Activation of the Sensory-Motor Pathways in the Premature Brain: A combined fMRI and DTI study

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Introduction

Functional MRI (fMRI) in pre-term and term newborns is a promising, but yet challenging, method to investigate brain function in the premature brain. Difficulties arise from hypothermia and dehydration during MRI, which can cause fussiness, and subsequently movement and physiological changes affecting the blood oxygen level dependent (BOLD) signal. To overcome these difficulties, we have utilized a novel MR compatible incubator (MRCI) with a special newborn RF head-coil. We used the MRCI to explore whether (i) sensory-motor pathways are already functioning and (ii) that sensory-motor lateralization is in-place in the premature brain. In order to test these hypotheses, we used passive sensory-motor fMRI for neuronal activation and diffusion tensor imaging (DTI) to visualize white matter tract development of the sensory-motor pathways. In an earlier study we demonstrated the feasibility of this approach and showed activation being present [1] without complete myelination (about 40% at 37 weeks [2]).

Methods

42 pre-term and term newborn patients of the NICU in need for routine MRI were enrolled in this study (GA 25-41, mean=37 weeks). All parents gave written consent for this IRB approved study. Patients were sedated before imaging using chloral hydrate (50mg/kg). Newborns were prepared and placed in the MRCI (Lammers Medical Technology, Lübeck, Germany and AIRI, Cleveland, OH) equipped with the newborn head-coil [3] . During imaging vital signs, movement, and sleep state was constantly monitored. Imaging was performed with a 1.5T MR system (CV/i, 8.4 software GE/MS Milwaukee). For functional acquisition we used a single shot gradient-echo echo planar imaging (GR-EPI) sequence (TR3000, TE50, FOV180, FA90, 64x64 matrix, 3x3x3 voxel resolution). 6 diffusion directions using 2D EPI (TR10000, TE85, FOV180, FA90, 128x128 matrix, 1x1x3 voxel resolution) were acquired. T2-weighted FSE images were used to overlay the functional results. Two experiments, passive sensory-motor stimulation (A) of the left and right hand, were conducted with the sleeping babies, provoking a grasp movement by repeated inflating/deflating of a rubber air-bulb (~2Hz) versus rest (R). We used an alternating block paradigm of RARARA lasting 30 s for each phase and a total scanning time of 3 minutes. Statistical Parametric Mapping software (SPM99) [4] was used for spatial pre-processing and t-test statistics. Individual brain maps of anatomy, fractional anisotropy (FA), and functional activation ($p<0.01$ uncorrected) were interpreted. Areas of activation/deactivation were identified and were accounted for hemispheric differences in the post- and precentral gyri and in the whole cerebrum.

Results

27 subjects with normal brain structure were investigated with fMRI and DTI. In 3 subjects we were unable to perform the tasks because of early awakening. 23 right hand and 17 left hand experiments have been successfully carried out. DTI was successfully performed in all these subjects. Head movement during fMRI was reported <4mm (translation) and <3° (rotation) and corrected. Brain maps show multiple areas of activation in the premature brain focused on the spinothalamic pathways in the brain stem and the ventrolateral thalamus and the thalamocortical pathways (Fig.1) in the posterior limb of the internal capsule and the corona radiata to the post and precentral gyri (Fig.1), and frontal lobe. FA confirmed age appropriate white matter tracts. We found 13% more contralateral BOLD changes in the sensory-motor areas whereas only 2% contralateral dominance overall in the cerebrum were found.

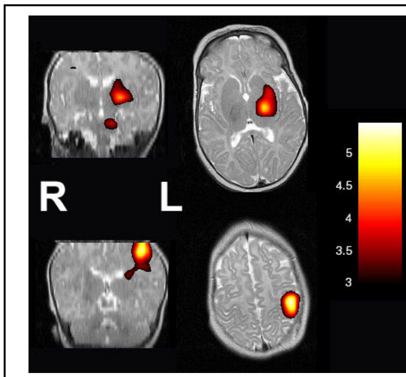

Figure 1: Right hand task in a 40-week (GA) old newborn activates the sensory-motor pathway, thalamus (top) to cortex (bottom).

Discussion

fMRI revealed an remarkably established sensory-motor response in the premature brains with incomplete myelination. (i) The presence of thalamic activation in the contra-lateral hemisphere suggests that unmyelinated regions along these pathways can activate surrounding areas. During the later development sheaths of myelin protect the fibers from co-activating adjacent regions. Missing thalamic activation in sensory-motor studies on infants of about 3 month of age [5] support this conclusion. (ii) Consistent evidence of deactivation suggests substantial differences between newborns and older children in blood oxygenation and tissue perfusion. (iii) Lateralization seems to be present in the premature sensory-motor cortex at near-term. In contrary the overall activation patterns for each hemisphere are not clearly lateralized at this age. Latter may be a results of (i). We conclude, that combined fMRI and DTI imaging is possible in the newborn and will reveal new insights of the functional development of the newborn and infant brain leading to novel basic developmental neurobiology and clinical applications.

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References

[1] Erberich SG, Friedlich P, Seri I, Nelson MD, Blüml S. Functional MRI in neonates using neonatal head coil and MR compatible incubator. NeuroImage 2003, 20:683-692

[2] Gilles, F. H., Leviton, A., and Dooling, E. C. 1983. The developing human brain – Growth and epidemiologic neuropathology. Chapter 12; *John Wright, PSG Inc.*, Boston

[3] Blüml S, Friedlich P, Erberich SG, Wood J, Seri I, Nelson MD. MR Imaging of Newborns Using a MR-Compatible Incubator with Integrated Radiofrequency Coils. Radiology 2003, in press.

[4] FristonK et al, Human Brain Mapping 1995; 2:189–210

[5] SouweidaneMM et al, P*ed. Neurosurg*. *30*:86-92