# Age-related Metabolite Changes in Healthy Spinal cord: A 1H MRS study at 3T

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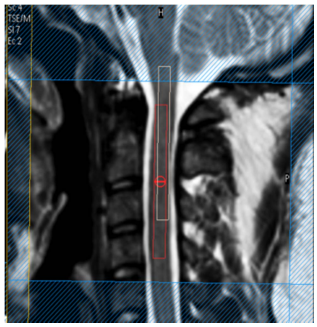
**Introduction:** Magnetic resonance spectroscopy (MRS) is a powerful, quantitative imaging tool, capable of characterising metabolic changes in the central nervous system (CNS), allowing us to study the pathophysiology of neurological diseases *in vivo*. However, it is important to understand how metabolite concentrations vary with normal aging to allow us to differentiate normal, age-related change from pathological changes associated with disease. Brain metabolite concentrations, derived using MRS, are thought to vary with age. Lower NAA concentrations, measured in the brain, are reported in older people when compared with younger subjects[1,2]. Additionally, glial cell proliferation is suggested to increase with age, resulting in higher brain concentrations of Cho and Cr with advancing age[3,4]. MRS of the human spinal cord (SC) is relatively novel, but growing numbers of clinical studies are reporting metabolic changes in the SC that are clinically relevant[5-9]. However, whether there is a relationship between age and metabolite concentrations measured in the SC is unknown. In this study we aim to investigate whether age related changes in metabolite concentrations are present in healthy human SC.

**Methods:** Written informed consent was obtained from 15 healthy participants, mean age 36.5years (range 23-65), 6M and 9F. MRS experiments were performed on a 3T Achieva system (Philips Medical Systems, Best), with a 16-channel neurovascular coil. To reduce motion during scanning, an MR compatible cervical collar was worn by all volunteers. A PRESS localisation sequence[10] (TE 30, TR 3RR) was used to excite a voxel positioned within the SC and centred on C2/3 intervertebral disc (Figure 1). Voxel volumes were altered when necessary (1.7 to 2.3 mls) to avoid CSF contamination. Triggered iterative shimming was performed and water signal was suppressed using MOIST. We collected 376 averages in a total scan time of 35 mins, including the localiser scans. Water scaled MRS data was quantified using LC model with basis sets simulated in GAMMA. The concentrations of the following metabolites were calculated: total N-acetyl-aspartate (NAA), Creatine plus Phosphocreatine (Cr), Myo-inositol (Ins), and Glutamate plus Glutamine (Glx). Cramer- Rao-Lower-Bounds (CRLB) values provided by LC model were used to assess the reliability of the fit. Metabolite concentrations fitted with < 20 % CRLB (tNAA, Cr, Cho, Ins) or 30 % (Glx) were considered in the analysis. A fat-suppressed 3D slab selective fast field echo (FFE) sequence was optimised with TR = 23 ms; TE = 5ms; flip angle α = 7°; FOV= 240 x 180 mm; voxel size = 0.5 x 0.5 x 5 $mm^3$; NEX = 8; 11 axial contiguous slices for calculation of SC volume. We assessed correlation between age and metabolite concentrations using Spearman's correlation coefficient. A linear regression model was used to explore the relationship between age (dependent variable) and SC metabolites (independent variables) when adjusting for gender, cord volume and voxel volume.

Figure 1: T2w Sagittal imaging indicting voxel positioning within the cord



**Results:** We achieved a reliable fit for tNAA, Cho and Cr in all participants and in 13/15 for Ins and 11/15 for Glx. Table 1 shows correlations between age and SC metabolites. Age was predicted by concentration of tNAA (βco-efficient = -0.52, $p < 0.05$, 95% CI= -7.0 to -0.26, PCC = -0.54) and Glx (β co-efficient= -0.72, $p = 0.01$, 95% CI= -7.6 to -1.2, PCC= -0.72) independently from cord volume and voxel volume. Figure 2 shows tNAA and Glx decline with age. There was a general trend for Cho, Cr and Ins to decrease with age, but this did not reach statistical significance.

| Metabolite | n | Rho | p |
|---|---|---|---|
| tNAA | 15 | -0.65 | **0.009** |
| Cho | 15 | -0.39 | 0.16 |
| Cr | 15 | -0.47 | 0.08 |
| Ins | 13 | -0.31 | 0.30 |
| Glx | 11 | -0.77 | **0.006** |

Table 1: Correlations (rho) and p values between age and metabolite concentrations

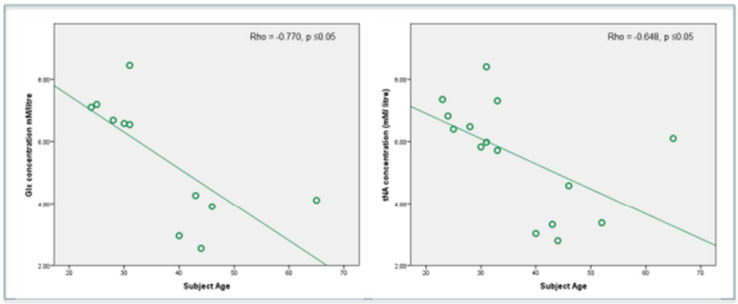



Figure 2: Scatterplots showing correlation between Age and Glx concentration (left ) and tNAA concentration right).

**Discussion:** Normal biological aging is associated with motor and somatosensory changes which are thought to reflect underlying changes in neurone numbers and changing neurobiology. We have demonstrated that SC tNAA and Glx concentration declines with age, which is in keeping with similar findings in the brain. However we found no increase in Cr and Cho contrary to previous reports in brain studies[3,4], which may represent a difference between patterns of glial proliferation in brain and SC with age.

**References**: [1] Christiansen et al. MRI, 1993. [2] Lim et al. MRM, 1997. [3] Soher et al. MRM, 1996. [4] Chang et al. Life sci,1996. [5] Carew et al. Amy lat scler, 2011. [6] Holly et al. Journal neurosurg, 2009. [7] Elliot et al. Spinal cord, 2011. [8] Ciccarelli et al. Neurology, 2010. [9] Kendi et al. Neurorad, 2004. [10] Solanky et al. NMR biomed. In press.