Scyllo-Inositol detection in the human spinal cord

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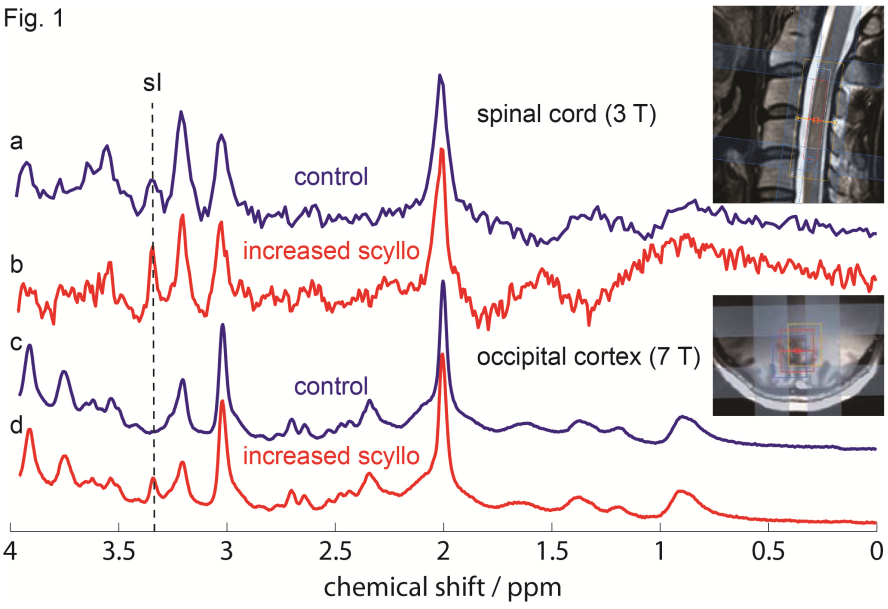
Introduction: Scyllo-Inositol (sI) is one of the stereoisomers of inositol consisting of six equivalent CH protons yielding a singlet resonance at the chemical shift of 3.35 ppm in MR spectroscopy (^{1}H MRS). The function of sI remains uncertain but changes compared to healthy subjects were observed in brain tumors (1), mitochondrial enzyme deficiency (2), chronic alcoholism (3), Alzheimer's disease (4) and HIV (5) indicating that sI is an important marker in many neurological disorders. **This work** represents the first report of sI detection in the human spinal cord, which was enabled by non-water suppressed ^{1}H MRS via metabolite cycling (MC) [6] at 3T.

Fig. 1



Methods: After approval from the local ethics committee, spinal cord ^{1}H MRS measurements were performed in 14 subjects (mean age ~28) using non-water-suppressed ^{1}H MRS via the inner-volume saturated PRESS localized MC technique (6) at 3T (Achieva, Philips Healthcare, Best, TE/TR = 30/2000 ms, voxel size = 1.2 ml) at the cervical level C3-4 (Fig 1). The MC method enables frequency alignment of each single FID even with the very low SNR available in the spinal cord, which improves the spectral quality (increased SNR and reduced FWHM of the metabolite peaks) and reproducibility of ^{1}H MRS measurements in the human spinal cord. Second order ECG-triggered FASTERMAP shimming as well as ECG triggering during F_0 determination and spectral acquisition was used. One female subject also participated in another study (7) where four healthy volunteers were scanned with a Philips 7T Achieva MR system (Philips Healthcare, Cleveland). In that study, the MRS voxel was placed in the occipital cortex, and SPECIAL (8) localization and VAPOR water suppression was used (TE/TR = 11.8/7000 ms, voxel size = 6.9 ml). This female subject showed a strongly increased sI peak in the spinal cord as well as in the brain. All MRS data were quantified using LCModel (9) and a set of basis spectra simulated including 20 metabolites using GAMMA (10).

Results and Discussion: Fig. 1 shows exemplary spectra of a control volunteer (a, c)) and the female volunteer with the increased sI peak (b, d) measured in the spinal cord (3 T) (a, b) and in the occipital cortex (7 T) (c, d). Although, sI is even hardly visible healthy control in Fig 1 c at 7 T, it was possible to identify sI in all 14 healthy subjects in the spinal cord at 3T (Cramér–Rao lower bounds (CRLB) < 25%). In addition, the increased sI resonance in spinal cord (b) and brain spectra (d) from the same female subject supports the assignment of the resonance line detected at 3.35 ppm in the 3 T spinal cord MRS measurements in all volunteers to sI, while a systematic artifact introduced by the MC technique was excluded. Table 1 shows metabolite ratios, standard deviations (SD) and the CRLB of NAA, choline (Cho), myo-Inositol (mI) and sI over Creatine (Cr) of the controls and the volunteer with the increased sI peak in the spinal cord. In addition, the fraction of mI and sI is shown in the last column. Brain sI concentrations measured in controls as published by Griffith et al. (posterior cingulate, grey matter, mean age ~67 Y, 3 T, TE = 32 ms) (4) and Michaelis et al. (cerebellum, white matter, age 18 – 28 Y, 2 T, TE = 20 ms) (2,11) are also displayed in table 1 for comparison. Concentration ratios of mI/Cr and sI/Cr in the spinal cord are higher compared to the brain (2,4,11), although NAA/Cr concentrations are quite similar, which is indicative for a slightly altered metabolism and tissue composition in the spinal cord. In addition, Michaelis et al. (2) noticed a proportionality of mI and sI concentrations of about 12-13 in healthy tissue. Our results in the spinal cord and the data of Griffith et al. (4) support this finding; however, measurements in the volunteer with increased sI shows reduced mI/Cr and increased sI/Cr resulting in a reduced mI/sI ratio of about 4. This may be an indicator of a mutated inositol epimerase. Seaquist and Gruetter (12) also reported an elevation of sI in proton MRS measurements in a healthy man and in this case they reported a reduction of mI/sI ratio to 5.

Table 1: *Note: Ratios from Michaelis et al. are calculated from the absolute values published in (2,11)*

volunteer(s)	NAA/Cr (mean ± SD, mean CRLB)	Cho/Cr (mean ± SD, mean CRLB)	mI/Cr (mean ± SD, mean CRLB)	sI/Cr (mean ± SD, mean CRLB)	mI/sI
controls (n=13)	**1.5** ± 0.2, 6%	**0.41** ± 0.06, 7%	**2.8** ± 0.43, 7%	**0.21** ± 0.048, 17%	**13.3**
elevated sI (n=1)	**1.8** ± -, 7%	**0.38** ± -, 9%	**1.5** ± -, 17%	**0.35** ± -, 13%	**4.28**
Michaelis et al.(2,11)(n=32)	**1.53** ± -, -	**0.33** ± -, -	**0.78** ± -, -	**0.06** ± -, -	**13**
Griffith et al.(4)(n=19)	**1.3** ± 0.1, -	**-**	**0.89** ± 0.16, -	**0.09** ± 0.042, -	**9.9**

Conclusion: SI was investigated for the first time in spinal cord MRS in vivo. The results show an increased mI/Cr and sI/Cr ratio compared to the brain which might be an indicator of a different metabolism in the spinal cord. This finding may help in better understanding the special tissue characteristics in the spinal cord.

Literature:

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