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Glucose Uptake Patterns in Exercised Skeletal Muscles of Elite Male Long-Distance and Short-Distance Runners

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Abstract

The aim of this study was to determine glucose uptake patterns in exercised skeletal muscles of elite male long-distance and short-distance runners. Positron emission tomography (PET) using 18F-fluoro-2-deoxyglucose (FDG) was performed to determine the patterns of glucose uptake in lower limbs of short-distance (SD group, n = 8) and long-distance (LD group, n = 8) male runners after a modified 20 min Bruce treadmill test. Magnetic resonance imaging (MRI) was used to delineate the muscle groups in lower limbs. Muscle groups from hip, knee, and ankle movers were measured. The total FDG uptake and the standard uptake value (SUV) for each muscle group were compared between the 2 groups. For the SD and LD runners, the 2 major muscle groups utilizing glucose during running were knee extensors and ankle plantarflexors, which accounted for 49.3 ± 8.1% (25.1 ± 4.7% and 24.2 ± 6.0%) of overall lower extremity glucose uptake for SD group, and 51.3 ± 8.0% (27.2 ± 2.7% and 24.0 ± 8.1%) for LD group. No difference in muscle glucose uptake was noted for other muscle groups. For SD runners, the SUVs for the muscle groups varied from 0.49 ± 0.27 for the ankle plantarflexors, to 0.20 ± 0.08 for the hip flexor. For the LD runners, the highest and lowest SUVs were 0.43 ± 0.15 for the ankle dorsiflexors and 0.21 ± 0.19 for the hip. For SD and LD groups, no difference in muscle SUV was noted for the muscle groups. However, the SUV ratio between the ankle dorsiflexors and plantarflexors in the LD group was significantly greater than that in the SD group. We thus conclude that the major propelling muscle groups account for ~50% of lower limb glucose utilization during running. Thus, the other muscle groups involving maintenance of balance, limb deceleration, and shock absorption utilize an equal amount. This result provides a new insight into glucose distribution in skeletal muscle, suggesting that propellers and supporters are both energetically important during running. Furthermore, for each unit muscle volume, movers of ankle are more glucose-demanding than those of hip.

Key Words: FDG, PET, muscle recruitment, glucose uptake, exercise

Introduction

Slow twitch (ST) muscle fibers and fast twitch (FT) fibers are mixed in a muscle, with different ratios in different muscles. For example, the average cross section areas of ST fibers are 43.5% and 73.4% for the surface of the lateral head of gastrocnemius and the surface of the tibialis anterior muscles, respectively, in young male adults (10). However, the mixing ratio varies with subjects. It has also been demonstrated that endurance athletes have predominantly ST fiber populations in their gastrocnemius and vastus lateralis muscles, whereas strength athletes have a higher percentage of FT fibers (1). In addition, endurance training improves exercise performance through the increase of muscle GLUT-4 content

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Table 1. Basic information of the runners

Runner Group	Number	Age (year)	Body Height (cm)†	Body Weight (kg)*	FDG Taken (MBq)	Treadmill Protocol Completed*
Long-Distance Runner	8	22.4 ± 3.2	171.0 ± 5.7	59.9 ± 5.1	32.8 ± 4.7	100.0 ± 0.0%
Short-Distance Runner	8	21.0 ± 1.5	176.6 ± 5.0	71.8 ± 6.0	34.4 ± 6.0	88.0 ± 7.5%

*Statistically significant difference found between the two runner groups.
$^{\dagger}P < 0.1$ found for the corresponding values between the two runner groups.

and hexokinase activity, and the decrease of muscle glucose-6-phosphatase activity. All of these adaptations lead to enhanced glucose uptake and phosphorylation (2, 7, 16).

Because electromyography and magnetic resonance imaging (MRI) techniques, which have been used to analyze the *in vivo* motion and contraction of skeletal muscle (4, 13), are not useful for evaluating muscle metabolism, positron emission tomography (PET) with [18F]-fluorodeoxyglucose (FDG) has been employed to determine metabolic activity of the dominant side and posterior compartment of legs in runners by Tashiro and colleagues (17). Recently, Ohnuma *et al*. investigated glucose uptake during a dash with FDG-PET, and found that "posterior thigh muscles were especially active" (15).

