

## CASE REPORT

# Glucose uptake of the spinal cord in patients with multiple sclerosis detected by $^{18}\text{F}$ -fluorodeoxyglucose PET/CT after walking

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**Study design:** Case report.

**Objectives:** To determine [ $^{18}\text{F}$ ]-fluorodeoxyglucose ( $^{18}\text{F}$ -FDG) uptake in the spinal cord of patients with multiple sclerosis (MS) was compared with healthy controls after treadmill walking.

**Setting:** Colorado Translational Research Imaging Center, University of Colorado School of Medicine, Aurora, CO, USA.

**Methods:** Eight mildly disabled patients with MS and eight healthy subjects performed 15 min of treadmill walking at a self-selected pace. Two minutes after walking began, each participant was injected with  $\approx 8$  mCi of [ $^{18}\text{F}$ ]-FDG into a catheter inserted into an antecubital vein. Immediately after walking positron emission tomography/computed tomography (PET/CT) imaging was performed on each participant. Images were analyzed to determine [ $^{18}\text{F}$ ]-FDG uptake within the spinal cord.

**Results:** Total spinal cord [ $^{18}\text{F}$ ]-FDG uptake was lower in patients with MS ( $1.48 \pm 0.36$  and  $1.55 \pm 0.33$ ,  $P = 0.04$ ), specifically within the thoracic ( $1.32 \pm 0.27$  and  $1.41 \pm 0.24$ ,  $P < 0.01$ ) and the lumbar ( $1.58 \pm 0.40$  and  $1.89 \pm 0.43$ ,  $P = 0.04$ ) spinal cord regions.

**Conclusion:** This is the first report of [ $^{18}\text{F}$ ]-FDG uptake in the spinal cord of patients with MS. The decreased [ $^{18}\text{F}$ ]-FDG uptake within the thoracic and lumbar spinal cord regions could be associated with autonomic nervous system and walking/motor dysfunctions that are often seen in patients with MS. PET/CT imaging with [ $^{18}\text{F}$ ]-FDG is highly useful for the demonstration of impaired glucose metabolism in the spinal cord of patients with MS.

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## INTRODUCTION

Multiple sclerosis (MS) is a progressive neurodegenerative disease affecting the central nervous system. Positron emission tomography (PET) and computed tomography (CT) are effective techniques to measure the metabolic activity of tissues at rest and after exercise. Using these techniques glucose uptake in tissues can be measured with the PET glucose analog, [ $^{18}\text{F}$ ]-fluoro-deoxy-glucose ( $^{18}\text{F}$ -FDG). A recent investigation showed lower [ $^{18}\text{F}$ ]-FDG uptake within the brain<sup>1</sup> of patients with MS, but there are no published studies on [ $^{18}\text{F}$ ]-FDG uptake within the spinal cord of these patients. The purpose of this study was to determine whether uptake of [ $^{18}\text{F}$ ]-FDG is also lower in the spinal cord of mildly disabled patients with MS. Knowledge about possible variations of [ $^{18}\text{F}$ ]-FDG uptake in the spinal cord of patients with MS may provide additional information related to variables of disability.

## CASE REPORT

Eight mildly disabled, but ambulatory, patients with relapsing remitting form of MS and eight healthy age-/sex-matched participants performed 15 min of treadmill walking at a self-selected comfortable speed. Two minutes after walking began, each participant was injected with  $\approx 8$  mCi of [ $^{18}\text{F}$ ]-FDG. PET/CT imaging was performed and image analysis was conducted using Analyze 11.0 (Mayo Clinic,

Rochester, NY, USA). Standardized uptake values ( $\text{SUV}_{\text{mean}}$ ) were calculated at mid-vertebral body level,  $\text{C}_1\text{--L}_1$ .<sup>2</sup> Spinal cord regions were defined as: whole  $\text{C}_1\text{--L}_1$ , cervical  $\text{C}_1\text{--C}_7$ , thoracic  $\text{T}_1\text{--T}_{10}$ , lumbar  $\text{T}_{11}\text{--T}_{12}$ , sacral  $\text{L}_1$ , to account for the mismatch between vertebral body and spinal cord segments.<sup>3</sup> Patients with MS walked at a slower self-selected speed than the healthy participants and [ $^{18}\text{F}$ ]-FDG uptake was lower throughout the whole spinal cord ( $1.48 \pm 0.36$  and  $1.55 \pm 0.33$ ,  $P = 0.04$ ) and specifically within the thoracic ( $1.32 \pm 0.27$  and  $1.41 \pm 0.24$ ,  $P < 0.01$ ) and lumbar ( $1.58 \pm 0.40$  and  $1.89 \pm 0.43$ ,  $P = 0.04$ ) regions.  $P$ -values were based on independent  $t$ -tests and Mann–Whitney  $U$ -test according to Kolmogorov–Smirnov tests of normality (Table 1) (Figures 1 and 2). Disability levels were determined by patient-determined disease step scores ( $1.9 \pm 1.6$ ) that correspond to Expanded Disability Status Scale<sup>4</sup> ( $3.0 \pm 1.7$ ). Images were analyzed retrospectively from a previous investigation looking at differences in [ $^{18}\text{F}$ ]-FDG uptake in patients with MS after walking.

