EXPLORING THE DIFFUSIVITY CHANGES OF DIFFUSE EXCESSIVE HIGH SIGNAL INTENSITY (DEHSI) IN PRETERM NEONATES BY USING TWO-COMPARTMENT WHITE MATTER MODEL BASED ON DKI

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Target audience: Pediatric radiologist and pediatrician

Introduction: Diffuse excessive high signal intensity (DEHSI) is extremely common in preterm infants on near-term images, expressed as long T1 and long T2 in diffuse white matter (WM) regions. It is still under debate about whether it represents a true WM abnormality or just the relative immature in WM. To the knowledge from the previous studies1,2, DEHSI regions in neonatal brain mainly distribute in the subcortical WM which present as the premyelination in perinatal period. Therefore, the differentiation of the axonal injury and increased free water in extra-axonal space is very important for clarifying the physiopathologic mechanism of DEHSI. Recently, Jensen et al. proposed a two-compartment non-exchange diffusion model of WM that is suitable for diffusion kurtosis imaging (DKI) analysis and provides analytical expressions for the intra- and extra-axonal diffusion tensors3. So the aim of this study was exploring the water diffusivity in DEHSI regions based on the two-compartment WM DKI model.

Methods: This study was approved by the local institutional review board. Subjects: 8 preterm neonates with DEHSI and 8 normal controls (matched with gestational age (GA), postmenstral age at MR scan (PMA) and birth weights (BW)) who underwent MRI at term-equivalent age were enrolled. Clinical details were given in Table 1. In addition, two severe hypoxic-ischemic (HI) neonates with DEHSI in WM and matched normal controls were also chosen. MRI acquisition: All neonates were all sedated (oral chloral hydrate, 25-50 mg/kg) before MRI scanning. Conventional MRI and DKI were performed on a 3T scanner (GE, Signa HDxt). DKI protocols were: 18 directions, b value=0, 50, 200, 500, 1000, 2000, 2500/1000/mm², TR/TE=8000/120ms, slice thickness= 4 mm without gap, field of view = 180mm×180mm, matrix = 256×256, voxel size = 0.70×0.70×4mm³. Image analysis: All DKI data were processed using a custom-written program in MATLAB, and all parameters (FA=fractional anisotropy, MD=mean diffusivity, AD= axial diffusivity, RD= radial diffusivity, MK = mean kurtosis, AK = axial kurtosis, RK = radial kurtosis, AWF = axonal water fraction, Da = intra-axonal diffusivity, De⊥ = axial extra-axonal space diffusivity, De⊥ = radial extra-axonal space diffusivity, α = tortuosity) were generated. 3 regions of interests (ROIs) were chosen in anterior, middle and posterior WM regions at the level of centrum semioval in axial b0 maps. 2 other ROIs were chosen in anterior periventricular WMs and posterior periventricular WMs (PPWM) at the level of the body of lateral cerebral ventricle. All ROIs were manually drawn as square shape with size of 49 voxels. Then all values of two-compartment WM DKI parameters were extracted for above 5 regions, and the difference of these diffusion parameters between DEHSI and control group, between severe HI and control group were analyzed by paired-sample t test. All tests were taken to be significant at p<0.05.

Results: Fig.1 exhibited the visible signal differences of WMs at the level of centrum semioval on FA, MD, AD, RD, De∥, De⊥ and α maps between a pair of DEHSI and control neonates. As shown in Fig.2, compared with control group, FA, α in DEHSI group were significantly decreased, while MD, AD, RD, De∥, De⊥ were significantly increased. MK, AK, RK, AWF, Da showed no significant difference between two groups. Fig.3 displayed changes of all these diffusion parameters in severe HI brain injuries. FA, MD, RD, De∥, De⊥, α have similar changes as DEHSI, while the MK, AK, RK, AWF in severe HI neonates were significantly increased.

Discussion: Although DEHSI has been studied for a few years, it is still unclear whether a diffuse WM injury exists. Previous DTI study has reported that DEHSI might represent an oligodendrocyte and/or axonal abnormality and exhibit the decreased FA and increased diffusivity4. However, DEHSI neonates manifested the normal neurodevelopmental outcome in a recent study5. In our result, the increased De∥, De⊥ and no significantly changed Da. AWF indicated an increased diffusivity mainly from extra-axonal space, which might be due to the increased water and/or enlarged extra-axonal space. Compared with severe HI neonates, MK, AK, RK, AWF in DEHSI neonates showed no significant increase, which suggested no direct injuries to axons or myelination. Conclusions: Based on the two-compartment diffusion model, this study demonstrated that the diffusion changes in DEHSI were mainly due to the increased water and/or enlarged space in extra-axonal space, rather than injuries to axons or the process of myelination.

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Table 1. Clinical characteristic of DEHSI and control neonates

<table>
<thead>
<tr>
<th>Demographics</th>
<th>DEHSI group</th>
<th>Control group</th>
<th>P</th>
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<tr>
<td>Gestational age, wks</td>
<td>34±1</td>
<td>34±1</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Postmenstral age at MR scan, wks</td>
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<td>38±1</td>
<td>&gt;0.05</td>
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<tr>
<td>Birth weight, g</td>
<td>2037</td>
<td>2298</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Fig.1 All diffusion parameters from a pair of DEHSI and control neonates

Fig.2 Differences of all diffusion parameters between DEHSI and normal group

Fig.3 Differences of all diffusion parameters between severe HI neonates and normal neonates