Since running is a basic skill of almost all athletes, which requires combined and accurately coordinated muscle contraction in every stride (17), the purpose of this study was to investigate if the glucose uptake pattern of the leg muscles differs between long-distance (LD) and short-distance (SD) runners at relatively higher exercise intensity. We hypothesized that glucose uptake is higher in LD runners because of their more abundant ST fibers and intense endurance training.

Materials and Methods

Subjects

Sixteen healthy young male elite SD (n = 8) and LD (n = 8) runners participated in the study. Most of the LD runners were competing in men's 5,000 meter or 10,000 meter runs, while the SD runners were competing in men's 110 meter hurdles. The demographic data of the runners are presented in Table 1. Written informed consent was obtained after the nature, purpose, and potential risks of the study were explained to the subjects. The study protocol was performed in accordance with Declaration of Helsinki and approved by the Institute of Research Board of the Taipei Medical University-Wan Fang Hospital.

Exercise Protocol

Every subject was fasting for at least 8 h before the exercise testing. A cup of 18F-FDG solution (radioactivity approximately 0.5 MBq/subject/kg) was ingested (5, 14) as fast as possible by each subject immediately before a Bruce Multistage Continuous Protocol (9) on a treadmill (Takasuma X-fit 7; Chi-Tai Health, Kaohsiung, Taiwan, ROC) under the supervision of a licensed physical therapist (PT). The test was modified so that the total test duration was 20 min, but the speed and slope remained the same if the subject felt uncomfortable to go to the next stage. A one minute cool down was allowed after the test, and then the subject rested in the supine position for 59 min before the PET scan.

FDG-PET

Multiple-frame step and pelvis-to-ankle PET imaging was performed using a dedicated PET scanner (SCANDITRONIX 4096 15WB Plus; General Electric, Milwaukee, WI, USA) with a 97.5 mm axial FOV. The acquisition time for each step was 5 min. Transmission scan then was done with the same area of the emission scan. All image data were reconstructed by a vendor-provided iterative reconstruction algorithm with correction of transmission scan.

MRI

One subject who had the nearest body weight and height to the average weight and height of all subjects was also scanned in a supine position in a 1.5 T Horizon scanner (General Electric) using a standard body coil with conventional T1-weighted spin echo MR pulse sequences. Continuous 4 mm axial slices were taken from the iliac crest to just below the ankle. Each display matrix was 256 × 256 with a pixel size of 1.56 × 1.56 mm.

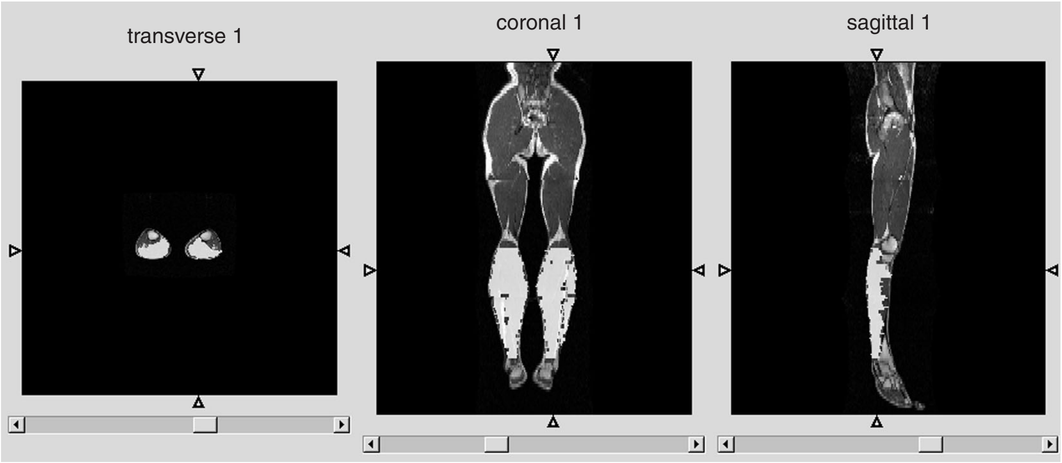

Fig. 1. An example of muscle group delineation from the magnetic resonance (MR) image set. A manually drawn region of interest (ROI) for the ankle plantarflexor group is shown in white. The interface of AMIDE shows, from left to right, axial, coronal, and sagital views of the lower legs of a subject.

