Evaluation of Skeletal Muscle Activity of Power Limb Based on Surface and Deep Layers in Humans in vivo: A PET Study

VIII. 18. Evaluation of Skeletal Muscle Activity of Rower Limb Based on Surface and Deep Layers in Humans *in vivo*: A PET Study

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Introduction

Nowadays, the physiological research involving skeletal muscle demonstrates a growing interest in sport medicine and rehabilitation science. Positron emission tomography (PET) is a useful imaging tool which elucidates individual skeletal muscle activity in humans *in vivo*. Reduction of radiation exposure to the healthy human volunteers is an advantage of this three dimensional positron emission tomography technique (3-D PET). 2-Deoxy-2-[18F]fluoro-D-glucose ([18F]FDG), an analogue of glucose, has been established as a valuable tracer for glucose metabolism[1,2]. After administration in the body, [18F]FDG is trapped inside the cell after phosphorylation up to [18F]FDG-6-phosphate in the presence of hexokinase enzyme. Therefore, the trapped [18F]FDG-6-phosphate inside cell reflects glucose metabolism at rest and after any task. This trapping nature of [18F]FDG is beneficial for imaging evaluation of skeletal muscle activity. Previous investigators assessed individual skeletal muscle activity of lower limb after exercise task (running) using [18F]FDG and PET technique[3,4]. However, until now, the imaging evaluation of lower limb skeletal muscle activity associated with surface and deep layers has not been done elaborately using [18F]FDG and PET technique.

In the present investigation, we tried to elucidate the skeletal muscle activity of thigh in respect of surface and deep layers using PET imaging technique.

Materials and methods

Ten healthy male volunteers (average age, 21.2±1.6 years) were enrolled in this investigation. A written informed consent was taken from each subject before the

investigation was started. The study protocol was approved by the Ethics Review Committee of Tohoku University Graduate School of Medicine. All the subjects abstained from eating or drinking at least 5 h prior to the start of the investigation. Each subject was studied twice – at rest and after exercise (ergometer bicycle pedal at 55% $\dot{V}O_{2max}$ workload).

In task condition, each subject was studied on two separate days within 3-week-long period with an interval of at least 2 days. Subjects' $\dot{V}O_{2max}$ was measured after an intermittent ergometer bicycle exercise task (Monark 818E, Monark, Varberg, Sweden). The oxygen consumption rate was determined by an automated metabolic unit machine (AE280-S, Minato, Osaka, Japan). The $\dot{V}O_{2max}$ was measured by the discontinuous method (5) and the power (watt) of the workload was determined at 55% $\dot{V}O_{2max}$. Before investigation, subjects rested for 20 min in a dimly lit and quiet room. A Teflon catheter was inserted into the antecubital veins of left hand to measure plasma radioactivity and glucose. Another Teflon catheter was inserted into the antecubital veins of opposite hand for [^{18}F]FDG injection (dose, 1.15 ± 0.11) (mean $\pm$ SD). The subjects performed ergometer bicycle pedal for 30 min following after [^{18}F]FDG injection to accomplish a total of 40 min exercise task.

After exercise and urination at around 45 min following intravenous [^{18}F]FDG injection, a set of whole-body emission scan was done with transaxial spatial resolutions of 4.4, 5.4, and 3.9 mm at full width half maximum in the tangential, radial and axial directions, respectively. Whole-body emission scan (3 min×9 frames) was performed from the knee joint to the vertex followed by transmission scan (3 min×9 frames). The post-injection transmission scan was performed with a ^{68}Ge/^{68}Ga external rotating line source (370 MBq at purchase).

In addition, all the subjects were studied at resting control condition maintaining the similar study protocol with exercise task. In resting control study, subjects sat on chairs with eyes open following after intravenous [^{18}F]FDG injection (40.7 ± 7.0 MBq) (mean $\pm$ standard deviation, SD) for 40 min in a dimly lit and quiet room.

MRI measurement

MRI scan was performed in the thigh region (from knee joint to the hip joint) using Spin Echo Sequence (MR Vectra, GE Yokogawa, Tokyo, Japan) at 0.5 or 1.0 Tesla. The measurement conditions are mentioned as following:

Repetition time/Echo time was 330/20 ms, number of excitations was 3, the field of view

was 45 cm, number of matrix was 224×128, slice thickness was 10 mm and a gap between slices was 3 mm.

Data analysis [ROI]

PET image data was analyzed based on regions of interest analysis (ROIs) on the skeletal muscles of thigh region. ROIs were drawn on quadriceps group muscles of thigh region – vastus lateralis (VL), vastus intermedius (VI), VM (vastus medialis), based on surface and deep layers. Here, VM muscle was analyzed according to surface and deep layers by drawing an imaginary line between mid-points at transaxial direction, referring VMs (vastus medialis surface) and VMd (vastus medialis deep), respectively. The location of individual skeletal muscle was determined from their respected MRI images, as anatomical reference. Therefore, coregistration of PET data (thigh) to the MRI data (thigh) was performed using statistical parametric mapping software (SPM 5)[6]. ROIs analysis was done by using image processing software, Dr. View (Asahikasei Joho System Co. Ltd. Tokyo, Japan).