## Imaging protocol

The PET/CT scans were performed with a Philips Hybrid Gemini TF 64 scanner (Philips Healthcare, Cleveland, OH, USA). The PET images were acquired in list mode and in three-dimensional mode, utilizing time-of-flight technology. The PET scans were immediately

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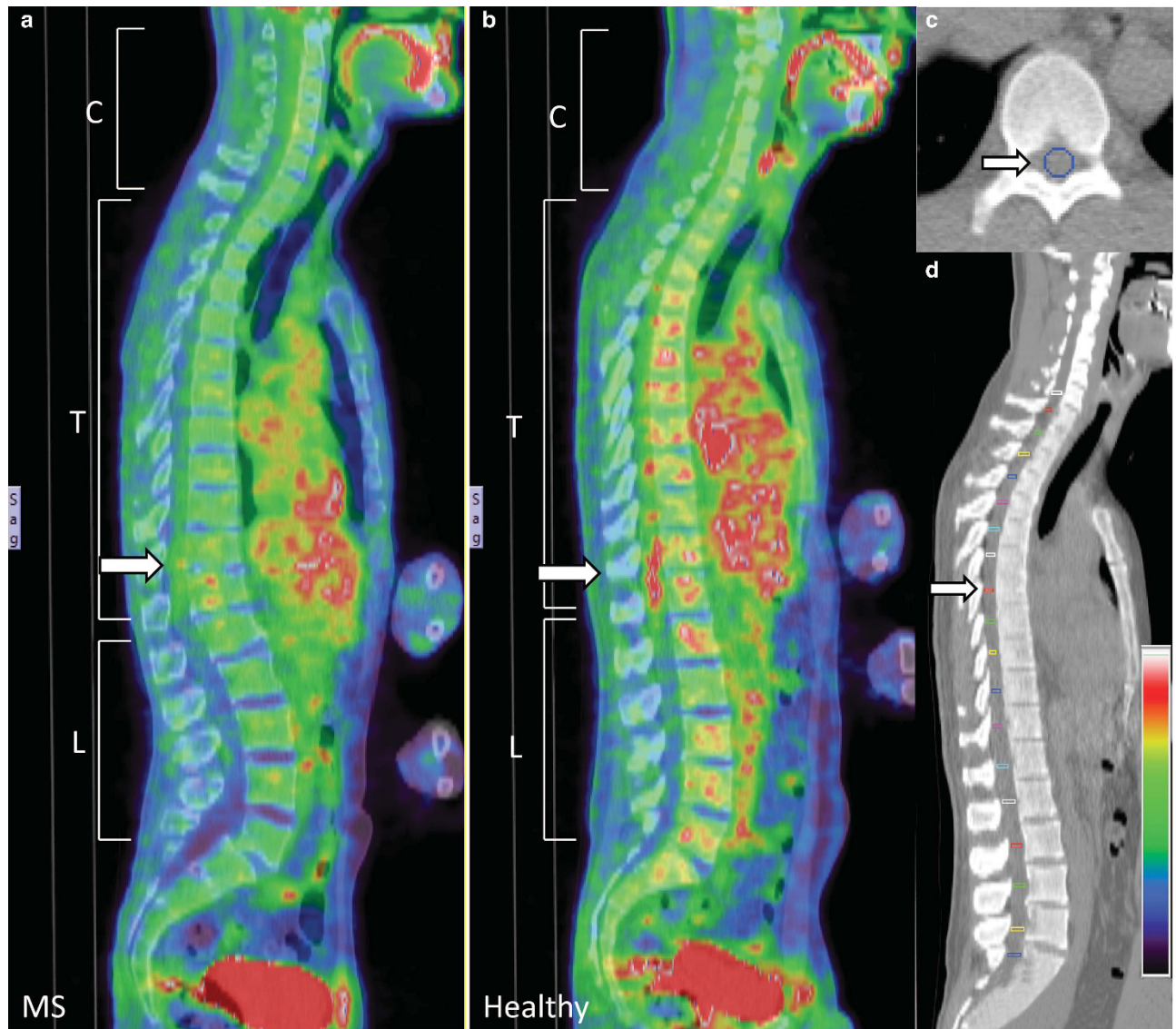
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**Table 1** Participant walking speed and spinal cord standard uptake values (SUV)

Group	Walking speed ( $m s^{-1}$ )	Whole	Cervical	Thoracic	Lumbar	Sacral
MS	1.1 ± 0.2	1.48 ± 0.36	1.72 ± 0.30	1.32 ± 0.27	1.58 ± 0.40	1.25 ± 0.43
CON	1.4 ± 0.1	1.59 ± 0.33	1.69 ± 0.28	1.41 ± 0.24	1.89 ± 0.43	1.27 ± 0.22
P-value	0.01	0.037	0.60	0.003	0.04	0.33

Abbreviations: CON, control; MS, multiple sclerosis.  
Values represent mean ± s.d.