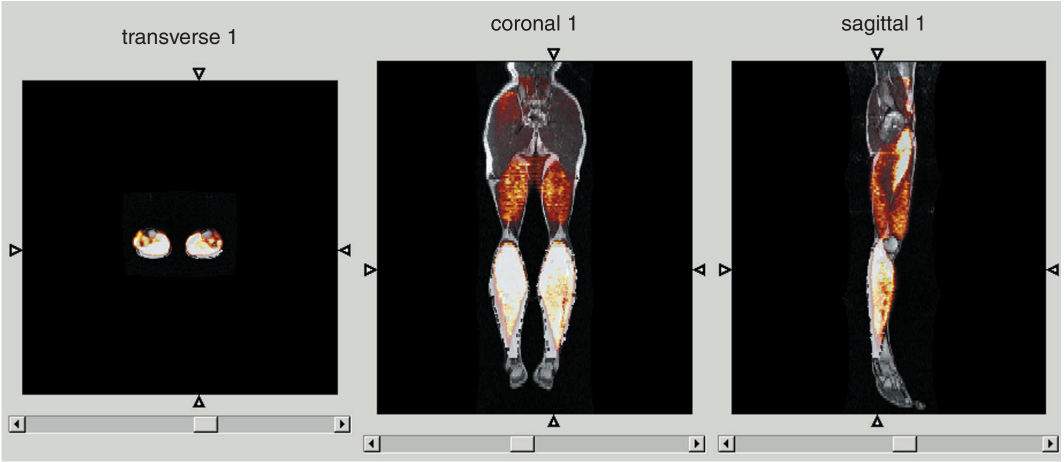

Fig. 2. The registered MR and PET image sets of the same subject shown in Fig. 1 are presented in a gray and red color spectrum, respectively. The manually drawn ROI of the ankle plantarflexor group is also shown in white as in Fig. 1.

Image Procedures

Both the reconstructed PET and MRI data were transferred to a personal computer in native and DICOM (Digital Imaging and Communications in Medicine) format, respectively. The multi-frame images were then stacked together and converted to the Mayo Clinic Analyze 7.5 format by programs written by one of the authors (C-H Chen) using IDL 6.3 (available from ITT Corporation, White Plains, NY, USA). In addition, PET images were decay-corrected to the start of the first scan step.

The MRI image set (Fig. 1) was first manually registered to the PET image set with a public-domain medical image processing tool, AMIDE (12), by a PT. The amount of FDG uptake in different muscle groups for each subject were then manually analyzed with AMIDE based on the registered MRI image set by the same PT, as shown in Fig. 2. The muscle groups included the extensors and flexors of the hips and knees, the abductors and adductors of the hips, ankle dorsiflexors, and ankle plantarflexors. The muscles included in each muscle group are listed in Table 2.

Statistical Analyses

Two-tailed *t*-test was applied on demographic data, percentage FDG (%FDG) uptake, standard uptake value (SUV), and antagonist ratios. The SUV is the most often used PET index, and is described elsewhere (11, 17). The antagonist ratios are ratios between absolute FDG uptake in MBq of hip adductors and abductors, hip flexors and extensors, knee flexors and extensors, and ankle dorsiflexors and plantar-

Table 2. Muscles in each muscle group

Joint	Abductor	Adductor	Extensor/Plantarflex	Flexor/Dorsiflexor
Hip	Gluteus medius Gluteus minimus Piriformis	Adductor magnus Adductors brevis Adductor longus Pectineus Gracilis	Gluteus maximus	Psoas major Iliacus Tensor fasciae latae Adductor brevis Adductor longus Pectineus
Knee			Rectus femoris Vastus intermedius Vastus lateralis Vastus medialis	Biceps femoris Semimembranosus Semitendinosus
Ankle			Gastrocnemius Peroneus brevis Peroneus longus Plantaris Soleus Tibialis posterior	Tibialis anterior

The ankle plantarflexors are considered extensors and the dorsiflexors flexors.

flexors. We also applied two-way analysis of variance (ANOVA) using a free statistical software program, R (18). The two factors were joint mover and sport type. The former had 8 levels (hip adductor, hip abductor, hip flexor, hip extensor, knee flexor, knee extensor, ankle dorsiflexor, and ankle plantarflexor), while the latter had only 2 levels (SD and LD). Therefore, it was an 8×2 factorial experimental design. We applied the analysis to both %FDG and SUV to see if any of the factors had a significant effect on them. If a factor was shown to have a significant effect, the different effects among different levels of that factor were checked by the Tukey test (19), again, using the freeware R. Data were presented as mean ± standard deviation (SD) or number and percent. A P value of < 0.05 was considered to indicate statistical significance.

