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PET-CT of the Normal Spinal Cord in Children

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Abstract

Rationale and Objectives—To assess the correlation between age and spinal cord metabolic activity in children using positron emission tomography-computed tomography.

Materials and Methods—The cohort included 128 children imaged from January 2003 through April 2007, excluding those with spinal disease. Using axial images we subjectively graded as minimal, moderate or intense, the fluorodeoxyglucose activity in the pons and three cervical, three thoracic, and two lumbar spinal cord levels. From regions of interest at each level, we determined the maximum standardized uptake value. Patients were grouped by age: Group 1, < 5 years; Group 2, 5 to < 10 years; Group 3, 10 to < 15 years; and Group 4, 15 < 22 years. We compared subjective grade and standardized uptake values at each level and for each level between age groups. Alpha was set at 0.0046 based on the Bonferroni correction for multiple comparisons.

Results—There were 16 patients in Group 1, 19 in Group 2, 33 in Group 3, and 60 in Group 4. Subjective grade and standardized uptake values were higher in the pons, mid cervical and low thoracic areas than elsewhere in all age groups. Subjective grade significantly increased with age in the cervical and thoracic cord ($P < 0.0005$). Standardized uptake values in the pons and all cord levels significantly increased with increasing age ($P = 0.0008$).

Conclusions—In children, metabolic activity of the spinal cord increases with age. On positron emission tomography, the cord can appear intensely avid in the mid cervical and low thoracic areas.

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Keywords

positron emission tomography-computed tomography; spinal cord; children

Introduction

This study was prompted by the observation of substantial variability between children in spinal cord fluorodeoxyglucose (FDG) uptake on positron emission tomography-computed tomography (PETCT) performed at our large children's cancer hospital. We also noted variability in FDG uptake between the cervical, thoracic, and lumbar spinal cord levels. There is no literature describing the PET-CT appearance of the spinal cord during childhood development. Therefore, to characterize the FDG metabolic activity of the normal, developing spinal cord, on PET-CT, we sought to determine whether the subjective appearance or standardized uptake value (SUV) of the spinal cord correlated with patient age or spinal cord level in this patient population. Such information may help distinguish benign from pathologic spinal cord activity and may be useful in monitoring the response of the cord to therapies aimed at nerve root regeneration.

Materials and Methods

Patient Selection

We searched our diagnostic imaging database for patients who underwent PET-CT from January 2003 to April 2007. After institutional review board waiver of informed consent, and in compliance with the Health Insurance Portability and Accountability Act of 1996, we reviewed their medical records and recorded demographics, primary diagnosis, date of diagnosis, and date of initiation of chemotherapy or radiation therapy. To avoid the potential effect of chemotherapy or radiation therapy on the spinal cord, we included only PET-CTs obtained before the initiation of therapy. Patients who had more than one PET-CT were included only once, and the first PET-CT was used. Patients with tumors involving the spine or spinal canal were excluded.

PET-CT scanning parameters and image review

Patients were instructed to fast for 4 or more hours before receiving an intravenous (IV) injection of 0.15 mCi/kg of FDG. Patients receiving total parenteral nutrition or IV solutions containing dextrose or glucose had those solutions withheld for a minimum of 4 hours before FDG administration. Serum glucose levels were obtained from patients who were diabetic or had received IV fluids containing dextrose or glucose within 4 hours of the scheduled FDG injection. Such patients were not administered FDG if the serum glucose level was above 200 mg/dl. After injection of FDG, patients lay on a cart in a quiet room, and the patients and guardians were instructed to have the patients refrain from talking, chewing, and using their arms and legs. Approximately 60 minutes after FDG administration, PET-CT was performed on a Discovery LightSpeed scanner (GE Healthcare Technologies, Waukesha, WI). The CT was obtained with a maximum of 90 milliamperereconds (adjusted for body weight), 120 kiloelectron-volts peak, and slice thickness of 5 mm, without IV or oral contrast unless clinically indicated. Two-dimensional positron emission imaging was performed for 5 minutes per bed position. PET and CT images were obtained from the top of the skull through the toes in most patients and reviewed at a Xeleris workstation (GE Healthcare Technologies) in reconstructed axial, coronal, and sagittal planes. Patients needing sedation were sedated for scanning only and not during the FDG uptake phase.

