Evidence for Detection of Ascorbic Acid in the Human Brain at 3T

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Introduction

Ascorbic acid (Asc) commonly known as vitamin C in the human body plays an important role in the storage of iron, has a stimulating effect on the immune system and is indispensable for the generation of collagen. In the healthy adult its plasma concentrations are in the order of 10 μM [1)]. Within the brain these are actively increased by a factor of roughly 100 leading to concentrations detectable via MRS. With its resonances at 3.73 ppm (CH_2), 4.01 ppm and 4.50 ppm (CH) a quantification of Asc is not trivial due to strong overlap with the spectra of other metabolites as for example Glutamate, Glutamine and myoInositol. However detection of vitamin C was recently reported by Terpstra et. al. in human subjects at 4T via spectral editing [3)] and in rats at 9.4T using LCModel fitting [5)]. The aim of this study is to evaluate the potential of standard 3T MRS for detection of vitamin C *in vivo* in the human brain. Therefore we examined spectra of 37 healthy volunteers and evaluated vitamin C concentrations via LCModel [2)]. Additionally we observed the time dependency of vitamin C concentration after an inter venous application of Ascorbic acid.

Material and Methods

All spectra were acquired on a 3T Siemens Magnetom Trio using IRS-PRESS [4)], a voxel size of 8 cm^3, TE of 30ms and a TR of 3000ms. 37 spectra of healthy volunteers from the 4 locations occipital (10), parietal (7), frontal (10) and cerebellum (10) were evaluated. They were fitted with LCModel with a frequency range of 4.2 – 0.2 ppm using a standard basis set excluding (w/o) and including (w) an ascorbic acid basis spectrum. Creatin (Cre) ratios were used for quantification since for absolute quantification none water saturated scans are required, which were not available for all data sets.

Additional a vitamin C bolus of 3g was given i.v. to 2 healthy volunteers. Spectra with an bi-occipital voxel (27cm^3) location were acquired before and up to 33 hours after the bolus was applied and fitted as described above. Asc/Cre ratios where normalised to the baseline measurements which were conducted at approximately 9am.

Results

LCModel was able to detect ascorbic acid in 35 of 37 spectra. In these spectra the Creatin ratio for all 4 locations was determined to be in the order of 0.5 with an average error of (11.5 +/-2) % given through the cramer rao lower bounds from LCModel (see Figure 1). Asc/Cre exhibits an average standard deviation of 0.11 over the 4 locations. This is comparable to the inter individual variance of other metabolites, e.g. Phosphoholine and Glycerophosphocholine (GPC+PCh) with 0.01, Glu+Gln with 0.23 and mI with 0.01 (see Figure 2). A correlation of 1/Cre metabolite concentration-differences between LCModel fits excluding and including ascorbic acid in the basis set with the evaluated Asc/Cre concentration is displayed in Figure 3. Most metabolite concentrations were not affected if Asc was included in the basis set (e.g. PCh+GPC and mI). Whereas if Asc is excluded from the basis set Glucose (Glc), Gln and Glu show an increase in concentration. The sum (Glx) of the latter three metabolites and Gln concentrations are plotted as examples in Figure 3. With a coefficient of correlation of 0.91 the sum highly correlates with the determined Asc/Cre ratios. Figure 4 depicts the Asc/Cre and Glx/Cre concentrations in an occipital voxel after an i.v. bolus. Although only two measurements have been performed so far a rise of vitamin C concentration is detected around 10 hours after the bolus, whereas Glx concentrations remain within their error margins.

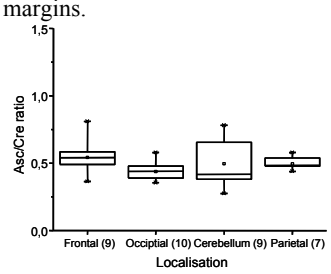

Figure 1: inter individual reproducibility of vitamin C in dependency of voxel location.

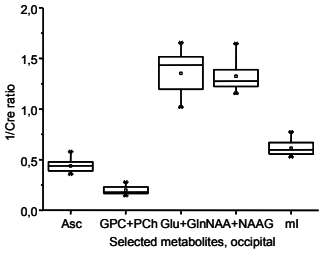

Figure 2: Comparison of inter individual reproducibility of vitamin C with other metabolites.

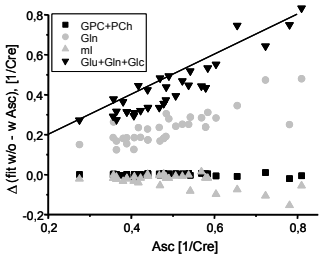

Figure 3: Concentration differences (w/o-w Asc included in basis set) of selected metabolites vs Asc concentration.

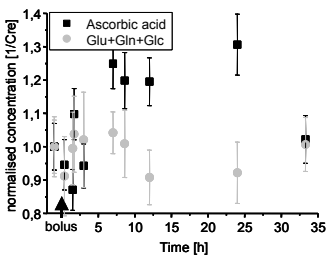

Figure 4: Normalised time dependency of Asc and Glx after bolus of 3g ascorbic acid.

Discussion

The location independent value of approximately 0.5 Asc/Cre and the comparable variance with other metabolites depicted in Figure 2 indicates that LCModel reliably determines a value for ascorbic acid. But the strong correlation with the rise in Glx concentration if Asc is excluded from the fit observed in Figure 3 confirm the difficulties in discriminating vitamin C from those metabolites. The Glx values closely follow the bisecting line. This shows that most of the signal originating from vitamin C is fitted through Glx if Asc is excluded and is due to their overlapping resonances at 3.7 ppm. Vice versa the estimated ascorbic acid concentrations could possibly rely on a "stealing" effect from Glx. However the comparably low errors for Asc in the volunteers as well as the significant rise of Asc/Cre and the roughly constant remaining values for Glx/Cre in the bolus measurement indicate that this is not the case. Therefore this data provide strong evidence that ascorbic acid can be detected in the human brain at 3T via LCModel.

References

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