Results

The mean body weight of the LD group was significantly different than that of the SD group (59.9 ± 5.1 kg *vs*. 71.8 ± 6.0 kg, respectively, $P <$ 0.05). There were no statistical differences in the comparison of other demographic data between the 2 groups (Table 1). Although there appears to be a difference in body height (171.0 ± 5.7 cm *vs*. 176.6 ± 5.0 cm), there was only a "weak" difference ($P < 0.1$). [Note: This is not really appropriate or correct. If P is set as < 0.05, and P value of the comparison is not below that level, then there is no difference. The term "weak" difference is not accurate or appropriate.]

The percent of runners completing the Bruce treadmill protocol (100.0 ± 0.0 LD *vs*. 88.0 ± 7.5% SD) was significantly different ($P < 0.05$). Data are presented in Table 1. The data of the completion of the treadmill protocol for the SD group implies that most SD runners reached 16% or more inclination, and all of them reached an inclination of at least 14%. For those who completed the protocol, the estimated VO_2 was approximately 60 ml/kg/min. The VO_2 for those who reached inclinations of 14% and 18% was approximately 35 ml/kg/min and 52 ml/kg/min (also the average for SD group), respectively.

The absolute and relative FDG uptake, the SUV, and the antagonist ratio for each muscle group are shown in Tables 3 and 4 for LD and SD runners, respectively. Table 3 indicates that the FDG uptake of the knee extensors and ankle plantarflexors for the LD group are 632 ± 246 kBq (27.2 ± 2.7% of the total FDG uptake of the 8 joint movers) and 508 ± 86 kBq (24.0 ± 8.1%), respectively. For SD runners, these values are 597 ± 321 kBq (25.1 ± 4.7%) and 584 ± 367 kBq (24.2 ± 6.0%), as shown in Table 4. The sum of knee extensor and ankle plantarflexor %FDG uptake for the LD and SD groups are 51.3 ± 8.0% and 49.3 ± 8.1%, respectively. The FDG uptake for the other muscle groups in descending order are knee flexor, hip extensor, hip adductor, hip abductor, ankle dorsiflexors, and hip flexor, as shown in Tables 3 and 4, and Fig. 3. Using the two-tailed t-test, no statistical differences in muscle glucose uptake and antagonist FDG ratio were found for any muscle groups or ratios between the 2 runner groups. This result is also

Table 3. The FDG uptake pattern of long-distance (LD) runners

Joint Movers		FDG Uptake (kBq)	FDG Uptake (%)	Antagonists FDG Ratio	SUV	Antagonists SUV Ratio
Hip	Adductor	214 ± 98	9.2 ± 1.7%	2.3 ± 1.9	0.26 ± 0.08	2.1 ± 1.7
	Abductor	187 ± 175	7.0 ± 4.9%		0.26 ± 0.27	
	Flexor	53 ± 46	2.0 ± 1.4%	0.1 ± 0.1	0.21 ± 0.19	0.6 ± 0.5
	Extensor	290 ± 142	12.2 ± 4.5%		0.27 ± 0.14	
Knee	Flexor	332 ± 149	14.0 ± 1.9%	0.5 ± 0.1	0.30 ± 0.14	1.0 ± 0.2
	Extensor	632 ± 246	27.2 ± 2.7%		0.30 ± 0.10	
Ankle	Dorsiflexor	90 ± 25	4.4 ± 2.2%	0.2 ± 0.0†	0.43 ± 0.15	1.1 ± 0.2*
	Plantarflexor	508 ± 86	24.0 ± 8.1%		0.38 ± 0.08	
Total		2,307 ± 816				

FDG: 18F-fluror-2-deoxy glucose; SUB: standard uptake value.
*Statistically significant difference ($P < 0.05$) found for the corresponding values between the two runner groups.
†$P < 0.1$ found for the corresponding values between the two runner groups.

