23Na-MRI contrasts for application in muscular sodium channel diseases

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Introduction

Sodium (23Na) MRI has the potential to noninvasively detect sodium content changes in vivo [1]. In previous 23Na-MRI studies of pathological changes either the total tissue 23Na concentration (TSC) was measured [2], or a T1-weighted approach was used to increase the SNR [3]. Furthermore, it has been demonstrated that in the healthy human brain 23Na fluid signal (e.g. liquor) can be suppressed with an inversion recovery sequence [4]. In this study, these three 23Na-MRI contrasts were applied and compared with regard to the information they provide about the compartments from which the 23Na signal originates. In particular, it was evaluated if the used techniques are capable of providing a strong weighting of the intracellular 23Na. Therefore, the model disease hypokalemic periodic paralysis (HypoPP), a muscular 23Na channelopathy, was selected. In HypoPP, cooling causes an increased open probability of the mutant sodium channels resulting in intracellular 23Na accumulation and muscle weakness [5].

Methods

Two patients with confirmed HypoPP and two healthy volunteers were examined on a 3.0 T clinical MR system (Magnetom Tim Trio, Siemens Medical Solutions, Erlangen, Germany). Images were acquired using a double-resonant (32.59 MHz/123.2 MHz) birdcage coil (Rapid Biomed GmbH, Würzburg, Germany).

Three different sodium MRI techniques based on a 3D density adapted projection reconstruction sequence [6] were used. First, a 23Na T1 weighted 23Na images were acquired with the following parameters: TE/TR = 0.3/6 ms; α = 40°; voxel size: 5x5x5 mm; 14000 projections; 4 averages; 5 min 36 s.

An Inversion Recovery (IR) sequence was used to suppress sodium signal emanating from 23Na ions in unrestricted environments (e.g. pure sodium chloride (NaCl) solution). Parameters: TE/TR = 0.3/124 ms; TI = 34 ms; voxel size: 6x6x6 mm; 5000 projections; 10 min 20 s.

Furthermore, the TSC was measured, providing a basis to compare the 23Na-T1 and 23Na-IR sequences. Parameters: TE/TR = 0.2/100 ms; α = 90°; 5000 projections; voxel size: 5x5x5 mm; 8 min 20 s. For the 23Na-T1 and the 23Na-IR sequence an ‘apparent’ concentration was calculated, using a reference tube (2) containing 0.3% NaCl and 5% agarose gel. Additionally, 1H-imaging with a T2-TIRM sequence was performed. In between the first and second measurement one lower leg was cooled for 25 min, followed by a short exercise (≈ 2 min), provoking an intracellular 23Na-accumulation in the patients’ cooled leg. Prior to each measurement the muscle strength was measured according to a grading system proposed by the British Medical Research Council. Taking the concentration weighted images, ROI’s (musculus soleus) were selected in 13 slices. In the 23Na-T1 and 23Na-IR images ROI’s were selected automatically at the same position, to prevent a biased selection.

Results

Edemata, which are also visible in the 1H T2-TIRM images (Fig. 1a, e), lead to an elevated sodium concentration (Fig. 1d, h) and to hyper-intensity in the 23Na-T1 (Fig. 1b, f) images. With the 23Na-IR sequence, edema and the reference tube containing NaCl solution (1) are suppressed (Fig. 1c, g). The patients showed significantly higher (apparent) sodium concentrations compared to the volunteers (Fig. 2), with less distinct differences for the 23Na-IR images (Fig. 2c), since edema are suppressed. The cooled leg of the patients showed decreased muscle strength; no changes concerning the strength were observed for the volunteers (Tab. 1). The total sodium concentration remained constant after provocation (Fig. 2a), whereas the T1 weighted measurements showed slightly increased signal intensity (Fig. 2b). The most pronounced changes after cooling were observed in the 23Na-IR images (Fig. 1c, g; Fig. 2c). The volunteers showed no significant changes after cooling in all measurements.

Discussion and Conclusion

This study demonstrates that the 23Na-IR sequence is well suited to highlight an intracellular sodium accumulation caused by provocation of the lower leg muscles in HypoPP. The increase in signal intensity can be attributed to shorter T1 relaxation times in the intracellular space compared to extracellular sodium compartments. This is also well in accordance with the tendency of an increased signal intensity in the 23Na-T1 images and unchanged total sodium concentrations. The less pronounced signal increase for the 23Na-T1 sequence when compared to the 23Na-IR sequence can be explained with the fact that the latter provides stronger T1-weighting. Furthermore, the 23Na-IR sequence suppresses background signal of muscular edema that affects the interpretation of conventional sodium images. It was shown that with the 23Na-IR sequence a strong weighting of the intracellular space can be obtained and together with a concentration weighted approach, valuable information as to from which compartments the sodium signal originates can be provided.

References

[4] Stobbe and Beaulieu; MRM (2005); 54: 1305-10

Fig. 1. Images from patient #1 with HypoPP. The reference tubes are labeled by numbers (1: 0.3% NaCl solution; 2: 0.3% NaCl and 5% agarose gel). Edema in m. soleus and m. gastrocnemius are marked by yellow arrows. In the lower row, the left lower leg (marked by blue arrows) was cooled before the measurement.

Tab. 1. Muscle strength in patients (pat.) with HypoPP and volunteers (vol.). The strength was scored according to the grading system proposed by the British Medical Research Council. (0 = complete paralysis, 5 = full strength).

<table>
<thead>
<tr>
<th>Measurement</th>
<th>pat. #1</th>
<th>pat. #2</th>
<th>vol. #1</th>
<th>vol. #2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (reference)</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>2 (one leg cooled)</td>
<td>5</td>
<td>3.5</td>
<td>5</td>
<td>5</td>
</tr>
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Fig. 2. ROI analysis of the musculus soleus. 1: reference measurement; 2: one lower leg was cooled. Red blue symbols were used for the non-cooled/ cooled leg. For the 23Na – IR and the 23Na-T1 sequence an ‘apparent’ concentration was calculated with the reference tube containing 5% agarose gel.