Metabolic Trends in Thalamic Development from Infancy to Adulthood Measured using Magnetic Resonance Spectroscopy

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Target Audience

MR physicists specializing in spectroscopy, neuroscientists, neurologists, neuroradiologists, and neonatologists interested in brain development.

Purpose

Quantitative assessment of metabolite changes within the developing brain enhances the understanding of normal brain development beyond morphological imaging. Proton magnetic resonance spectroscopy (1H MRS) is capable of measuring biochemical data within specific regions of the brain. As an important component of the default mode or 'resting state' network, the thalamus is particularly important as thalamocortical connections may be impaired in preterm-related neurodevelopmental delay (1) and its connections with the cingulate, form part of the parietal white matter "crossroads" which are known to be vulnerable in preterm infants (2). This study examines normal development of metabolite concentrations in healthy individuals from birth to young adulthood using 3T 1H MRS within a posterior thalamus-specific voxel with both parietal grey matter (including posterior medial cingulate cortex) and parietal white matter voxels.

Methods

Term control infants (18 male, 13 female; PCA 41.5±3.8 wks), pediatric healthy controls and adult healthy volunteers (1-25 years of age, mean: 15 years; 15 male, 26 female) were included in this study. MRS was performed on a 3T scanner with selective voxels placed in the posterior thalamus, parietal white matter (p-WM) and parietal grey matter (p-GM). All processing was performed using fully automated LCModel software (Version 6.1-4F, Stephen Provencher Inc.) looking at 6 major metabolites (NAA, Cr, Cho, mI, Glu, Tau). Group differences were identified using the Student's *t-test* and logarithmic regression analysis of metabolites with age using SPSS (Version 20, IBM Corp.).

Results

Statistical analysis revealed significant differences in most major metabolites between neonate and older age groups, summarized in Table 1. Logarithmic regression analysis relationship between age and metabolite concentration in thalamic voxels (NAA, Cho, mI, Glu, Glc), white matter (NAA, mI, Glu) and grey matter (NAA, Cr, Cho, mI). Generally, NAA increased rapidly whereas choline and myo-inositol decreased substantially following the neonatal period. Of note, the absolute concentration of NAA and choline were significantly thalamus compared to GM and WM voxels ($p < .01$).

Table 1: Mean Metabolite Concentration Change from Neonatal Period to Older Age

	NAA	Cr.	Cho.	mI	Glu	Glc
Thal.	+3.31‡	+0.05	-0.45*	-2.93‡	+3.31‡	-1.07*
W.M.	+4.96‡	+0.82	-0.67*	-4.14‡	+4.96	-1.29*
G.M.	+3.07‡	+0.20‡	-0.23	-3.09‡	+3.07‡	-3.23

t-test results: ‡ $p < 0.001$, * $p < 0.05$

Discussion

MRS is capable of clarifying changes in metabolites within the developing brain. Using 3T MRS, we identified biochemical trends within the GM, WM and thalamus that differ between neonates and older individuals. As demonstrated in work performed by our group at 1.5T (3), the majority of changes occur following the neonatal period. For this reason, we examined differences between neonates and a combined group of children and adults.

Particularly important is the demonstration of a critical period in the metabolic development within the posterior thalamus, which plays a key role in integrating cortical activity with thalamocortical connections seen by functional connectivity and diffusion tensor tractography (3, 4). Moreover, preterm infants appear to have impairment in these connections (1), and in normal individuals these connections increase with age, suggesting they are key to normal development. In neonates, we noted relatively greater absolute metabolite concentrations of NAA within the thalamus compared with other voxels, a finding consistent with known earlier maturation of the thalamus relative to parietal regions. In addition, there were differences in the rate of change of metabolites within the thalamus compared to GM and WM voxels, suggesting a critical period in the metabolic development of overall parietal network connectivity.

Conclusion

We have defined metabolic postnatal development of the posterior thalamus in conjunction with an overall critical period in metabolic development of the parietal region. Future work attempting to integrate the observed thalamic metabolic changes in neurodevelopment with the formation of posterior thalamocortical connections on diffusion tensor and functional connectivity imaging will aid in clarifying parietal development and identify events prone to disruption in the preterm brain.

References

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