Table 4. The FDG uptake pattern of short-distance (SD) runners

Joint Movers		FDG Uptake (kBq)	FDG Uptake (%)	Antagonists FDG Ratio	SUV	Antagonists SUV Ratio
Hip	Adductor	201 ± 98	8.6 ± 1.3%	1.3 ± 0.5	0.29 ± 0.12	1.1 ± 0.4
	Abductor	184 ± 114	7.7 ± 3.5%		0.30 ± 0.18	
	Flexor	44 ± 19	2.0 ± 0.5%	0.2 ± 0.0	0.20 ± 0.08	0.8 ± 0.2
	Extensor	237 ± 126	10.2 ± 1.6%		0.26 ± 0.12	
Knee	Flexor	342 ± 179	14.1 ± 3.3%	0.6 ± 0.1	0.35 ± 0.16	1.1 ± 0.2
	Extensor	597 ± 321	25.1 ± 4.7%		0.33 ± 0.15	
Ankle	Dorsiflexor	78 ± 50	3.3 ± 0.8%	0.1 ± 0.0†	0.42 ± 0.24	0.9 ± 0.2*
	Plantarflexor	584 ± 367	24.2 ± 6.0%		0.49 ± 0.27	
Total		2,267 ± 1,214				

FDG: 18F-fluror-2-deoxy glucose; SUV: standard uptake value.
*Statistically significant difference ($P < 0.05$) found for the corresponding values between the two runner groups.
†$P < 0.1$ found for the corresponding values between the two runner groups.

supported by the two-way ANOVA results. The significant factor that determines FDG uptake in a muscle group is the different joint movers ($P < 0.001$), as shown in Fig. 3, and not the different type of running. Note Fig. 3 indicates median and quartiles instead of mean and standard deviation. The Tukey test showed that the %FDG of hip flexors was significantly lower than that of hip extensors, knee flexors, ankle plantarflexors, and knee extensors. There was no statistical difference of %FDG among other muscle group pairs.

The SUV for each muscle group, as shown in Tables 3 and 4, falls between 0.21 ± 0.19 (hip flexor) and 0.43 ± 0.15 (ankle dorsiflexor) for LD runners, while values for SD runners are 0.20 ± 0.08 (hip flexor) and 0.49 ± 0.27 (ankle plantarflexor). Note that the highest muscle group SUV is different for the 2 groups. However, the two-tailed *t*-test failed to show a significant difference of SUV for any muscle groups between the 2 groups of runners. Two-way ANOVA testing again revealed that the significant factor affecting SUV in a muscle group was the different joint movers ($P < 0.001$), instead of the type of running.

Figure 4 shows the combined SUV for each muscle group for all the subjects. The Tukey test showed that the SUVs of both ankle dorsiflexors and plantarflexors were significantly higher than that of hip flexors. No statistical difference in SUV was found between other muscle group pairs. However, the *P* values of the comparison between the SUVs of hip extensors and the ankle movers were < 0.1.

The antagonist SUV ratios varied between 0.6 ± 0.5 (hip flexor/hip extensor) and 2.1 ± 1.7 (hip adductor/

