31P MRS Shows Low Phosphocholine/Glycerophosphocholine in Paediatric Optic Pathway Gliomas

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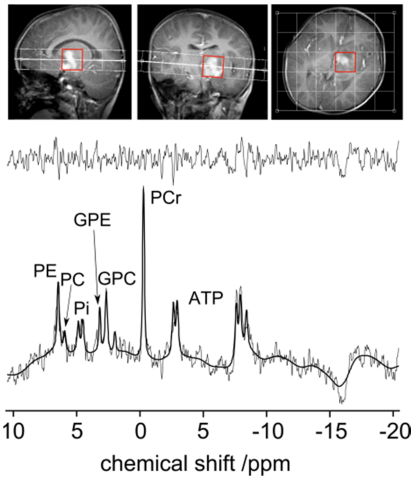
Introduction and Aims

In-vivo 31P magnetic resonance spectroscopy (MRS) is able to profile high energy phosphorus-containing metabolites in the brain. However, translation of this technique into clinical practice has been hampered by poor SNR, lack of technical development and the absence of evidence for clear benefit for pathologies such as brain tumours. 1H MRS is able to measure total choline (tCho) which has previously been linked to tumour malignancy [1]. 1H MRSI however suffers from problems such as difficult shimming, lipid contamination and water suppression optimisation all of which are exaggerated at higher fields. Improved biomarkers of tumour aggressiveness may be obtained by resolving the total choline peak measured by 1H MRS into constituent resonances phosphocholine (PC) glycerophosphocholine (GPC), and phosphoethanolamine (PE) glycerophosphoethanolamine (GPE) using 31P MRS. For some tumours this is especially important such as paediatric optic pathway gliomas, which have high tCho and enhance with Gd contrast despite being low grade. The location of these tumours centrally within the brain makes this technique particularly challenging for surface coils. The aim of this study is to develop and test a 31P MRS protocol which can be used to investigate metabolite levels in brain tumours from all locations on a clinically-realistic timescale and apply it to optic pathway gliomas in chldren. This will hopefully provide further insight into choline metabolism in tumours resulting in more specific biomarkers for diagnosis, prognosis and treatment monitoring.

Methods

All measurements were conducted on a Philips 3T TX Achieva system using a dual-tuned 1H/31P head coil (Rapid Biomedical). Imaging consisted of a T1-weighted localiser. The protocol was optimised using a combination of phantom and volunteer examinations. A 31P MRSI sequence using ISIS localisation was employed. The voxel sizes were either 30 × 30 for volunteers or 35 × 35 for some patients with a slice thickness of 30 mm (matrix size varied). The TR was 4000 ms and the TE was 0.31 ms with 8 signal averages acquired. Broadband decoupling and NOE enhancement were employed to improve spectral resolution and SNR. An eliptical k-space mask was employed with an 80 % sampling rate. All data was fitted using the TARQUIN[2] fitting software with a newly-optimised basis set including PE,PC, GPC, GPE, inorganic phosphate (Pi), phosphocreatine (PCr) and adenosine triphosphate (ATP). The automated processing of 31P MRSI was found to be easier to implement than 1H MRSI due to the aforementioned issues. The optimised protocol was tested on 6 healthy volunteers investigating metabolite ratios in various regions of the brain in an examination time of 22 minutes. Significant differences in metabolite ratios were found when analysing the data using an ANOVA test to look for variance and a Tukey's significant difference test to allow for multiple comparisons. The protocol was also implemented in three paediatric patients with unbiopsied brain tumours (presumed optic pathway gliomas) with an examination time of 12 minutes.



Results

The volunteer studies were sensitive enough to detect minor differences in metaboloite ratios across different structures in the brain. Good quality spectra were obtained across a multitude of stuctures including the cerebellum, brain stem, basal ganglia and the frontal lobe which would be challenging for 1H MRSI in a single examination. For example: a significantly lower PCr/ATP ratio was found in the basal ganglia when compared to both the brain stem ($p < 0.05$) and the cerebellum ($p < 0.005$). This differences in choline metabolites were also detected such as a significantly higher PE/GPE was found in both the basal ganglia ($p < 0.05$) and the frontal lobe ($p < 0.05$) compared to the brain stem.

An example spectra obtained from a paediatric patient with an optic pathway glioma is shown in the figure on the left. Similar quality scans were obtained from the two other patients. In all cases, the PCh/GPC was low, in keeping with a low grade tumour[3]. An example of this is shown in the figure on the left hand side.

Discussion

The detection of subtle differences in metabolite ratios in volunteers is encouraging for the sensitivity of the protocol and to our knowledge has not previously been reported in the literature. There is limited research into these metabolite levels and further investigation is required. This data will undoubtedly help in further studies into brain tumours and disorders in various brain regions. The data obtained from patients was good quality across the whole brain also providing an internal control from "normal" age-matched brain included in the MRSI grid. Importantly we were able to resolve the choline-containing peaks which we hope will help us to understand the role of these metabolites in tumours. We believe this is the first report of 31P MRS from unbiopsied optic pathway gliomas and yielded excellent quality data which confirmed their low grade nature.

Conclusions

We have developed and implemented a 31P spectroscopy protol for the study of paediatric brain tumours on a realistic timescale. As part of the optimisation, a volunteer study has highlighted the differences in metabolite ratios in various regions of the brain. The protocol will now be used to further investigate childhood brain tumours.

References

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