To obtain representative data from throughout the spinal cord, we examined the second, fourth, and seventh cervical (C2, C4, and C7); the second, fourth, eighth, 11th, and 12th thoracic (T2, T4, T8, T11, and T12); and the first lumbar (L1) vertebral levels. To ensure that the entire length of the cord was evaluated, we also examined the pons and filum terminale at the fourth lumbar (L4) level. PET image intensity was standardized for each patient by using a consistent window setting across all images. On axial PET images, the FDG avidity of the pons and spinal cord were compared with that of the cervical paraspinal muscle and subjectively graded as 1) minimal if FDG uptake was ≤ 1.5 times that of the paraspinal muscle, 2) moderate if FDG uptake was > 1.5 times but ≤ 3.0 times that of the paraspinal muscle, or 3) intense if FDG uptake was > 3 times that of the paraspinal muscle. The maximum SUV of the pons and each spinal cord level was determined by drawing a region of interest (ROI) around the structure of interest on the CT image, avoiding the margins of the skull base and vertebrae (Fig. 1A). The ROI was then copied to the corresponding PET image (Fig. 1B).

Statistical Analysis

Patients were placed into one of four age groups: 1) < 5 years, 2) 5 years to < 10 years, 3) 10 years to < 15 years, and 4) 15 years to < 22 years. The Shapiro-Wilk test was used to test the normality of continuous variables, and in many cases the data were found not to be normal. The differences in the subjective grade and maximum SUVs between age categories in the pons and each spinal cord level were investigated using the Kruskal-Wallis test. Alpha was set at 0.0046 based on the Bonferroni correction for multiple comparisons [1].

Results

Patient Characteristics

One hundred twenty-eight patients met the inclusion criteria. There were 74 males and 54 females ranging in age from 1 to 21 years (mean, 12.9 years). By age, 16 patients were in Group 1, 19 in Group 2, 33 in Group 3, and 60 in Group 4. Primary diagnoses were Hodgkin lymphoma (n=58), rhabdomyosarcoma (n=14), non-Hodgkin lymphoma (n=9), Ewing sarcoma family of tumor (n=8), osteosarcoma (n=6), germ cell tumor (n=5), neuroblastoma (n=5); Wilms' tumor, malignant melanoma, Langerhans' cell histiocytosis, nasopharyngeal carcinoma, Sertoli-Leydig cell tumor, and synovial sarcoma (n=2 each); and hepatoblastoma, clear cell sarcoma, leiomyosarcoma, adrenocortical carcinoma, desmoplastic small round cell tumor, hepatocellular carcinoma, desmoid tumor, neuroepithelial sarcoma, high-grade sarcoma (not otherwise specified), renal cell carcinoma, and malignant peripheral nerve sheath tumor (n=1 each; tumor located in the inguinal canal). These primary malignancies do not have a propensity to metastasize to the spinal cord.

PET-CT assessments

As shown in Figures 2 and 3, by visual assessment, FDG activity increased with age in the pons and all spinal cord levels. These differences were significant in the cervical and thoracic areas (all $P \leq 0.0005$). Results of SUV measurements are shown in Figure 4. SUVs significantly increased with age in the pons and all spinal cord levels (all $P \leq 0.0008$). SUV measurements were highest in the pons (median = 5.1), followed by the C4, T11, and T12 spinal cord levels (all three medians = 1.6) (Fig. 5).

Discussion

We found that, by both subjective and SUV assessments, the metabolic activity of the normal pons and all spinal cord levels in children significantly increases with increasing age. Our findings agree with others who have assessed cortical brain, brain stem and spinal cord

evoked potentials in healthy children [2–5]. Those investigators found that conduction velocities from peripheral nerves to the brain or brain stem increase with increasing age. The increases in conduction velocity parallel normal increases in spinal cord length and fiber myelination that occur during childhood development [2,3]. Importantly, during childhood, the spinal cord demonstrates plasticity, or changes in evoked potentials, in response to descending activity from the brain (learned motor skills) and peripheral input from the environment, such as painful stimuli [2–7]. In addition to these changes, Moskowitz and colleagues [8] found significant increases in cervical and thoracic spinal cord cross-sectional area and volume in children, measured on magnetic resonance images, with increasing age, height, and weight. These investigators found that increases in cord volume were more closely correlated with patient age than increases in cross-sectional area. This finding suggests that the longitudinal growth of the cord during childhood development is greater than cross-sectional growth. We have shown that the spinal cord also develops increasing metabolic activity that may coincide with acquisition of learned motor activity, linear spinal cord growth, and increasing fiber myelination.

