Temporal evolution of brain metabolic substrates differs among major anatomical lobes during the first months of life in human

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Introduction

^{1}H MR spectroscopy (MRS) has been widely used to assess cellular biochemistry and metabolism noninvasively. In addition to providing valuable information to study and monitor neurometabolic disorders in patients[1], MRS can also provide insight into early brain development. Using single voxel MRS, several studies demonstrated that the concentration of several major metabolites (NAA, Cho, mI) might undergo a period of rapid changes during the first several months of life[2]. It remains unknown, however, if the development of brain metabolic substrates differs among anatomical lobes during this critical period of time of early brain development. In this study, we sought to investigate early brain metabolic development in different functional lobes during the first six months of life using a 3D MRSI approach.

Methods

Nine full term healthy infants (6 males and 3 females) were studied with an approved IRB and written consent was obtained from parents prior to imaging. Subjects were scheduled to be scanned every 3 month starting from within one month to six months after birth. All images were acquired using a Siemens 3T whole body MR system and a 32 channel head coil. All subjects were scanned while they were sleeping without sedation. 3D MRSI was acquired using a PRESS sequence with TR =1.6s, TE =30ms, 1024 points, 1200Hz bandwidth, 16×16×8 matrix size, 0.56ml[3] nominal spatial resolution after interpolation and ~8.5 min. In addition, high-resolution (1mm^3) T1-weighted MP-RAGE images were collected to provide anatomic reference. The 3D MRSI data was processed using LCModel[3] to obtain concentration of several metabolites. Five ROIs encompassing five anatomical lobes: frontal lobe (FL), parietal lobe (PL), occipital lobe (OL), temporal lobe (TL) and sub-cortical region (SR) were pre-defined in an age matched T1 template and then aligned onto T1 images of each subject using a nonlinear registration [4]. Relative concentration change of metabolites were computed as $([C]_T-[C]_{1mon})/[C]_{1mon}$, where $[C]_{1mon}$ is the concentration of neonate (within 1month), and $[C]_T$ is the concentration of a metabolite at either the 3 month or 6 month scan.

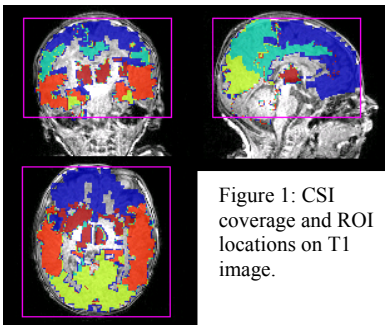

Figure 1: CSI coverage and ROI locations on T1 image.

Results

Fig 1 showed the CSI coverage and ROI locations on T1 images from a representative subject. We have successfully acquired 3D CSI and T1w from 3 subjects at 1 month old (30±8.8 days), 7 subjects at 3-month (age: 86±2.9 days) and 3 subjects at 6-month (age: 197±3.6 days). The growth rates of NAA, Cho and mI to Cre ratios for the five anatomical lobes were shown in the Fig.2. Continuing decreases of the concentration of Cho/Cre and mI/Cre were observed throughout the first six months after birth although the decrease of Cho/Cre appears to be linear with age while a marked decrease of mI/Cre was observed from neonates to 3 months followed by only a slight reduction from 3 to 6 months. Moreover, different lobes had similar decrease rates. Conversely, with the exception of the occipital lobe which exhibited a stable NAA/Cre through the first 6 months of life, the NAA/Cre increased in the four remaining lobes for the first 3 months of life. Among all five ROIs, the parietal lobe had the fastest increase rates of NAA within the first three months followed by temporal lobe, sub-cortical region and frontal lobe. Between 3 to 6 months, all five lobes show only slight changes.

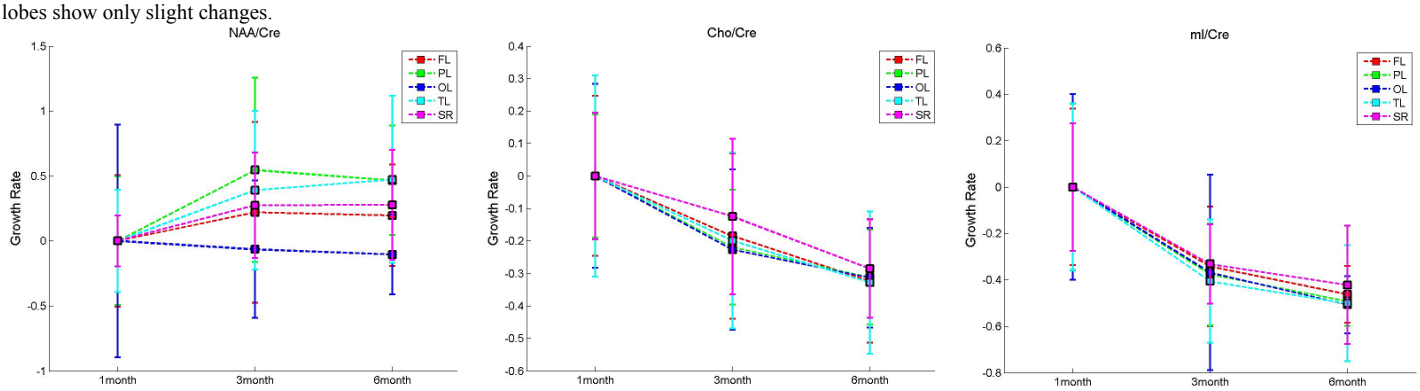

Figure 2 Normalized growth rates of NAA, Cho and mI to Cre ratios for FL (front lobes), PL (parietal lobe), OL (occipital lobe), TL (temporal lobe) and SR (sub-cortical regions) at neonate, 3-month and 6-month. The boxplots were generated at various time points for 5 lobes.

Discussion and Conclusions

It has been demonstrated that NAA is a marker for neurons and axons[5] and could be used to probe the neuronal functional development of the brain. Given the rapid development of neuronal functions during the first year of life, it is not surprising that an increased of NAA/Cre is observed in our study. However, two features deserve additional discussion. First, it appears that the development of neuronal functions largely occurs during the first 3 months of life, followed by a plateau from 3 to 6 months, which is in agreement with literature[1]. Second, the rather stable NAA/Cr ratio in the occipital lobe may suggest that a large part of metabolic substrate of visual function may have already completed by the time of birth. Since the spatial resolution of MRS data is low, we have focused our analysis in large size functional lobes, which may result in a diminished sensitivity in detecting subtle changes of occipital lobe. On the other hand, Cho/Cre and mI/Cre are expected to be altered in response to alteration of membrane metabolism or damaged membrane. Consistent with published results, we found that their concentrations are high in neonates and continues to decrease throughout the first 6 months after birth. The early brain metabolic maturation finding reported in this study needs to be confirmed in a large subject population with a wide span of ages.

References

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