean value was 1.23 ± 0.05. Values for the LC did not change in relation to insulin infusion rate by ANOVA ($P = 0.33$). A regression plot of fractional extraction of FDG and fractional extraction of [^{3}H]G is shown in Figure 2. A highly significant correlation was observed ($r = 0.95$, $P < 0.001$), and the slope of this plot represents the value for the LC and is 1.22 ± 0.08 ($P < 0.001$), when forcing the y intercept through 0. This value is nearly identical to the arithmetic mean. A comparable value was obtained when the intercept was not forced through 0 (slope = 1.10 ± 0.16, $P < 0.001$; intercept 0.06 ± 0.05, $P = 0.85$), and exclusion of the data of the one apparent outlier had minimal effect on these results (slope = 1.20 ± 0.04, $P < 0.001$; nonzero intercept: slope = 1.21 ± 0.09, $P < 0.001$; intercept −0.01 ± 0.03, $P = 0.85$).

To examine whether the duration over which the arteriovenous differences were determined affected the values for the LC, we also conducted the aforementioned analyses using fractional extraction values from 0–60 min. This had essentially no effect on fractional extraction values for FDG and [^{3}H]G or for calculation of the LC. The correlation between values measured at 0–90 min versus those measured at 0–60 min was 0.99 for fractional extraction of FDG, 0.99 for fractional extraction of [^{3}H]G and 0.98 for the LC.

Extrapolating Fluorodeoxyglucose to Glucose Metabolism Using Lumped Constant

Examples of a basal and insulin-stimulated PET scan and the corresponding model fit are shown in Figure 3. Compared to the basal state, insulin stimulated a nearly 10-fold increase in FDG uptake (0.14 ± 0.03 mg/100 mL/min versus 1.29 ± 0.24 mg/100 mL/min, respectively, $P < 0.001$). LGU and the MRGlc (determined using the arterial glucose level, FDG uptake and the calculated LC) were highly correlated ($r = 0.85$, $P < 0.001$).

DISCUSSION

PET imaging of the uptake of the glucose analog FDG within skeletal muscle has been used by several groups of investigators to examine insulin action in muscle and to investigate insulin resistance of skeletal muscle in diabetes mellitus, obesity and other disorders (*3,5–8,14,37*). The regional specificity of glucose metabolism that can be obtained by PET imaging of FDG can be of great potential value for the study of insulin resistance in skeletal muscle. However, to properly interpret findings using FDG, it is necessary to understand both the potential analog effects of FDG in skeletal muscle and the potential effect of insulin on analog effects of FDG. Deoxyglucose has a higher affinity for membrane transporters than does actual glucose, yet it has a lower affinity for hexokinase (*15,16*). Accordingly, FDG may have differing quantitative uptake in skeletal

TABLE 2
Insulin-Stimulated Glucose Metabolism

Insulin dose* (mU/min/m^2 body surface area)	Plasma insulin (pmol)	Arterial glucose (mmol)	Systemic glucose infusion (μmol/min/kg)	Leg glucose uptake (mg/min/100 mL leg tissue)	Leg blood flow* (mL/min/100 mL leg tissue)
0	48 ± 12	4.9 ± 0.1	0 ± 0	0.24 ± 0.06	2.1 ± 0.4
20	179 ± 17	4.7 ± 0.12	25.6 ± 7.5	4.28 ± 1.53	3.7 ± 0.7
40	448 ± 13	5.3 ± 0.3	46.8 ± 4.3	4.85 ± 1.54	2.7 ± 0.2
120	1270 ± 63*	5.1 ± 0.1	46.0 ± 2.3*	6.30 ± 0.77*	2.9 ± 0.3

*$P < 0.01$, analysis of variance for significant change with respect to insulin dose.
Values are mean ± SEM.

TABLE 3
Fractional Extraction of Glucose, [^{3}H]G and FDG and Calculated LC Across Insulin Doses over 90 Minutes

Insulin dose (mU/min/m^2 body surface area)	n	Glucose (%)*	[^{3}H]G (%)*	FDG (%)*	LC (FDG/[^{3}H]G)
0	4	2.4 ± 0.3	10.5 ± 4.3	11.4 ± 4.4	1.04 ± 0.28
20	4	22.7 ± 5.6	31.1 ± 3.1	34.6 ± 4.5	1.11 ± 0.07
40	5	32.1 ± 7.5	31.8 ± 7.8	48.8 ± 7.8	1.90 ± 0.56
	4†	35.7 ± 8.5	37.1 ± 7.5	49.5 ± 10.0	1.34 ± 0.04
120	3‡	42.1 ± 2.2	38.8 ± 8.6	44.0 ± 3.2	1.16 ± 0.10