Semiquantification analysis (standardized uptake value, SUV) for individual skeletal muscle of thigh (surface and deep layers) was performed by using the following formula:

$$SUV = \frac{Mean\ ROIcts\,(cps/pxls) \times Body\ weight(g)}{Injected\ dose\,(MBq) \times Calibration\ factor\,(cps/MBq)}$$

Statistical analysis

For statistical analysis, nonparametric Wilcoxon signed rank test was performed for two conditions (resting control and exercise task), in terms of skeletal muscles of surface and deep layers. The significant difference was set at $P < 0.05$.

Results

SUV ([18F]FDG uptake) was shown significantly increased ($p < 0.50$) in the skeletal muscles of both surface and deep layers (surface: VL, VMs, and deep: VI, VMd) after exercise (55% $\dot{V}O_{2max}$), when compared with the resting condition (Fig. 1). In another, SUV in thigh skeletal muscles based on surface and deep layers was shown in Fig. 2 and Fig. 3, respectively. In the resting condition and after exercise (55% $\dot{V}O_{2max}$), SUV was significantly increased ($p < 0.05$) in the deep muscles (VI and VMd) than surface muscles (VL and VMs) (Fig. 2 and Fig. 3). In another, SUV ([18F]FDG uptake) of exercise to rest

ratio in the surface and deep skeletal muscles was shown in Fig. 4 and Fig. 5, respectively. It revealed that SUV of exercise to rest ratio was relatively higher in the surface muscles (VL and VMs) than deep muscles (VI and VMd) of thigh (Fig. 4 and Fig. 5).

Discussions and Conclusion

The present investigation evaluated glucose metabolic distributions in different skeletal muscles of thigh (quadriceps group) at two conditions – at rest and after exercise (ergometer bicycle pedal at an intensity of 55% $\dot{V}O_{2max}$). [^{18}F]FDG and PET imaging technique was applied for the evaluation of skeletal muscle activity, based on surface and deep layers. It was found that [^{18}F]FDG uptake (SUV) by the thigh skeletal muscles of both surface (VL, vastus lateralis and VMs, vastus medialis surface) and deep layers (VI, vastus intermedius and VMd, vastus medialis deep) was significantly higher ($p < 0.05$) after ergometer bicycle exercise (55% $\dot{V}O_{2max}$) when compared with the resting condition. In another, [^{18}F]FDG uptake (SUV) by the skeletal muscles of deep layer (VI and VMd) was higher ($p < 0.05$) than surface layer (VL and VMs) both at resting condition and after exercise. However, [^{18}F]FDG uptake (SUV) of exercise to rest ratio by the surface muscles (VL and VMs) was higher than deep muscles (VI and VMd).

Quadriceps group muscles of thigh has a dominant role in locomotion (walking, running, jogging or bicycle pedal). Therefore, it is noteworthy to assess the skeletal muscle activity of thigh (quadriceps group) based on layer arrangement (surface and deep), which would persuade the self-care of musculoskeletal system. Previous investigators already revealed the skeletal muscle activity of lower limb and pelvis after exercise task using [^{18}F]FDG and PET imaging technique[3,4]. They assessed energy metabolic changes (glucose metabolism) of lower limb skeletal muscles induced by exercise. However, to date, no studies have assessed the skeletal muscle activity of lower limb associated with surface and deep layers.

Some, physiological factors such as blood flow distribution, glucose transporter and plasma metabolite affect the glucose uptake of working skeletal muscle during exercise task[7,8]. Present study revealed that glucose uptake by the skeletal muscles of deep layer (VI and VMd) was higher than skeletal muscles of surface layer (VL and VMs) of thigh (quadriceps group) at rest and after exercise (55% $\dot{V}O_{2max}$). This variation in glucose uptake of skeletal muscle of thigh associated with surface and deep layers might be caused by the effects of blood flow distribution or nerve function.

In another, it was found that [^{18}F]FDG uptake (SUV) of exercise to rest ratio by the surface muscles (VL and VMs) was higher than deep muscles (VI and VMd), suggesting of higher glucose uptake of skeletal muscles of surface layer than skeletal muscles of deep layer of quadriceps group of thigh after exercise (55% $\dot{V}O_{2max}$). We were able to confirm that the functional levels of skeletal muscles of surface and deep layers of thigh (quadriceps group) serve as dynamic homeostatic control, and exercise may adjust uniform energy distribution.

