Relationship between whole body oxygen consumption and skeletal muscle glucose metabolism during walking in older adults: FDG PET study

Hiroyuki Shimada¹, Daina Sturnieks², Yosuke Endo³, Yuichi Kimura⁴, Takao Suzuki⁵, Keiichi Oda⁶, Kenji Ishii⁶ and Kiichi Ishiwata⁶

¹Section for Health Promotion, Department of Health and Medical Care, Center for Development of Advanced Medicine for Dementia, National Center for Geriatrics and Gerontology, Aichi, Japan, ²Prince of Wales Medical Research Institute and School of Medical Sciences, University of New South Wales, Sydney, Australia, ³Honda R&D Co., Ltd., Fundamental Technology Research Center, Saitama, Japan, ⁴Image Analysis Team, Biophysics Group, Molecular Imaging Center, National Institute of Radiological Sciences, Chiba, Japan, ⁵Research Institute, National Center for Geriatrics and Gerontology, Aichi, Japan, ⁶Positron Medical Center, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan

ABSTRACT. Background and aims: The purpose of this study was to determine the relationship between whole body energy metabolism measured as oxygen consumption (VO₂) and local muscle activity measured by positron emission tomography (PET) and [¹⁸F]fluorodeoxyglucose (FDG). Methods: Ten community-dwelling older women (73-83 yrs) had FDG PET and VO₂ measured while walking at a comfortable speed. Results: A significant positive correlation was found between VO₂ and FDG uptake in the biceps femoris (r=0.83), gluteus minimus (r=0.67), gluteus medius (r=0.77) and pelvis section muscles (r=0.76). The subjects who showed high FDG uptake in the hip muscle group had significantly higher VO₂ while walking, compared with subjects without high FDG uptake in the hip muscles. Conclusions: These results indicate that FDG PET provides an index which reflects whole body energy metabolism during walking, and revealed that excess muscle activity in the hip muscles during walking plays a key role in increasing VO₂ in older adults.

INTRODUCTION

Restriction in outdoor activities has a strong association with deterioration of physical function in healthy or frail older people (1-6). In Japan, more than 50% of older people aged 65-69 years leave their house at least once a day, but this rate declines with age to less than 40% of people aged 70-79 years and 30% of people 80 years and over (7). A two-year prospective study in Japan showed an association between a low frequency of going outdoors at baseline and incident disability in initially non-disabled elderly individuals. The adjusted risks of incident mobility impairment (odds ratio (OR)=4.02) and disability in instrumental activities of daily living (OR=2.65) were significantly higher in older individuals who went outdoors once a week or less, compared with an active subgroup who went outside once a day or more often (4). Outdoor activity is probably restricted by difficulties in walking for extended periods (8).

Previous studies have recognized that oxygen consumption (VO₂), which provides an index of walking efficiency, is greater in older adults than young adults while walking, even when no gait impairment is present (9-12). Whole body metabolic cost reflects mainly mechanical energy cost due to muscle activity during exercise. Aging is associated with relatively greater muscle activity and increased levels of coactivation of opposing muscles during physical activities (13, 14). Older adults have been shown to work at a higher level of effort, relative to their maximum capability, which contributes to difficulties in performing activities of daily living (14).
Knowledge about muscle activity during exercise was gathered by surface electromyography (EMG) or kinetic analysis of walking. However, these techniques have some limitations to our understanding of the etiology of metabolic cost, as they do not measure the activities of deep layer muscles and isolated synergistic muscles, respectively. In recent years, positron emission tomography (PET) and [18F]fluorodeoxyglucose (FDG), a technique which provides images of the spatial distribution of skeletal muscle metabolism, have been used to monitor muscle activity during exercise (15-22). FDG PET enables the observation of continuous activity, such as extended walking, because it can measure cumulative muscle metabolism during unrestricted physical activities.