*$P < 0.05$ for comparison across insulin doses.
†Excludes one outlier with very low fractional extraction of tritium.
‡Because study terminated at 60 min for 1 participant, n = 3. For 60-min period, this participant had the following fractional extractions: glucose 46.9%, FDG 54.0% and tritium 47.2%. Calculated LC for this participant was 1.14.
[^{3}H]G = [^{3}H]glucose; FDG = [^{18}F]fluorodeoxyglucose; LC = lumped constant.
Values are mean ± SEM.

muscle. Therefore, to derive quantitative data concerning glucose metabolism using the analog FDG, we conducted this study to obtain empirical values for the LC within skeletal muscle and to examine whether insulin influenced LC. The LC was assessed by bolus coadministration of FDG and [^{3}H]G, followed by arterial and venous sampling to study respective fractional extractions across the leg. The cumulative arterial and femoral venous radioactivity concentrations were determined, using data obtained for 90 min after injections, and included delineation of the initial bolus phases of the curves based on a high frequency of 10 samples per minute. Insulin stimulated a significant increase in the fractional extraction of FDG, [^{3}H]G and actual glucose. This is consistent with the known effect of insulin to potently increase glucose metabolism in skeletal muscle (*38,39*). Within-subject correlation between fractional extraction of FDG and [^{3}H]G and that of actual glucose were quite strong (correlation coefficients of approximately 0.9). The value for the LC of FDG across the leg in these lean participants was approximately 1.2, reflecting a slight preferential uptake of FDG, but this value was not significantly affected by insulin. These data indicate that the LC for FDG in skeletal muscle is fairly constant across a broad range of physiologic and supraphysiologic insulin concentrations and that the quantitative uptake of FDG is only modestly different than that of glucose.

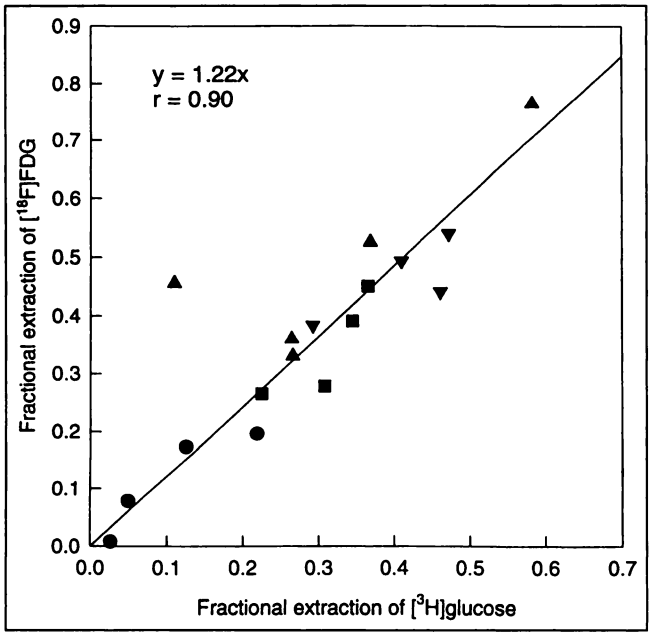

FIGURE 2. Plot of relationship between [^{18}F]fluorodeoxyglucose (FDG) extraction and [^{3}H]G extraction during insulin infusion of 0 (●), 20 (■), 40 (▲) and 120 mU/min/m^2 (▼). Slope of line, 1.22 ± 0.08, is approximation of LC for human skeletal muscle.

PET imaging of FDG has been extensively used to investigate glucose metabolism in the brain (*1,2*) and myocardium (*3,4,6*), and for each organ there has also been considerable research to determine the value for the LC (*17–19*). In the brain, the value of the LC is less than 1.0; based on broad acceptance of prior studies, an empiric value of 0.52 ± 0.03 is generally used (*17*). The fact that the LC in the brain is significantly less than 1 is attributed to the relative importance of glucose phosphorylation as a locus of control for glucose metabolism. This is thought to result from the lesser affinity of FDG than glucose for hexokinase (*40*), whereas glucose transport, for which FDG has a higher affinity, is not considered to be rate limiting for glucose metabolism by brain (*23*). It is interesting to note that, during hypoglycemia, when glucose transport does limit rates of cerebral metabolism of glucose, values for the LC can increase markedly (*22,23*). Even though glucose metabolism in the brain is insensitive to insulin (*20,21*), and thus insulin is unlikely to affect the LC for this tissue, the issue of whether insulin influences the LC in myocardium is more controversial.

