Evaluation of white matter development and small world anatomical networks in fetal brain by sBTFE sequence from MRI.

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Target audience: It is generally accepted that fetal magnetic resonance imaging (MRI) is becoming an increasingly powerful tool for studying brain development in vivo. The steady state free precession (SSFP) techniques are basically gradient echo sequences with facilitating image acquisition. Balanced turbo fast echo (BTFE) is one of SSFP and the most frequently commercially used fast sequences. Very fast imaging in milliseconds can be achieved by BTFE sequences using a large flip angle and very short time of repetition (TR). Furthermore, another technique, k-space and time (k-t) sensitivity encoding (SENSE) imaging, can be combined with BTFE to further reduce both maternal and fetal motion artifact as well as subject discomfort. High quality images in fetal MRI without resultant aliasing can be generated from this ultrafast sequence through a combination of SENSE and BTFE.

Purpose: To assess the developmental changes or myelination in white matter signal intensity across gestational age by sBTFE, one of superfast MRI sequences, in living unsedated fetuses in utero. And to evaluate the complex brain networks in fetus under exploring connectivity patterns based on fetal brain white matter of small world properties.

Materials and Methods: 146 normal singleton fetuses underwent sBTFE sequences on a 1.5 T MR scanner. Signal intensity values of 15 regions of interest (ROIs) at the deep white matter of each fetal brain were obtained. Signal intensity ratios (SIR) were calculated by dividing the signal intensity from CSF in the posterior part of bilateral ventricles. The SIRs were plotted against the gestational weeks (W21～W39)for each region. In order to explore the network in fetal brain, the statistical similarity in SIR between too ROIs was measured by the Pearson correlation coefficient across subjects and interregional correlation matrix. A graph theoretical analysis was performed by Pajek software to explore the small world properties in fetal brain white matter. All of the ROIs were abbreviated to Fron.L,Fron.R,occi.L,occi.R, temp.L, temp.R, PreC.L, Post.L, PreC.R, Post.R, Pons, Cere.L, Cere.R, Thal.L, Thal.R.

Results: At W21～W23 gestational weeks, SIR of bilateral frontal lobes was significantly lower than those of other lobes and SIR of frontal, occipital, and parietal lobes increased significantly at W28 ($P < 0.05$). The human fetal brain anatomical network had small-world properties in every GA with cohesive neighborhoods and short path length between regions ($\gamma > 1$, $\lambda \sim 1$,higher Cp and lower Lp). The average degree shows significantly different between groups in every GA except between W28 and W33 ($P<0.05$). The degree in W25 is lowest among all of groups and there is not significantly statistical different for the degree between W28 and W33 ($P>0.05$). The connection network was mapped in the anatomical space by using Pajek software package with Pearson correlation $r \geqq 0.7$.

Discussion: This is the first study, to our knowledge, to demonstrate the large scale human fetal brain white matter development and anatomical connectivity patterns using signal intensity measurements from sBTFE ultrafast sequence in MRI. Firstly, we found the SIR for the frontal lobe white matter was smaller than other regions during W21 to W23 might be explained by the germinal matrix present only in the frontal lobe white matter at that time. Secondly, the cellular migration in temporal lobes, pons and cerebellar WM might be earlier than other regions owing to the higher SIR for these regions than others in W25. Thirdly, the cellular migration was unsynchronized in temporal, pons and cerebellar white matter in W25 and there were similar pattern of the small world properties in W28 and W33, indicating the fetal brain was going to maturation after 28 weeks.

In our study, sBTFE sequence with 2-mm slice thickness and very short TR-TE supplied very good contrast between CSF-WM-gray matter and high spatial resolution. Scanning time is quite short, getting 1 slice in 2 seconds, the structure of fetal brain are depicted clearly. The shortened TR reduces flow void artifacts, fetus motion, further increasing the brightness of fluids; it also decreases the scan time while preserving high fluid signal, making less time available for flow voids caused by CSF motion and recovery of magnetization at the end of a long echo train.

It has been demonstrate that the first WM fibers to show high-order organization and myelin deposition are concentrated in the ascending sensory spinocerebellar and spinothalamic tracts, which are located in the posterior part of the brainstem and make connections to the cerebellar hemisphere and to the lateral parts of the thalamus. The myelin deposition shortened the T1 value in the tissue and this correlates well with the facts that (1) The SIR for the pons and thalamus increased significantly from GA of 25 weeks, and (2) both these regions show a very similar maturational time course.

We found that the fetal brain white matter network had small world properties from W21 to W39 with cohesive neighborhoods and short path length between regions. The higherst γ and Cp in the group of W33～W39 than the group before W33 implied the small world properties were stronger and stronger during the development of fetal whiter matter. The lowest γ and Cp is in the group of W25 among W23 and the week after W25 can be explained by the unsynchronized cellular migration with temporal, pons and cerebellar WM firstly development, which in consistent with our former part findings.

Conclusion: Myelination-related changes during the course of pregnancy can be reflected by SIR on fetal MR imaging with sBTFE sequence. The cellular migration was unsynchronized in temporal, pons and cerebellar white matter in W25 and there were similar pattern of the small-world properties in W28 and W33, indicating the fetal brain was going to maturation after 28 weeks.

Key words: cerebral maturation, small world networks, ultrafast sequence, prenatal diagnosis

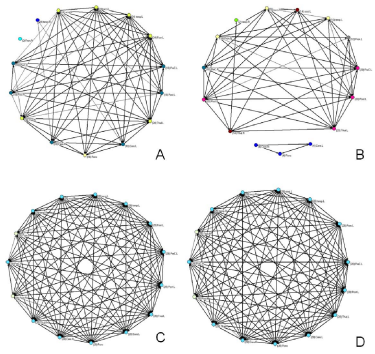

Figure 1- The connection network were mapped in the anatomical space by using Pajek software package to visualize the hubs in fetal brains white matter. Here we only shows the nodes with Pearson correlation $r \geqq 0.7$ for corresponding matrix map in each GA group. The nodes in green represent the ROIs as flowing: Fron.L, Fron.R, occi.L,occi.R, temp.L, temp.R, PreC.L,Post.L, PreC.R, Post.R, Pons, Cere.L, Cere.R, Thal.L, Thal.R. The number in parentheses besides the node name represents the degree for each node. Figure A is for W23, B is for W25, C is for W28 and D is for W33. A Kamada-Kawai layout algorithm was applied here. The figure 7 C and D shows the similar pattern with undirected nodes (n) and edges (k), where nodes represent ROIs and edges represent undirected connections between ROIs. The figure B for W25 shows less nodes (n) and edges (k) than W23, W28 and W33 groups, which is certified by the degree analysis.