Associations between tissue sodium concentration, age and cross-sectional area in the healthy spinal cord

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Synopsis

Tissue sodium concentration has recently come into the spotlight for a number of neurological conditions, given its potential role in neurodegeneration and due to the advances in MRI technology. This has led to many studies in the brain, but there is a shortage of studies characterising sodium in the spinal cord. Here we use 23Na-MRS to measure sodium in the healthy spinal cord and look at the association between tissue sodium concentrations with age and spinal cord cross-sectional area.

Introduction

Sodium channels have recently undergone intense scrutiny in neuropathology, due to their potential role in axonal conduction, and therefore energy failure and axonal degeneration. 23Na-MRI has been used successfully to study neurological conditions including Multiple Sclerosis (MS) and Alzheimer’s disease1,2. However, evidence of similar applications of 23Na-MRI in the spinal cord (SC) are lacking due to the small size of the structure and the intrinsically low SNR. Here we overcome these challenges to report on sodium concentrations in the SC of a healthy control cohort, together with measures of age and cross-sectional area (CSA), and find whether: a) inter-subject variations in cervical SC sodium in a healthy population are related to age; b) a correlation between spinal cord CSA and sodium exists, given the known effect of age on spinal cord atrophy, and c) if sodium concentration in the cervical SC can be predicted based on age and CSA.

Methods

Subjects: Twenty-four healthy control subjects (age range 23-68y) were recruited. All participants gave informed written consent.

23Na-MRS: All MRI scans were acquired on a 3T Achieva TX system (Philips Healthcare, Best). Sodium data were acquired using fixed-tuned transmit-receive sodium head coil (Rapid, Germany). Using the Q-body coil, 1H images were first acquired in the sagittal and coronal planes for MRS planning. Using ISIS, a voxel (9x12x35mm3) centered at the level of the C2-3 intervertebral disc was planned to measure sodium concentration, TR=300ms, effective TE=0.26ms, n=800 (Figure 1). Saturation pulses were placed to extend over the edges of the voxel to suppress signal from cerebrospinal fluid (CSF) and the effects of any protruding intervertebral disc3. An example sodium spectrum is shown in Figure 2.

23Na Quantification: Immediately following the 23Na-MRS, volunteers were removed from the scanner and replaced with an external concentration reference phantom containing 44.8mM 23Na, on which an identical scan was performed. Data were processed with jMRUI, using first and second order phasing, apodisation=20Hz, and zero-filling=2048. Signal amplitudes for volunteers and phantom were measured using the AMARES algorithm. Differences in the performance of the ISIS sequence due to differing amounts of white and grey matter and varying extracellular volume fractions, which would contribute to a higher sodium concentration.

Analysis: Correlations between sodium and age and sodium and CSA were investigated using the Pearson correlation coefficient. In addition, multiple regression analysis was run to examine whether sodium concentration in the cervical SC could be predicted based on age and CSA.

Results

Figure 4a and 4b show the distribution of sodium with age and CSA. Mean±SD total sodium was 40.8±13mM, age 39±12years, and CSA was 83±6mm2. As can be seen in figure 4a and b the correlation between sodium and age, or sodium and CSA appeared weak with Pearson coefficients of 0.34 (p>0.05) and -0.18 (p>0.05) respectively. However, using multiple regression analysis, it was found that age and CSA statistically significantly predicted cervical SC sodium concentration. Using a 3D-cones imaging technique (40.8±13mM versus 31.4±2.3mM), it is similar to cortical grey matter (41.8±3.2mM) and deep grey matter (34.4±2.5mM), and considering its standard deviation it is not dissimilar to brain concentrations7. The higher standard deviation is probably due to age as well as differing amounts of white and grey matter and varying extracellular volume fractions, which would contribute to a higher sodium concentration.
Conclusion

Structurally related changes have a lower impact on sodium concentration in the cord than age. This knowledge will inform future studies looking to use this technique to measure sodium in the SC for neurological conditions such as MS and spinal cord injury.

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References


Figures

Figure 1. Sagittal (left), coronal (middle) and axial images (right) showing the exact 23Na voxel placement and also the placement of saturation bands used to suppress the effects of cerebrospinal fluid (CSF) and other tissues types in the proximity.

Figure 2. 23Na-MRS spectrum from an in vivo tissue voxel in the spinal cord stacked together with the corresponding signal from a saline phantom containing 44.8mM NaCl for one of the subjects.

Figure 3. Axial view of the cervical cord acquired using the 3D gradient echo (left), and the corresponding automatic segmentation (right) used to calculate CSA.
Figure 4. Relationship between cervical cord total sodium concentration and a) age (Pearson coefficient=0.34 p>0.05) and b) cervical cross sectional area (CSA) (Pearson coefficient=-0.18 p>0.05) for the healthy control cohort with the shaded area showing the confidence intervals.