Independent spinal cord atrophy measures correlate to motor and sensory deficits in individuals with spinal cord injury

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Introduction

MRI can effectively detect lesions on the spinal cord but it has been difficult to find sensitive markers for specific functional deficits. Spinal cord atrophy due to loss of white matter can be measured as the transversal area at a given level of the spinal cord distal to the focal lesion and correlations to global functional scores has been reported in multiple sclerosis [Losseff et al, Brain, 1996]. We hypothesize that motor and sensory deficits will be accompanied by atrophy along different axes of the spinal cord due to the location of the main sensory tracts in the dorsal column and motor tracts mainly in the lateral columns, see figure 1. One motor and two sensory qualities as well as walking ability was evaluated in our SCI group and correlated to the respective measures. To accurately extract quantitative measures from the images, gradient nonlinearity correction was applied and long-term inter-scan reproducibility was assessed.

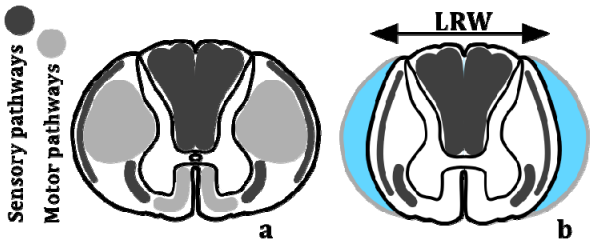

figure : a) the approximate locations of some sensory and motor pathways of the human spinal cord at the level of C2. Hypothetic situations with atrophy in only motor tracts (b) and only sensory tracts (c) may result in decrease in different widths of the spinal cord. Any combination of b) and c) is plausible as a result of a real lesion.

Methods

We enrolled 19 individuals with incomplete chronic SCI (15 cervical, 3 thoracic and 1 lumbar) and 16 healthy controls. All participants were scanned using a MPRAGE sequence (TR = 1540 ms, TE = 3.93 ms, flip angle 9°) on a Siemens Trio 3T system using a 1ch head coil. The sequence covered the whole brain and the upper cervical spinal cord. Two of the healthy controls were scanned 7 and 12 times respectively at different days spread over 18 months. Patients underwent the International Standards for Neurological Classification of Spinal Cord Injury including a motor score (MS) based on the collective muscle strength of the extremities, light touch sensory score (LTSS) and pinprick sensory score (PPSS) [Marino et al, J. Spinal Cord Medicine, 2003]. The patients also performed a 6 minute walking test (6MWT) where the total walking distance over 6 minutes was recorded [van Hedel et al, Arch. Phys. Med. Rehab., 2005]. Images were corrected for gradient nonlinearities using in-house software based on previous work [Jovicich et al NeuroImage, 2006] and verified in an fMRI study [Skimminge et al, ISMRM 2009]. A transversal spinal cord mask was created according to earlier work on multiple sclerosis [Losseff et al, Brain, 1996] but with the spinal process of C2 as caudal landmark instead of the C2/C3-disk. Spinal cord area (SCA), left-right width (LRW, see figure b)) and antero-posterior width (APW, see figure c)) were extracted from the mask and used for the statistical analysis.

Results

Reproducibility: As a consequence of the gradient nonlinearity correction, the coefficient of variance for the inter-scan variability in the two subjects scanned over 18 months was reduced from 8.05% to 1.01% for SCA, 4.33% to 0.95% for LRW and 4.03% to 0.93% for APW. The mean SCA for the whole healthy control group was estimated to 74.0 mm^2 without correction compared to 88.1 mm^2 for the corrected images.
Patients vs controls: The group with SCI had a significantly lower SCA compared to the healthy group (mean 67.3 mm^2 vs 88.1 mm^2, $p<0.001$), APW (mean 7.63 mm vs. 8.95 mm, $p<0.001$) and LRW (12.3 mm vs. 13.1 mm, $p=0.04$).

r/p-value	LTSS	PPSS	MS	6MWT
SCA	0.65/0.003*	0.72/0.0008*	0.53/0.02*	0.58/0.008*
APW	0.66/0.002*	0.75/0.0003*	0.30/0.2	0.42/0.07
LRW	0.07/0.8	0.03/0.8	0.59/0.01*	0.42/0.08

Functional correlations: Results are presented in the table. SCA was significantly correlated with all functional parameters. APW was correlated to LTSS and PPSS but not MS. LRW was correlated to MS but not LTSS and PPSS. 6MWT was stronger correlated to SCA than APW and LRW.

Discussion

We present a robust method for extracting clinically relevant and specific spinal cord atrophy measures to monitor the integrity of sensory and motor pathways independently. As hypothesized and in accordance to the location of the main sensory and motor pathways, sensory qualities were correlated to APW and muscle strength was correlated to LRW. However, it is not surprising that a global measure like the 6MWT is better correlated to SCA than APW and LRW as locomotion involves sensory feedback with central motor command at both supraspinal and spinal level.

The analysis could due to the use of a standard head scan easily be applied to data from existing clinical and experimental protocols without demanding extra scan time with tailored sequences. It is observed that gradient nonlinearity correction provides improved geometrical consistency and excellent reproducibility. In perspective, high resolution imaging combined with more elaborate techniques for shape analysis could possibly be used to decompose even more specific atrophy components in different subsystems within the motor and sensory pathways.