Intracellular Volume Fraction Measurements using Single Quantum Sodium MRI.

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Introduction

In-vivo quantification of brain extra- and intra-cellular space changes can provide valuable insights into the cellular mechanisms underlying brain aging and neurological diseases. Since current methods are invasive (1-3), a relatively simple and accurate non-invasive method of determining intracellular volume fraction non-invasively has been long sought in order to quantify the extent of tissue damage in any given tissue sample.

Sodium MRI has been shown to be a specific tool for quantifying brain tissue damage in several pathological conditions (4-6). In healthy tissue, extracellular (ESC) and intracellular sodium concentrations (ISC) are tightly regulated around 140 mmol/L and 10-15 mmol/L, respectively. As a result, tissue sodium concentration (TSC) represents a weighted average of the extracellular and intracellular sodium contents and is sensitive to intracellular sodium volume fraction (ISVF) changes. Therefore, sodium MRI can provide valuable non-invasive information about tissue damage via the intracellular sodium volume fraction measurement. The aim of this study was to show the feasibility of sodium MRI at 3 Tesla in assessing brain ISVF in healthy subjects.

Theory

Assuming that the brain tissue can be described by the intracellular and extracellular compartments only, it is possible to relate TSC (ρ_T) with intracellular sodium volume fraction (ISVF) (η_{in}):

$$\rho_T = \frac{M_{in} + M_{ex}}{V_{in} + V_{ex}} \Rightarrow \eta_{in} = \frac{V_{in}}{V_{in} + V_{ex}} = \frac{\rho_{ex} - \rho_T}{\rho_{ex} - \rho_{in}} \qquad [1]$$

where M_{in} and M_{ex} are the intra- and extra-cellular sodium contents (in moles) occupying volume V_{in} and V_{ex} respectively, ρ_{in} /ρ_{ex} stand for ISC and ESC. Since ESC and TSC are much larger than ISC the use of 12.5 mmol/L will lead to no more than 2% error in ISVF quantification (see eq [1] and Figure 1.).

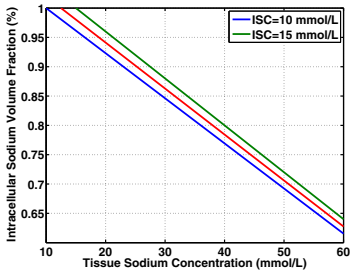

Figure 1. ISVF versus TSC plot. Imprecise knowledge of ISC causes small (less than 2%) error in ISVF measurement.

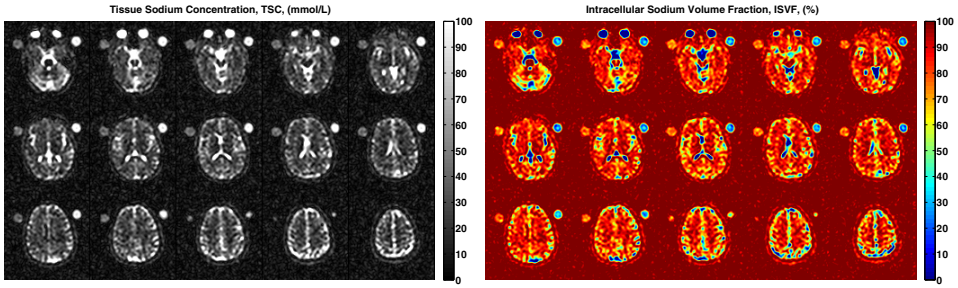

Figure 2. Selected axial TSC and ISVF maps from a healthy volunteer. TSC and ISVF values are in agreement with previous reports based on invasive studies (1,3,6,7-12).

Methods

Ten healthy volunteers (5 women, mean age 27±3 yrs) were recruited for this IRB-approved study. All experiments were performed on a whole body 3T Tim Trio scanner (Siemens AG, Erlangen, Germany) with a custom-built, transmit-receive dual-tuned $^{1}H/^{23}Na$ head coil (Stark Contrast, Erlangen, Germany). The MRI protocol included: a) T1-weighted magnetization prepared rapid acquisition gradient-echo (MP-RAGE) sequence with TE/TR/TI: 2.6/2250/1100 ms; 192 1.0 mm-thick slices, 256x256 matrix with 240x240 mm2 field of view (FOV); b) A modified GRE sequence for 3D single-quantum sodium images with a FOV of 240x240x240 mm3 with 5x5x5 mm3 voxel volume using a non-selective excitation. Other acquisition parameters were TE=12.0 ms., TR=100 ms. Eight averages were acquired for the sodium imaging making this part of protocol about 31 min. TSC maps were obtained from sodium images using procedure described in (6,7). Long T_2^* correction of 20 ms was applied to correct for signal decay. (13). TSC and MPRAGE images where co-registered using FSL (5) and corresponding GM and WM masks were applied to TSC maps.

Results and Conclusions

Figure 2 shows selected TSC and ISVF maps from a healthy brain. The average TSC value (mean±SEM) for the GM was 37±6 mmol/L and for the WM was 24±3 mmol/L inline with previously reported values. (4,6,9). Assuming that the ESC=140 mmol/L and ISC=12.5 mmol/L, we obtain $ISVF_{GM}$=81±5 % and $ISVF_{WM}$ = 91±2%. Our ISVF results are in a good agreement with the previously reported values between 80% and 95% (1-3,10-12). Note that the systematic error in our measurements due to imprecise knowledge of ISC cannot bias the ISVF values by more than 2 % (see Figure 1).

In summary, ISVF can be assessed by means of sodium MRI.

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