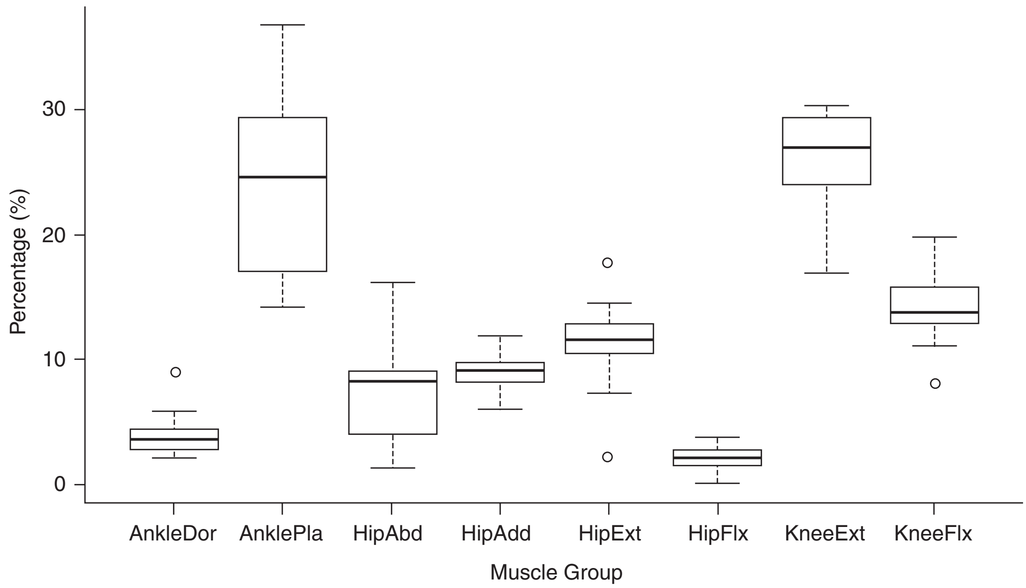

Fig. 3. Percent FDG uptake (%FDG) for each muscle group generated by the statistical software R. The plot shows the median as the thick horizontal bar, quartiles as the rectangles and bars, while the small circles are outliers. The %FDG of hip extensor (HipExt), knee flexor (KneeFlx), ankle plantarflexor (AnklePla), and knee extensor (KneeExt) were all significantly higher than that of hip flexor (HipFlx). There was no statistical difference between any other muscle group pairs with respect to %FDG.

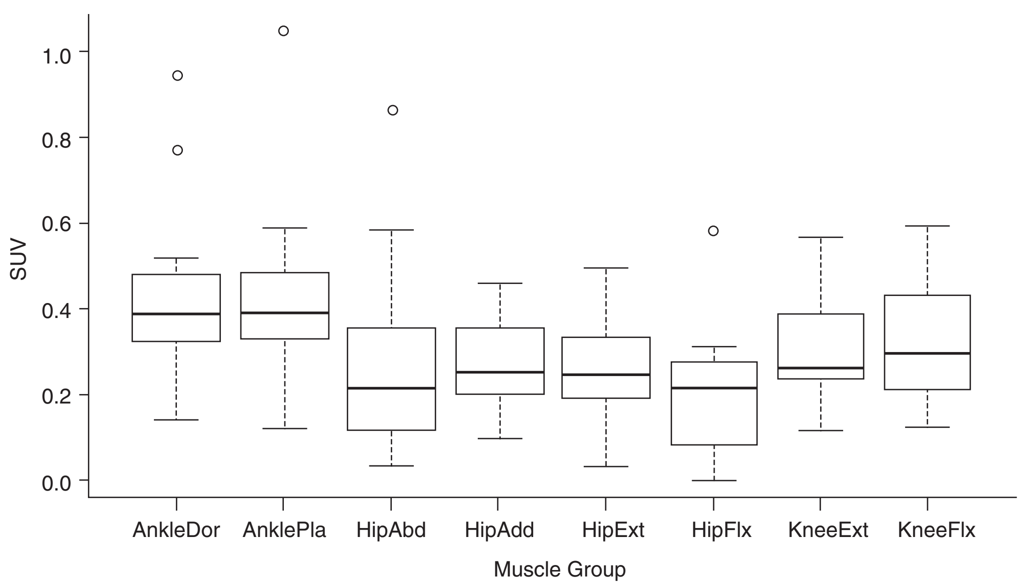

Fig. 4. Standard uptake value (SUV), which represents normalized glucose uptake per unit muscle volume per unit FDG intake per body weight, for each muscle group generated by R. The plot shows median, quartiles, and outliers as in Fig. 3. The SUVs of ankle dorsiflexors (AnkleDor) and plantarflexors (AnklePla) are significantly higher than hip flexors (HipFlx) in Tukey test. There was no statistical difference between any other muscle group pairs with respect to SUV.

hip abductor) for LD runners, as shown in Table 3. For SD runners, the ratios varied between 0.8 ± 0.2 (hip flexor/hip extensor) and 1.1 ± 0.4 (hip adductor/hip abductor), as shown in Table 4. Note that a significant difference was found in the dorsiflexor-plantarflexor antagonist SUV ratio between the 2 groups (LD 1.1 ± 0.2 *vs*. SD 0.9 ± 0.2).

