Multiple Sclerosis alters Intra-cellular Sodium Concentration and Intra-cellular Volume Fraction: an in-vivo 7T MRI study.

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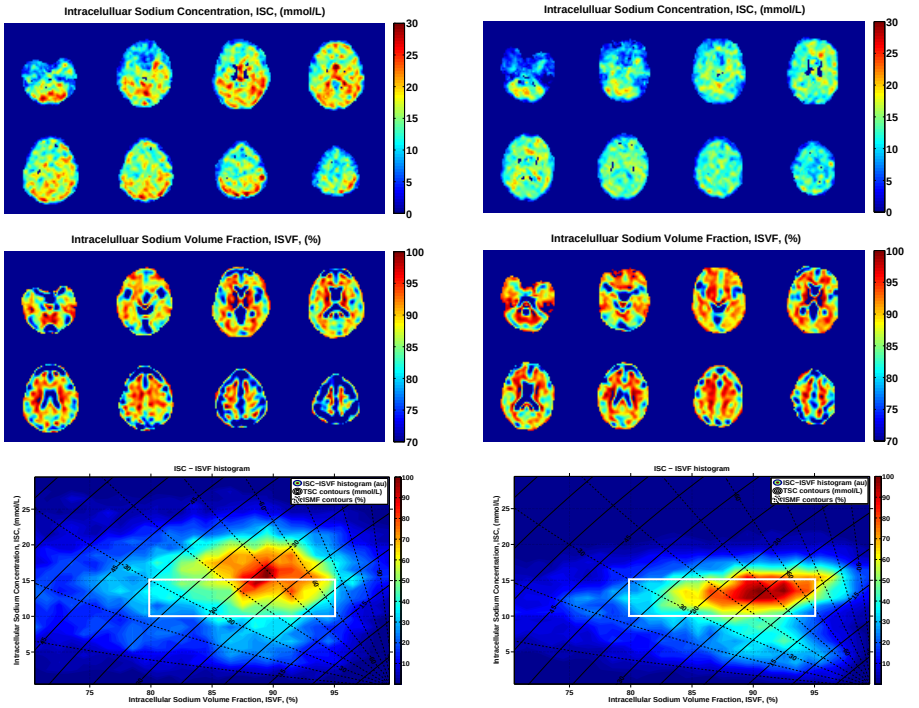
Introduction

Axonal degeneration has been recognized as the main cause of irreversible disability in patients with multiple sclerosis (MS) (1,2). Although the mechanisms of neurodegeration are poorly understood, it has been suggested that an increase of sodium (^{23}Na) in chronically demyelinated axons can lead to calcium mediated degeneration (3). Indeed, increased intracellular sodium concentration (ISC) causes "reversal" of the Na/Ca exchanger and a lethal rise of the intracellular calcium concentration. Since extracellular sodium concentration remains relatively constant as long as there is adequate tissue perfusion, ISC and the intracellular sodium volume fraction (ISVF) provide important information about tissue viability. Increased brain total sodium concentration (TSC) has been recently measured in MS patients using 23Na MRI at 3 Tesla (4). However, TSC is a compound measure of the ISC and ISVF and, therefore, it is sensitive but not specific to variations in ISC and ISVF. The aim of our study was to evaluate ISC and ISVF in MS patients and healthy controls using single- (SQ) and triple-quantum-filtered (TQF) ^{23}Na MRI (5).



Methods

Eight relapsing-remitting (RR) MS patients (mean±SD age: 48±13 yrs; disease duration: 10±5 yrs and median EDSS score: 3.2, range 1.5-5.0) and eight age-matched controls (46±11 yrs) were enrolled in this IRB-approved study after signing an informed consent. Experiments were performed on a 7T whole-body MAGNETOM scanner (Siemens Healthcare, Erlangen, Germany) with a custom-built dual-tuned TX/RX ^{1}H/^{23}Na head coil (6). Acquisition parameters for TQF imaging (5) were 240x240x240 mm^3 FOV with 30x30x24 encoding matrix; TR=150ms, TE=6.8ms, FA=90^o and τ_1=6.8ms τ_2=150μs N_{ave}=2. SQ sodium imaging was performed with the same imaging parameters as TQF imaging. The data were processed according to (4,5,7,8).

Results and Conclusions

The Figure depicts ISC and ISVF maps for a 42-year-old MS patient (left) and an age-matched healthy control (right). ISC and ISVF values for the healthy volunteer are well within the "healthy" bounds obtained in invasive studies (9-11) (marked by the white frame). As a result of this study, we found that ISC values for the RR MS patients (13.6±3 mmol/L) are higher than those for the healthy controls (11.9±2 mmol/L) indicating accumulation of intracellular sodium in agreement with disease model (3). In addition, the patients' ISVF values (86.6±3 %) are slightly lower than those of the healthy controls (88.6±3 %) indicating loss of the intracellular volume. Even though the coarse resolution of the obtained images did not allow analysis of ISC and ISVF values in the MS lesions, the loss of the intracellular volume and accumulation of sodium in the intracellular space are evident in the normal-appearing brain tissue which is in line with the diffuse nature of the disease.

In summary, we will report the results of the first ongoing non-invasive study assessing ISC and ISVF distribution non-invasively in MS patients using 7T MRI.

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