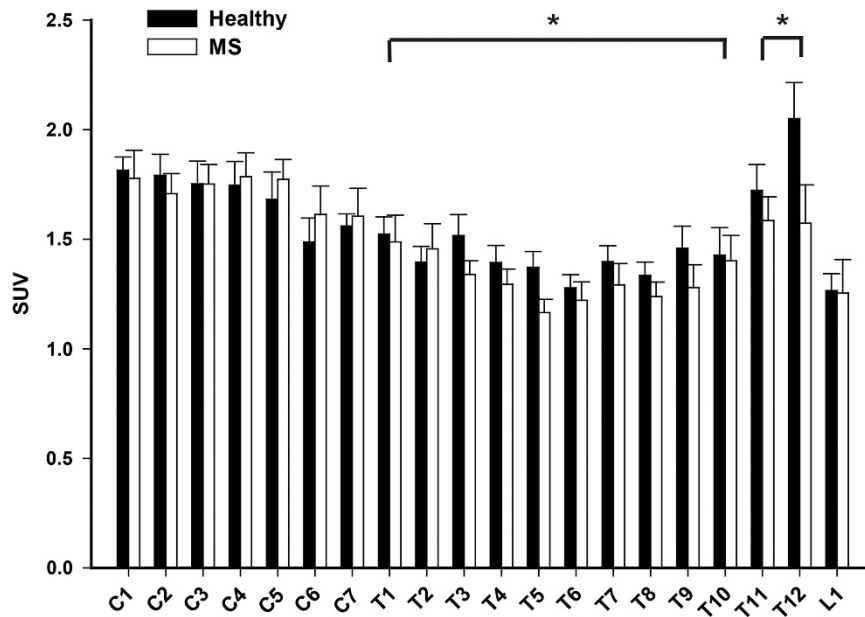


**Figure 1** PET/CT images for a patient with MS (a) and a healthy participant (b). Increased [ $^{18}F$ ]-FDG uptake is indicated by red and lower intensity indicated by blue. Note the difference between  $T_{11}$  and  $T_{12}$  and the reduced ( $^{18}F$ )-FDG uptake in this area in the patient with MS. (c) A transverse image from the CT scan shows a region of interest (ROI) drawn at the mid-vertebral body level. (d) A sagittal view of the CT image demonstrating ROI drawn throughout the spinal cord at the mid-vertebral body level.

preceded by CT scans for attenuation correction and for anatomical reference. Consecutive scans were performed to maintain co-registration. The data sets were reconstructed using an iterative method (ordered subset expectation maximization) with 33 subsets and 3 iterations with a Gaussian filter.

## DISCUSSION

The spinal cord is the link between the brain and peripheral effector organs and muscles; however, it can be overlooked in disease diagnosis/progression and rehabilitative strategies in patients with MS. Our main finding was lower [ $^{18}F$ ]-FDG uptake within the whole



**Figure 2** Average SUV<sub>mean</sub> ± s.e. at each vertebral level for patients with MS and healthy controls. [<sup>18</sup>F]-FDG uptake is lower between C<sub>1</sub> and L<sub>1</sub> as well as from T<sub>1</sub> to T<sub>10</sub> and T<sub>11</sub> to T<sub>12</sub>.

spinal cord and specifically within thoracic and lumbar spinal cord segments. Sympathetic branches of the autonomic nervous system (ANS) and motor neuron pools of the lower limbs are located within these regions. ANS dysfunction is one of the most common side effects in MS. Furthermore, failure to activate central pattern generators and lower motor neuron pools during walking could be contributing to the impaired walking ability of patients with MS. Figure 1 displays high activity of the lumbar spinal cord within the healthy controls but is absent in patients with MS. Alterations in glucose metabolism/uptake might be a contributing factor to ANS side effects and alterations in walking ability, but there is no published literature regarding this.

Cheng *et al.*<sup>5</sup> demonstrated the use of [<sup>18</sup>F]-FDG in the diagnosis of spinal cord neuropathies. Their investigation showed the usefulness of this technique in investigating nervous system dysfunctions and functional outcomes. Applying these methods in the study of MS could provide useful data in determining changes in disability associated with ANS and peripheral effectors, allowing for new estimates/predictions of disability in this population. Further studies are needed to determine whether the lower [<sup>18</sup>F]-FDG uptake in the spinal cord during walking is due to the reduced walking speed of patients with MS or whether it is pathological to their disease. Studies at rest and during exercise are also needed to correlate these results with disability levels, motor performance, age, sex, duration and disease type.

## CONCLUSION

These data provide the justification to continue work on investigating the metabolic activity of the spinal cord, at rest and during exercise,

and how it affects measures of disability in diseased populations, especially MS. With an extended knowledge on this subject, it is possible that new drug and rehabilitative strategies may improve the condition of common side effects in MS.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## ACKNOWLEDGEMENTS

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