Discussion

The purpose of this study was to evaluate the glucose uptake patterns in exercised skeletal muscles of elite runners, and determine if there are differences in glucose uptake patterns between LD and SD runners while performing the same task. We found that the major propelling muscle groups accounted for approximately 50% of lower limb glucose utilization during running. The rest of muscle groups involving maintenance of balance, limb deceleration, and shock absorption utilize an equal amount of glucose as the propellers. This implies that propellers and supporters are both energetically important during running. We also found that, for each unit muscle volume, movers of the ankle expended more energy than those of hip during the Bruce test protocol.

The time interval from FDG oral administration to PET scan varied from 40 to 90 min in previous studies (5, 14). The time in our study was 80 min (20 min exercise, 1 min cool down, 59 min rest). A longer time interval usually results in better differential uptake between target and background tissues (3). Since the subjects engaged in little activity after exercise, FDG remaining in the blood is usually not a concern, as discussed in the report published by Iemitsu *et al*. in 2000 (8) where the authors state that "although the whole body scanning was performed under resting condition, tissue radioactivity reflects metabolic level during exercis".

Tashiro and colleagues (17) demonstrated that the mean FDG uptake ratio between the posterior and anterior compartments of the lower leg was 7.67. Since ankle dorsiflexors occupy most of the posterior compartment of the lower leg, and plantarflexors most of the anterior compartment, this value is compatible with those of our study. Our results indicate that the ankle dorsiflexor-plantarflexor FDG uptake ratios are 5 and 10 for LD and SD runners, respectively. Note that in Tables 3 and 4, the corresponding antagonist ratios are plantarflexor-dorsiflexor, instead of dorsiflexor-plantarflexor ratios. Therefore, the values 5 and 10 were derived from the inversion of 0.2 and 0.1, respectively. The groups of Fujimoto (6) and Tashiro (17) have shown that the highest increase of 18F-FDG uptake is in the most exercised muscles of ankle plantarflexors. In addition to these muscles, the knee extensors in our subjects also took up the same amount of FDG as the ankle plantarflexors. Since nearly maximal and submaximal VO_2 for the SD and the LD groups, respectively, were achieved in our study, we speculate that the difference might be due to higher exercise intensity and up-slope running. This speculation is at least partly supported by the study of Fujimoto and colleagues 2003 (7). In that study, the glucose uptake by quadriceps femoris was significantly higher than that of the hamstrings with the increase in exercise intensity. In the same study, they also showed that the skeletal muscle glucose uptake difference between trained and untrained men was increased with moderate-to-high intensity exercise, but not with low intensity exercise; thus, we chose high intensity exercise for our study.

Our SUV results are again compatible with those of Tashiro (17). Both studies showed that the highest SUV appeared over ankle movers of lower leg, with approximately the same SUV in our study as theirs. However, the mean SUV ratio in our study between ankle dorsiflexor-plantarflexors was 1.1 and 0.9 for LD and SD runners, respectively, while the similar ratio in Tashiro's study was approximately 0.6 (1:1.59). We suspect that the difference is due to different exercise types used in the two studies. Although there were significant differences of %FDG uptake in different muscle groups, which represents different work done by different muscle groups, SUVs were about the same for most muscle groups in our study. Because of the high intensity and generalized muscle use of the lower limbs, this might indicate that the maximal force and energy consumption per unit muscle volume for different muscles in the lower extremities may not be very different.

Unlike the above mentioned studies, Ohnuma *et al.* (15) revealed that FDG accumulated significantly more in the posterior thigh muscles than the lower leg muscles after 10 min repeated dash running. All of the studies suggest different muscle recruitment patterns in different sports, and that FDG-PET is a good tool for evaluating muscle glucose utilization. However, in our study, we have shown that while performing the same high-intensity task, athletes with different endurance capacities and training demonstrate about the same muscle recruitment pattern, except for the ratio between ankle dorsiflexors and plantarflexors. Our study also indicated that the ratio between antagonists may be a more sensitive index than FDG uptake and SUV themselves to detect different muscle glucose usage patterns in speed and endurance type athletes.

Based on our findings, stretching and strengthening both the ankle movers and knee extensors are important to avoid most sports injuries related to non-dash running. On the other hand, the same stretching and strengthening should be advised to protect the hamstrings for athletes who participate in the dash.

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