FDG is taken up by cells from the circulatory system through glucose transporters 1-4 and is phosphorylated into FDG-6-phosphate by hexokinase, the first enzyme in the glycolytic pathway (23). As FDG-6-phosphate is a poor substrate for glucose-phosphate isomerase, which converts glucose to fructose, it escapes from further metabolism, is trapped within the cells (24), and can thus be detected by gamma rays (25). FDG has a half-life of 110 min, which makes it ideal for observing cumulative muscle activity during endurance exercise. FDG PET can also be used to compare task-specific muscle activity, because FDG uptake is closely correlated with exercise intensity in healthy adults (17, 26, 27). For example, Pappas et al. reported that a five-fold increase in resistance during elbow flexion increased FDG uptake in the biceps brachii by a factor of 4.9 (26). Our previous study confirmed that FDG PET is an appropriate method to measure muscle activity during walking (19). However, the relative contribution of different muscle groups to whole body energy consumption during walking is not known. Understanding whole body energy consumption and its relationship with muscle activity during walking in the elderly will help healthcare practitioners who prescribe specific muscular endurance training to increase walking endurance capacity in older people.

The purpose of this study was to examine the relationship between lower-limb muscle activity measured by FDG PET and whole body energy metabolism measured as VO2 during walking in older women. During the propulsive phase of walking in young adults, the ankle plantar flexors perform most of the work (28). In contrast, in older adults, the hip and ankle muscles perform the same amount of work (28), because the power-generating capacity of the ankle plantar flexors is impaired (29). In fact, our previous FDG PET study revealed that older adults walked with greater muscle activity in hip muscles than young adults (22). We hypothesized that the activity of the hip muscles causes an increased oxygen demand of the body during walking in older adults.

METHODS

Subjects

Ten community-dwelling older women (average age 77.8, 73-83 yrs) participated in this study. Their height and weight (mean±standard deviation (SD)) were 148.8±5.1 cm and 51.0±7.4 kg, respectively. Inclusion criteria were women aged 70 years and older. Exclusion criteria included symptomatic cardiovascular disease, hypertension (systolic blood pressure >160 mmHg or diastolic blood pressure >100 mmHg), heart failure, diabetes mellitus, disability in instrumental activities of daily living (ADL) or disability in gait capacity. Disability in instrumental ADL was defined as an impairment in at least one subscale of the Tokyo Metropolitan Institute of Gerontology index (30). Gait capacity was defined as <90 m/min in 5-m maximum walking speed test or a self-reported discontinuous 1000 m walk. All subjects had no other diseases and were independently mobile outdoors.

Subjects were fully informed about the purpose, nature and potential risks of the experiment. They gave their written, informed consent before participating in the study. The Ethics Committee of the Tokyo Metropolitan Institute of Gerontology approved the study protocol, which conforms to the Declaration of Helsinki.

Measurements

FDG PET and VO2 were measured in each subject during exercise on separate days within one week. Walk distances were measured during both FDG PET and VO2 measurements, and average walking speed was calculated for each. Subjects refrained from consuming food or drink containing sugar for at least six and two hours before the FDG PET or VO2 measurements, respectively. Subjects refrained from strenuous physical activity for at least two days before both measurements. A venous blood sample was taken at the time of FDG PET and VO2 measurements, to determine blood glucose level and HbA1C.

FDG PET. Subjects walked at a comfortable speed on a 940-m circular indoor track, marked every 1-m, for 50 minutes while distance was measured. The protocol involved preparatory walking for 30 minutes, followed by an intravenous injection of FDG, then another 20 minutes of walking, followed by a PET scan. The preparative walking was performed to obtain vivid PET images for reducing muscle glycogen before FDG injection. Glucose uptake is increased following exercise, presumably as a direct consequence of decreased muscle glycogen content (31). PET scans were started 49-59 minutes after injection of FDG on a Headtome-V device (Shimadzu Co., Kyoto, Japan) in the two-dimensional mode. PET scans of the area from the iliac crest to the ankle were made in 5 or 6 overlapping bed positions with a 7-minute emission time per position, with simultaneous attenuation correction. Images were reconstructed by a filtered-back-projection al-