Intra-cellular Sodium Concentration and Intra-cellular Volume Fraction Quantification in the Human Brain using 7T MRI in-vivo.

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Introduction

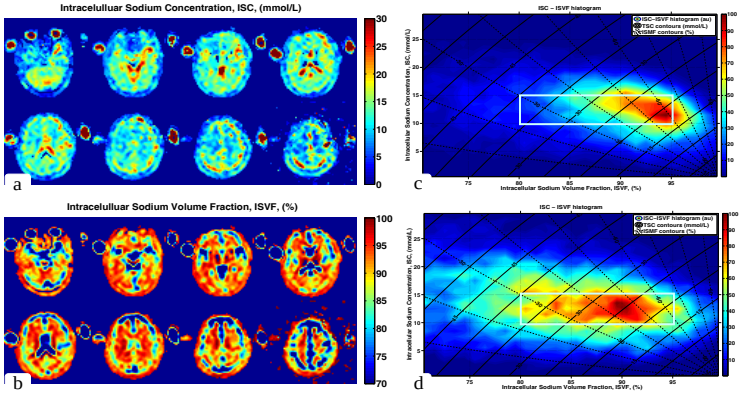
Sodium is involved in many cellular functions such as regulation of mitosis, cellular proliferation (1), sodium/calcium-exchange mediation (2) as well as cellular energy metabolism via active trans-membrane Na+/K+ transport (3). Most cell types maintain a large sodium ion concentration gradient across their membranes with an intracellular sodium concentration (ISC) of about 10 -15 mmol/L and an extracellular sodium concentration (ESC) of about 140 mmol/L (4). This cross-membrane difference in sodium concentration is essential for the generation and propagation of action potentials (5), cell volume regulation (6), and other cellular homeostatic and regulatory functions. Neurological disease processes may alter the trans-membrane sodium concentration gradient and the cell volume causing changes in ISC, intracellular sodium volume fraction (ISVF) and intracellular sodium molar fraction (ISMF) (see, for example, (7-10)). Therefore, non-invasive techniques for ISC, ISVF and ISMF quantification are important for monitoring the function of healthy and diseased brain tissue, its disease progression and treatment success. In this work, we combine ISMF and TSC measurements to obtain maps and histograms of ISC and ISVF in healthy volunteers. This work demonstrates the feasibility and robustness of spatially-resolved intracellular sodium quantification in vivo, paving the way for future clinical and research applications.

Theory

If the ESC (ρ_{ex}) is known, it is possible to obtain the values of ISC (ρ_{in}) and ISVF (η_{in}) from TSC (ρ_T) and ISMF (χ):

$$\begin{cases} \chi = \dfrac{M_{in}}{M_{in}+M_{ex}} \\ \rho_T = \dfrac{M_{in}+M_{ex}}{V_{in}+V_{ex}} \end{cases} \quad [1] \qquad \begin{cases} \rho_{in} = \dfrac{M_{in}}{V_{in}} = \dfrac{\chi\rho_T\rho_{ex}}{\rho_{ex}-(1-\chi)\rho_T} \\ \eta_{in} = \dfrac{V_{in}}{V_{in}+V_{ex}} = 1-(1-\chi)\dfrac{\rho_T}{\rho_{ex}} \end{cases} \quad [2]$$

where M_{in} and M_{ex} are the intra- and extra-cellular sodium contents (in moles) occupying volume V_{in} and V_{ex} respectively. Here, we have assumed that the tissue can be described by the two compartments only (11-13). Thus, ICS and ISVF can be obtained from TSC and ISMF [2] accessible to MRI through SQ and TQF imaging. The values of ρ_T and χ can be obtained from SQ and TQF imaging (12,14,19,20).



ISC map (a) and ISVF map (b) derived from MRI measurements in a healthy young volunteer. ISC-ISVF histogram from the same volunteer (c). The ISC and ISVF values are within the expected range (frame) for a healthy brain (16-18). The color in the panel represents voxel frequency count in the brain corresponding to ISC and ISMF values. For comparison, ISC-ISVF histogram from a healthy elderly volunteer is shown in panel (d). Comparing (c) and (d), ICS remains constant while ISVF decreases consistent with the normal aging.

Methods

Eight healthy volunteers (4 elderly (mean age 65.0±1.8) and 4 young (mean age 27.5±1.3)) were enrolled in this IRB-approved study. Experiments were performed on a 7T whole-body MAGNETOM scanner (Siemens Healthcare, Erlangen, Germany) with a custom-built dual-tuned TX/RX $^1H/^{23}Na$ head coil (15). TSC and ISMF were measured as described in (14,19,20). Acquisition parameters for TQF imaging 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. The RF excitation train was comprised of three non-selective pulses of 900 μs duration each. SQ sodium imaging was performed with the same imaging parameters as TQF imaging. Due to long TRs, T_1-weighting was ignored.

Results and Conclusions

The Figure depicts ISC and ISVF maps for a 27-year-old volunteer. ISCs of GM and WM regions are relatively uniform at 13.0±3.9 mmol/L and ISVF is 94.8±5.4%. As can be seen from the histogram, ISC and ISVF measured in-vivo are within the expected range (16-18). The ISVF for the WM is higher than for the GM consistent with previous findings (16) and the ISC remains within the expected range between 10 – 15 mmol/L. The ISC value for an elderly volunteer is 12.5±4.3 mmol/L, similar to that in the young brain, while the ISVF is decreased (86.7±6.6%)(see panel (d) of the Figure). This corresponds to a decrease in intracellular volume caused by normal aging while the ISC remains constant. The developed technique allows quantitative mapping of ISMF, ISVF and ISC in-vivo and may be used to study the function of healthy and diseased organs, monitor disease progression and guide treatment.

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