[^{18}F]FDG and PET is a useful imaging technique in evaluation of skeletal muscle activity of lower limb associated with surface and deep layers. The results of this investigation may contribute to rehabilitation science.

References

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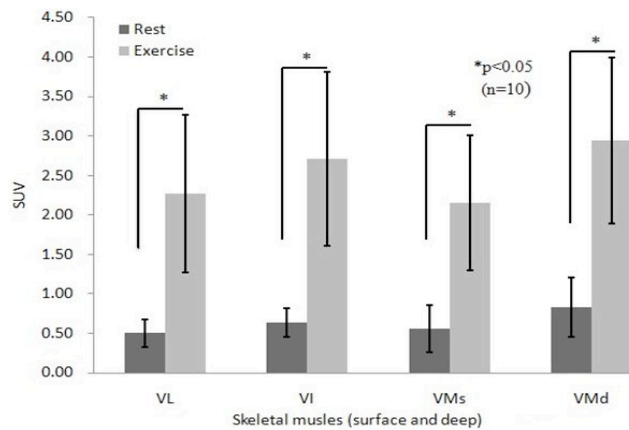
Figure 1. Glucose uptake (standardized uptake value, SUV) in the thigh skeletal muscles at rest and after exercise (55% $\dot{V}O_{2max}$). The x-axis shows the respective muscles (surface and deep) and the y-axis shows the SUV values.

VL = vastus lateralis, VI = vastus intermedius, VMs = vastus medialis surface and VMd = vastus medialis deep.
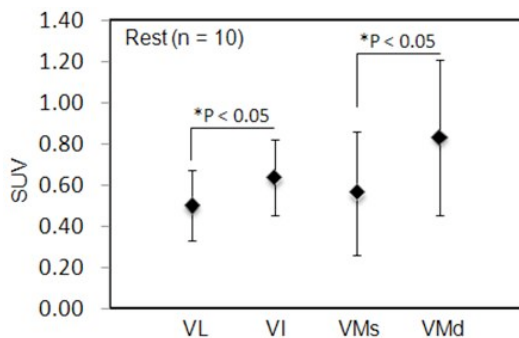

Figure 2. Glucose uptake (standardized uptake value, SUV) in the thigh skeletal muscles (surface and deep) at resting condition. The x and y-axis show the skeletal muscles and SUV values, respectively.

VL = vastus lateralis, VI = vastus intermedius, VMs = vastus medialis surface and VMd = vastus medialis deep.
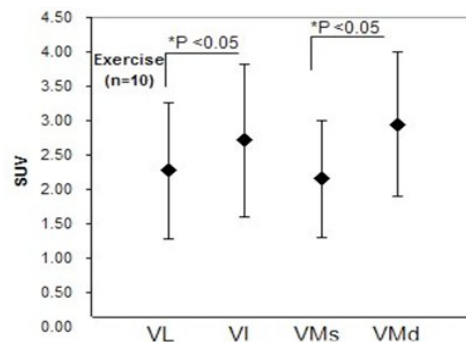

Figure 3. Glucose uptake (standardized uptake value, SUV) in the skeletal muscles of thigh (surface and deep) after exercise (55% $\dot{V}O_{2max}$). The x and y-axis show the skeletal muscles and SUV values, respectively.

VL = vastus lateralis, VI = vastus intermedius, VMs = vastus medialis surface and VMd = vastus medialis deep.
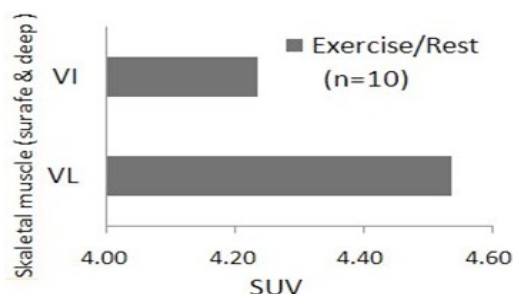

Figure 4. SUV (standardized uptake value) of exercise to rest ratio of VL (surface) and VI (deep) skeletal muscles of thigh.

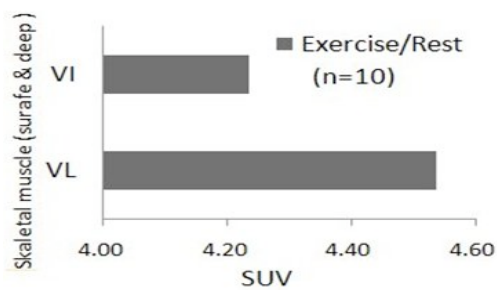VL = vastus lateralis, VI = vastus intermedius.

Figure 5. SUV (standardized uptake value) of exercise to rest ratio of VMs (surface) and VMd (deep) skeletal muscles of thigh.

VMs= vastus medialis surface, VMd = vastus medialis deep.