A recent study in myocardium, which examined the fractional extractions of FDG and glucose across the heart in vivo in humans and, therefore, was of similar design to this study using arteriovenous balance across the leg, reported that the value for LC in the heart is approximately 1.4 (*4*). Botker et al. (*24*) found that insulin induced a linear decrease

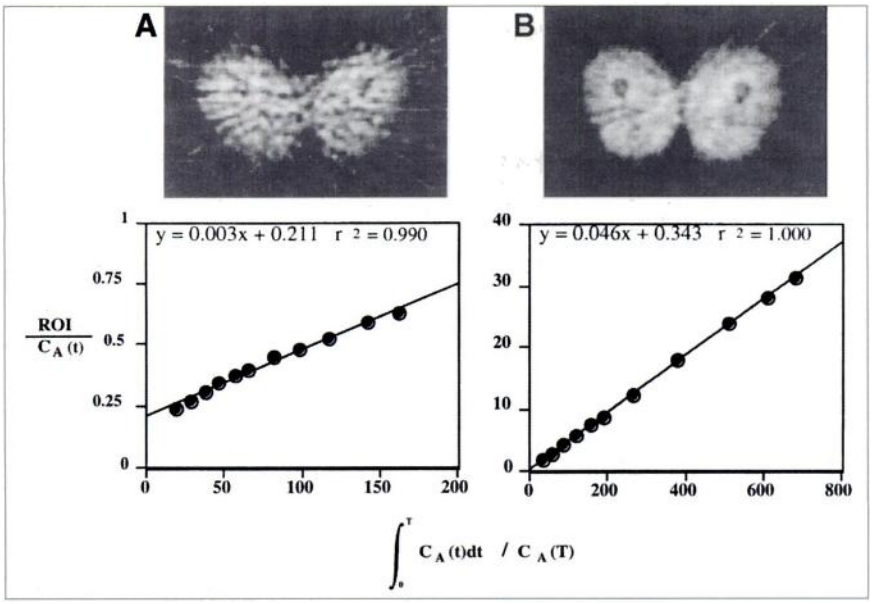

FIGURE 3. Quantitative parametric images (top row) and corresponding regional results of Patlak analysis (bottom row) under basal (A) and insulin-stimulated (B) conditions. In images, each pixel represents overall uptake of FDG in skeletal muscle. Graphs are corresponding Patlak plots, determined from region-of-interest (ROI)-generated PET and measured time-activity data (C_A), with linear regression performed at 12–90 min after FDG injection. T = study duration.

in LC for myocardium with values at maximal insulin stimulation being approximately threefold lower than during fasting conditions. They found that fatty acid concentration also affected the value for the LC during fasting conditions. One limitation of the data of Botker et al. is that simultaneous rates of glucose metabolism or arteriovenous fractional extraction of glucose were not empirically determined for the participants. During in vitro studies in myocardium, Russell et al. (*25*) also observed in vitro that insulin diminished the LC and proposed that the mechanism for the decrease was an insulin-induced decrement in the affinity of deoxyglucose for hexokinase.

There have been relatively few studies of the LC for FDG in skeletal muscle. In the one prior clinical investigation that examined the issue, measurements of glucose uptake across the forearm during one dose of insulin infusion resulting in insulin concentrations in the upper physiologic range were compared with simultaneous FDG uptake determined by PET imaging of muscle in the upper arm (*13*). A value of approximately 1.0 was found for the LC, which is similar to the value of approximately 1.2 found in this study. In rat skeletal muscle, insulin did not alter the value of the LC of deoxyglucose; the value was slightly less than 1.0 (*27*). For PET imaging, it is customary to administer FDG as a bolus injection. That approach was used in this study, although the resulting non–steady-state concentrations do pose methodologic challenges for ascertainment of arteriovenous differences that were used to estimate the LC. We used the classic approach to this issue that was articulated by Zierler (*36*), which was that of sampling throughout the non-steady-state phase and until basal conditions were reestablished and then using integrated data to determine fractional extraction. Furthermore, to calculate the LC, fractional extraction of FDG was related to that of [^{3}H]G, which was administered in an identical bolus manner and assayed within the same blood samples, after allowing for dissipation of the more short-lived radioactivity of FDG. The data obtained revealed good concordance between fractional extractions of FDG and [^{3}H]G and, indeed, with that of actual glucose (though the latter was measured in steady-state conditions). Another methodologic consideration is the fact that, ideally for dose-response studies, each participant would be studied at all four insulin doses. However, within this study, ethical considerations of potential risks of repeated femoral venous and arterial cannulations caused us to favor the random assignment of different participants to each insulin dose, while attempting to match participants for clinical characteristics. Despite potential interindividual differences in insulin sensitivity, which could confound interpretation of dose-response data, the expected effect of insulin to increase glucose uptake and fractional extractions of FDG and [^{3}H]G across the leg was observed.

CONCLUSION

Insulin does not appear to influence the LC for FDG in skeletal muscle. For the purposes of quantitative assessments of glucose metabolism based on imaging of FDG by PET methods, our data indicate that the value of the LC in healthy lean volunteers is 1.2, indicating a modest preferential uptake of FDG relative to glucose. Because of the potential usefulness of insulin-stimulated PET imaging of FDG metabolism for investigations of skeletal muscle insulin resistance, additional research is indicated to delineate the LCs for skeletal muscle in insulin resistance.

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