In vivo chlorine-35, sodium-23 and proton magnetic resonance imaging of the rat brain

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Introduction

Chloride (CI) is the most abundant *anion* in the mammal organism playing an important role in many cellular processes. For instance, plasma membrane Cl currents are important for the regulation of excitability in nerve and muscle. Moreover, Cl ions play a crucial role in controlling the ionic composition of the cytoplasm and the volume of cells [1]. In order to investigate the feasibility of combined in vivo 35Cl, 23Na and 1H MRI we developed a rf coil setup to measure ³⁵Cl, ²³Na and ¹H signals in one scanning session without moving the subject or changing the setup.

Material and Methods

For the ¹H and ²³Na measurements we used a linear double tuned volume resonator with an inner diameter of 7 cm from Bruker (Ettlingen, Germany). Additionally, we placed a surface coil on the head of the animal that operated at the resonance frequency of ³⁵Cl at 9.4 T of 39.2 MHz. This coil was constructed from silver wire with 3 mm diameter. A single loop of 35 mm diameter was bent on a 35 mm plexiglass half cylinder to achieve an optimal filling factor for a rat head. The 35Cl coil was built large enough to cover the whole brain for sure and is glued to the plexiglass half cylinder to which it was bent.

Proton imaging was performed using a multi slice multi echo (MSME) sequence with TR = 2000 ms, $TE_1 = 13$ ms and $TE_2 = 65$ ms (two images per slice). The field of view (FOV) was 64×64 mm² at a matrix of 256×256 with 9 coronal slices of 3 mm thickness and an inter-slice distance of 3.5 mm. The total measurement time (TA) was 6 min 24 sec.

The ²³Na and ³⁵Cl imaging was done using a slice selective ultra short echo time (UTE) pulse sequence with radial k-space acquisition [2]. For both nuclei 3 coronal slices with FOV = 64×64 mm², matrix of 64×64 , slice thickness = 3 mm and an inter-slice distance of 3.5 mm were measured. The positions of the 3 slices were matched with the slice positions of the corresponding ¹H images by means of the scanner software Paravision[®] 5. The parameters for the 23 Na imaging were TR = 40 ms, TE = 0.321 ms, readout bandwidth = 25 kHz/FOV, number of averages = 225 and $TA = 30 \text{ min } 17 \text{ sec. For the}^{-35}\text{Cl}$ imaging the following parameters were used: TR = 40 ms, TE = 0.448 ms, readout bandwidth = 25 kHz/FOV, number of averages = 455 and TA = 1 h 1 min.

1H 23Na 35CI 1H+23Na 1H+35CI

Results and DiscussionMultinuclear MRI of ³⁵Cl, ²³Na and ¹H was applied on the head of a healthy rat and on a rat displaying a focal cerebral infarction in the right hemisphere of the brain. Columns a-e show the results of the in vivo MRI on a healthy rat whereas columns f-j show the results measured on a rat displaying a focal cerebral infraction. In the T_2 weighted ¹H images the area of infarction can be identified by the brighter areas in the right hemisphere of the brain due to ischemic swelling. Similar behaviour is observed in the ²³Na and ³⁵Cl images. Compared to the healthy tissue, a signal enhancement of a factor of 2.9 (²³Na) and of 2.2 (³⁵Cl) is observed in the area of infraction. The increase in signal is attributed to an increase in concentration of sodium and chloride ions. Note, the ³⁵Cl images were measured with a surface coil therefore mainly the brain of the rat is visible in the corresponding images (column c + h).

The coil setup and the measurement parameters of the ³⁵Cl and ²³Na MRI were a compromise in order to achieve almost the same image quality (SNR and resolution). Despite the fact that the signal intensity of ³⁵Cl is expected to be approx. 9.6 times lower than the signal intensity of ²³Na, the ³⁵Cl signal was sufficient to perform in vivo ³⁵Cl MRI with acceptable image quality in a measurement time of 1h. The total measurement time for the multinuclear MRI was 2h. 35Cl MRI allows non-invasive in vivo studies on pathologies or physiological processes which result in a change of Cl concentrations. Since chloride and sodium ions are transported concurrently, combined in vivo 35Cl, 23Na and ¹H MRI may provide a new approach to study diseases like stroke, ischemia or cystic fibrosis.

[1] Jentsch TJ et al., Physiol. Rev. 2002; 82: 503-568.

[2] Robson MD et al., J. Comput. Assist. Tomogr. 2003; 27(6): 825-846.