The evaluation of the white matter development and small-world networks in the fetal brain MRI using sBTFE sequence

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TARGET AUDIENCE: obstetrician, neurologists and neuroradiologists.

Purpose: We aimed to examine the white matter development and small-world networks in the fetal brain across the different gestational weeks (GW) using sBTFE on MRI.

Methods: *Subject*: A total of 150 singleton fetuses ranging from 21 to 39 GW were imaged with sBTFE sequence in 1.5T MRI scanner (Achieva Nova Dual, Philips, The Netherlands). The fetal brain in utero was examined using a four-element, phased-array abdominal coil placed around the abdomen of pregnant mother.

Measurement: Signal intensity (SI) values from fifteen regions of interest (ROIs) were obtained and scaled by SI from cerebral spinal fluid (CSF). SI ratio (SIR) for bilateral prefrontal, occipital, temporal, parietal and pre central white matter regions and from thalamus, cerebellum and pons were plotted against GW (Fig.1). Two brain regions were considered connected if there were statistically significant correlations in SIR (r>0.8). We constructed the small-world network of such connectivity between every two brain regions (n=15,15×15/2 pairs of regions) across all subjects (n=150). Three parameters for the connections matrix were used: (1)the degree of connectivity; (2) the clustering coefficient (Cp); (3) the characteristic path length (Lp). Analysis of variance was used to compare SIR and the parameters. False discovery rate was applied for multiple comparisons,q=0.05.

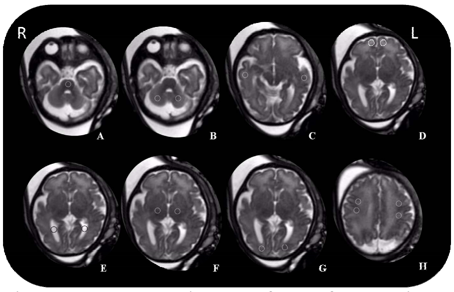

Fig.1 An example image of the fetal brain at gestational week 30, from sBTFE sequence in transversal plane. The circles demonstrate manual placement of ROIs in the center of the pons(A), bilateral white matter of cerebellum at the level of the cerebellar peduncle(B), temporal lobes(C), frontal lobes(D), CSF in lateral ventricles (E), thalamus(F), occipital lobes(G), white matter in the anterior and posterior parts of the central sulcus (H).

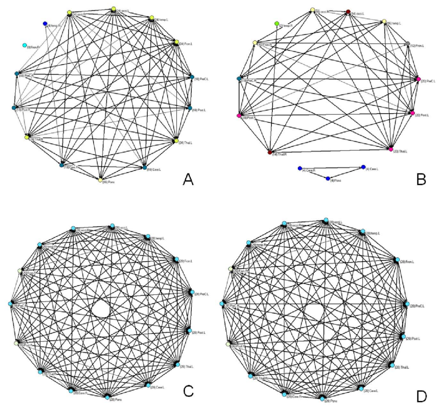

Fig.2 The connection networks were mapped in the 2D anatomical space. The nodes represent 15 ROI as follows: prefrontal, Occipital, Temporal, Parietal, Precentral, Pons, Cerebellum, and Thalamus. The color and the number in parentheses in front of the node name indicate the degree of connection for that particular node. The lowest degree of connections is seen in the gestational week 25 (B) as compared to weeks 21-23 (A), 28 (C) and 29-33(D). Similar (higher) connectivity pattern is retained in GW28 and 29-33 (C and D).

Results: The SIR did not change significantly during GW21-23 (Group A) and GW33-39 (Group D) (p > 0.05). In Group A, the SIRs for bilateral prefrontal lobes were lower than for the pre central, occipital, temporal and parietal lobes (P = 0.04). Conversely, in week 28 (Group C), the SIR for bilateral frontal lobe was higher than the pre central, occipital, temporal and parietal lobes (P = 0.03). In week 25 (Group B), the SIR for bilateral temporal lobe was the highest with respect to GW and also to the regions examined, respectively (P = 0.001). The degree of connections in Group B was lower than Group A, C and D (P < 0.05) (Table 1). The degree of connections did not differ between left and right hemisphere across the whole spectrum of gestational age. As the gestational age progressed, the fetal brain network pattern developed consistently with small-world properties (given that $\gamma>1$,and $\lambda\sim1$ when calculated with higher Cp and lower Lp) (Fig. 2).

Table 1 The averaged SIR (Means ± SD) in ROIs from bilateral hemisphere among groups.

Gestational week	Week 21-23	Week 25	Week 28	Week 33-39
Group	A	B	C	D
Number of fetus	n=16	n=15	n=15	n=50
SIR				
Prefrontal	0.25±0.03	0.29±0.02	0.43±0.01	0.29±0.06
Occipital	0.31±0.06	0.24±0.02	0.40±0.03	0.29±0.03
Temporal	0.28±0.01	0.34±0.02	0.40±0.06	0.30±0.01
Parietal	0.31±0.03	0.31±0.06	0.38±0.01	0.31±0.01
Pre Central	0.28±0.02	0.30±0.02	0.41±0.06	0.29±0.02
Thalamus	0.20±0.02	0.22±0.01	0.26±0.02	0.21±0.06
Pons	0.19±0.02	0.35±0.03	0.24±0.03	0.23±0.01
Cerebellum	0.27±0.01	0.43±0.01	0.29±0.01	0.30±0.03

Discussion: To our best knowledge, this is the first study in a large fetal brain cohort to demonstrate white matter development and connectivity patterns using relative signal intensity quantification measurements from sBTFE ultrafast MRI sequence. We found that the bilateral prefrontal SIR during gestational week 21-23 was characterized by significantly lower than other subplate zones. This finding could be explained by the germinal matrix being present exclusively in the frontal lobe white matter at this time point. Secondly, the lower degree of the connection pattern in brain network at gestational week 25 as compared to earlier and later gestational age could be due to the unsynchronized cellular migration within the temporal, pons and cerebellar white matter. Thirdly, we have observed similar pattern of the small-world properties between gestational weeks 28 and 33-39, indicating the fetal brain was maturating after gestational week 28.

Conclusions: sBTFE sequence is the optimal tool for the assessment of the changes in fetal brain white matter. Additionally, sBTFE sequence could be complementary to the DTI and functional MRI[3] and could contribute to the understanding of the connectivity and functional competence of the developing brain. Moreover, calculating the changes in SIR from sBTFE sequence can reflect the temporal order when and where the germinal matrix migrates and how myelination progresses as these two processes are very likely to affect the SIR values. Knowing this all can be useful for further refinement of the diagnosis while finding any abnormality on ultrasound.

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