

to estimate an unsuppressed-water signal area that could be used as a reference signal to quantify brain tissue water content. This cerebral water quantification technique is superior to the previous techniques because it does not require extra unsuppressed-water acquisitions, or corrections for variations in the sensitivity of the head coil as both the *in vivo* and reference signals are acquired from the same voxel position.

The developed referencing technique was subsequently used to accurately quantify cerebral water content in healthy volunteers and in psoriasis patients (for the first time).

In the healthy volunteers, the average water content, WC of frontal brain grey matter, GM was found to be higher than that of white matter, WM ( $GM/WM\ WC \pm SE = 46.37 \pm 2.58/42.86 \pm 2.46$  mol/kg;  $p = 0.02$ ); parietal voxels also showed a similar comparison ( $GM/WM\ WC \pm SE = 37.23 \pm 1.70/34.14 \pm 2.02$  mol/kg;  $p = 0.03$ ); both findings being consistent with previous reports [2]. Water content measured from five voxel positions in the brain did not show significant variation by one-way ANOVA ( $p = 0.60$ ); there was also no variation with age ( $p > 0.05$ ) and gender ( $p > 0.05$ ). Water content in the psoriasis patients did not also vary significantly (one-way ANOVA,  $p = 0.63$ )

Among five brain metabolites quantified using the cerebral water referencing method, only the mean concentration of creatine, Cr was found to be significantly lower in the frontal GM of the psoriasis patients, PsA compared to healthy controls, HC at baseline ( $PsA/HC \pm SE = 6.34 \pm 0.38/7.78 \pm 0.38$  mM/kg;  $p = 0.01$ ) and post-TNF- $\alpha$  blockade medication ( $PsA/HC \pm SE = 6.69 \pm 0.25/7.78 \pm 0.38$  mM/kg;  $p = 0.03$ ). No metabolite changed significantly with medication ( $p > 0.05$ ). The significant change in Cr concentration in psoriasis thus suggests that Cr may not be a reliable denominator in studies of psoriasis that express the metabolite concentrations as ratios.

T1 and T2 relaxation times of cerebral water and the metabolites were measured in the prefrontal GM ( $T1/T2 \pm SE = 1574 \pm 61/147 \pm 6$  ms) and bilateral hippocampi ( $T1/T2 \pm SE$ ; left =  $1475 \pm 68/178 \pm 83$  ms, right =  $1389 \pm 58/273 \pm 98$  ms). These estimates were consistent with reported values; relaxation times for cerebral water were however measured for the first time in those regions. The

measured relaxation times were used to correct the water and metabolite signals for relaxation effects in the absolute quantification studies discussed above.

The spectral processing technique was further validated in functional MRS studies focusing on the water peak. While healthy volunteers received a visual stimulus, the resulting BOLD effects on the metabolite and water spectral peaks were recorded, and were found to be comparable to previous reports [3]. For the first time, this study further investigated the impact of temporal resolution (determined by NEX) on the amount of the BOLD signal from cerebral water and metabolites. In a single visual activation paradigm, the BOLD effect resulted in increased water peak area which differed significantly between NEX values of 2 and 8 ( $p < 0.01$ ); this observation also was true for NAA and Glu. The findings thus suggest that temporal resolution of the MRS data could result in significant differences in the results of functional MRS studies.

#### IV. CONCLUSION:

This study has developed and implemented a referencing method for quantification of total cerebral water content, suitable as a reference for estimation of brain metabolite concentrations, *in vivo*. Validation studies show that the technique is appropriate for studies involving both patients and healthy subjects.

#### REFERENCES

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