Reproducibility of ^{1}H-MR spectroscopic imaging in the centrum semi-ovale in patients with multiple sclerosis

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Introduction

Multiple sclerosis (MS) is an autoimmune disease characterized by relapses and slowly progressive deterioration.[1] In general, it is difficult to measure the effects of medication in MS patients, and objective surrogate markers are highly useful to predict prognosis or to measure medication effects in these patients. In this respect, ^{1}H-MR spectroscopic imaging (SI) is a promising modality, since previous studies have shown that in MS patients abnormalities can be detected in lesions as well as in normal appearing white matter.[2] Although it has been shown that in healthy subjects ^{1}H-MR SI has a high intra-individual reproducibility which is needed for surrogate markers,[3] it is unknown whether this remains valid in patients with clinically stable MS. In the present study we investigated the reproducibility of ^{1}H-MR SI in clinically stable MS patients within a time span of 4 weeks.

Methods

Fifteen patients with relapsing MS (14 relapsing remitting, 1 secondary progressive with relapses), who participated in a trial to establish the effect of a novel therapeutic medicine, underwent ^{1}H-MR SI at baseline and received a follow-up exam after 4 weeks (before taking any study medication). All patients were relapse free in 4 weeks before the baseline scan and in the 4 weeks between the two scans. Mean age was 37 years (range 25 to 50 years). None did use immunomodulating medication. ^{1}H-MR SI was performed at 3T at the level of the centrum semi-ovale using the following parameters: TE=144ms, TR=2.5s, FOV= 230mm, slice thickness=20mm, matrix= 24x24, turbo factor=3, and outer volume suppression with 12 rest slabs. The total scan time was 8 minutes. To select voxels that mainly contained gray matter (GM) 12 SI voxels were selected in the midline gray matter in each subject. To select voxels that mainly contained white matter (WM) 24 SI voxels were selected (12 in each hemisphere) in the deep white matter in each subject. Metabolite peak areas of N-acetyl-aspartate (NAA) are expressed as ratios to creatine (Cr). The reproducibility after 4 weeks was tested by a coefficient of variation (CV= standard deviation of differences between two measurements/mean of measurements *100%).

Results

The figure shows a modified Bland & Altman plot indicating the difference of the two NAA/Cr ratios in the gray and white matter in all patients. The mean NAA/Cr ratio in the GM was 1.74 ± 0.11 (mean ± standard deviation) at baseline and 1.73 ± 0.12 at follow-up. In the WM, the mean NAA/Cr ratio was 2.11 ± 0.15 at baseline and 2.11 ± 0.16 at follow-up. The CV was 5.3 and 3.9% in GM and WM, respectively.

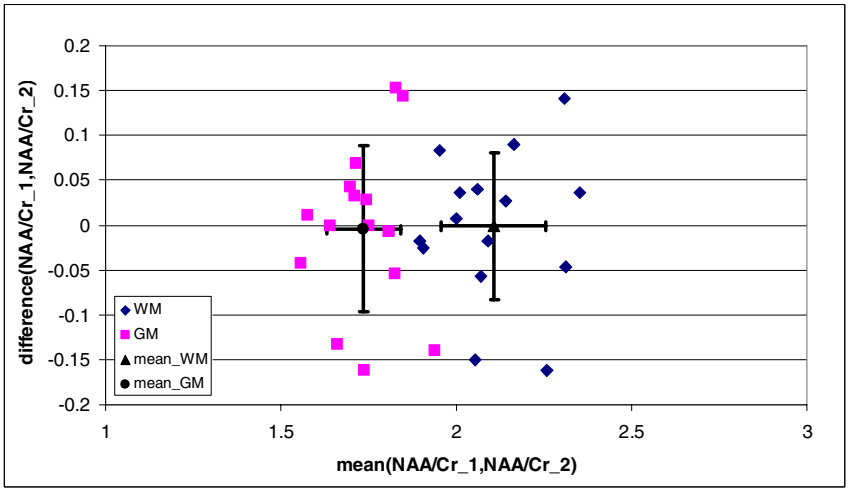

Figure: A modified Bland & Altman plot showing the difference between the two NAA/Cr ratios vs. the average of the two measurements.

Discussion

Our results are in agreement with a previous study in which ^{1}H-MR spectroscopic imaging at 1.5T was applied at the level of the centrum semi-ovale showing mean CV's ranging from 5.1 to 7.1% (N=5) for the NAA/Cr ratio in healthy volunteers.[3] The authors suggested that ^{1}H-MR SI could be used to monitor progressive axonal degeneration. In our study at 3.0T with MS patients the CV of NAA/Cr was comparable, which means that both biological variability and scan variability after 4 weeks is low in clinically stable patients. This indicates that ^{1}H-MR SI at the centrum semi-ovale can potentially be used as surrogate marker in MS.

References

1.Noseworthy JH, Lucchinetti C, Rodriguez M, Weinshenker BG. Multiple sclerosis. *N.Engl.J.Med.* 2000;**343**:938-52.

2. Filippi M, Rocca MA, Comi G. The use of quantitative magnetic-resonance-based techniques to monitor the evolution of multiple sclerosis. *Lancet Neurol.* 2003;**2**:337-46.

3. Rotondo E, Bruschetta G, Sacca A, Bramanti P, Di Pasquale MR. Straightforward relative quantitation and age-related human standards of N-acetylaspartate at the centrum semiovale level by CSI (1)H-MRS. *Magn Reson.Imaging* 2003;**21**:1055-60.