We found that, in all age groups, both the subjective and SUV assessments of FDG avidity in the mid cervical and lower thoracic cord showed significantly greater metabolic activity than other areas of the cord and can appear intensely FDG avid. These cord levels have the largest cross-sectional areas and are the neuronal origins of upper and lower extremity motor and sensory neurons [9]. Therefore, these levels of the spinal cord would be expected to be more metabolically active than other areas.

Our study has several limitations. We had a somewhat small sample size of two age groups (< 5 years, n=16; and 5 years to < 10 years, n=19). Also, the selection of age groups for our statistical analysis may not fully reflect physiological changes that occur at other time points during childhood development. Patients may have moved their extremities during the FDG uptake phase which might result in an increase in FDG uptake within the spinal cord. However, at our institution, we attempt to minimize patient activity by informing patients and their guardians of the need to have the patient remain quiet during the FDG uptake phase, and we provide a minimally stimulating environment. Furthermore, patients are monitored using a closed circuit television system during the uptake phase to assure minimal physical activity. An additional study limitation is the potential for incomplete recovery, that is, an underestimation of FDG activity, from regions of the spinal cord with smaller cross-sectional areas relative to those with larger areas. We expect this to have been a minor limitation, however, because changes in cross-sectional area of the spinal cord in children have previously been shown to be quite small [8,10,11] and thus unlikely to result in substantial underestimations of true FDG activity from those of smaller caliber. Because our study subjects had untreated hematologic and solid malignancies, it is possible that the distribution of FDG to the spinal cord was diminished due a relative flux of FDG to the primary tumor site. However, others have found that administration of granulocyte colony stimulating factor to women with breast cancer did not significantly affect the ability to detect changes in primary tumor SUV that correlated with the pathologic assessment of tumor response to therapy [12]. Therefore, within our cohort, we would not expect FDG avidity of the primary tumor to have significantly affected either the subjective or SUV assessment of spinal cord FDG activity.

In conclusion, we have shown that the FDG activity and PET-CT appearance of the normal spinal cord in children is related to patient age and probably reflects spinal cord plasticity and growth that occur during development. In children, the normal spinal cord can appear very intense, especially in the mid cervical and low thoracic areas where the brachial and lumbar nerve plexi arise. An awareness of the normal metabolic changes that occur within the spinal cord during childhood development, as well as the differences in metabolic

activity at each spinal cord level, should help in distinguishing normal from abnormal findings on PET-CT in this patient population. In the future, FDG PET-CT assessment of spinal cord metabolic activity may prove to be a valuable adjunct in the management of cord injury and in monitoring the efficacy of interventions aimed at nerve root regeneration.

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A

B

Fig. 1. For standardized uptake value determination, we first drew a region of interest (ROI) on (A) the computed tomography image, avoiding the margins of the skull base or vertebra. (B) The ROI was copied to the positron emission tomography image, and the maximum SUV was determined.

Fig. 2.

This graph shows results of the subjective assessment of fluorodeoxyglucose avidity in the pons and each spinal cord level for each age group. Note the increase in perceived activity with increasing age at each level. These increases were significant at all levels except in the pons and lumbar areas.

A

B

c

D

E

F

G

H

Fig. 3. Representative examples of lower cervical (top row; 3A–D) and lower thoracic (bottom row; 3E–H) spinal cord positron emission tomography-computed tomography images from each of four age groups. Arrows denote the spinal cord. Note the increase in fluorodeoxyglucose activity within the cord with increasing age.

Fig. 4.

This graph shows the median of maximum standardized uptake values (SUVs) at each spinal cord level for each age group. Note the increase in SUV with increasing age for each level. These increases were significant in the pons and all cord levels.

Fig. 5.

This bar graph shows that the median of maximum standardized uptake values (SUVs) was higher in the pons, lower cervical, and low thoracic areas than elsewhere.