Feasibility of functional resting-state measurements of the fetal brain

V. Schöpf[1,2], G. Kasprian[1], C. M. Mitter[1], P. C. Brugger[3], and D. Prayer[1]
[1]Department of Radiology, Division of Neuroradiology, Medical University Vienna, Vienna, Vienna, Austria, [2]MR Centre of Excellence, Medical University Vienna, Vienna, Vienna, Austria, [3]Center of Anatomy and Cell Biology, Integrative Morphology Group, Medical University Vienna, Vienna, Vienna, Austria

Introduction:
The evolution of resting-state networks and the development of connectivity have recently been studied in premature infants (<41 GW) and older children (9-12 years) (for a review see Power et al., 2010). While it has been proposed that the neuronal mechanisms underlying these activity networks evolve *in utero* and are supposed to be strongly connected to gestational age, this aspect has not yet been investigated.
In this study, we aimed to demonstrate the feasibility of studying spontaneous resting-state activity of the fetal brain. Functional connectivity analyses allowing the characterization of interregional neural interactions during spontaneous activity during rest was used to study those underlying mechanisms. Furthermore, we proposed at describing subplate specific activity patterns and interactions with subcortical structures for different developmental stages.

Methods:
Functional images of 10 fetuses with morphologically normal brain development, aged from gestational week (GW) 20-39, were acquired on a 1.5 T Philips Intera MR scanner using single-shot gradient-recalled echo-planar imaging.
Between 10 and 15 axial slices (5mm thickness) with a matrix size of 144 x 144, FOV of 250 x 250 mm and TE/TR of 50/1000 ms and a flip angle of 90°. Image preprocessing was performed with SPM8 (http://www.fil.ion.ucl.ac.uk/spm/) including motion correction. Brains were extracted as implemented in BET (Brain extraction tool) version 2.1, as implemented in FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). Data sets were inspected for "jerk-like" head movements, in which the fetal brain moved out of its original position and returning to in space to its previous position after a few seconds. As realignment algorithms are not able to cope with "out-of-slice" movements affected image volumes were removed from the data sets and the remaining volumes were treated as one continuous data set.
Postprocessing was performed using functional connectivity analysis implemented in Matlab (Matlab 7.8.0, Release 2009a, Mathworks Inc., Sherborn, MA, USA). Correlation maps were converted to z values by Fisher's r-to-z transformation to enable parametric statistical comparison. Seed voxels were positioned by an experienced Neuroradiologist.

Results:
Bilateral resting-state activity could be proved in cortical frontal, occipital, and temporal regions. Throughout the whole group subplate temporal, frontal and occipital seed regions could be proved to evoke bilateral activity patterns situated in corresponding subplate regions. Furthermore, temporal, frontal and occipital subplate regions showed high and consistent correlations with thalamic regions.
We were able to categorize cortical activity projections for cortical seed regions into projections before and after GW 26.

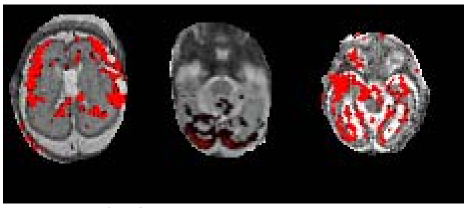

Figure: left: GW 27, seed voxel position in the frontal subplate; middle: GW 27, seed voxel position in the occipital cortical plate; right: GW 22, seed voxel position in the temporal subplate.

Conclusion:
We were able to show that resting-state measurements are possible *in utero* and can be analyzed by means of functional connectivity analysis. Resting-state measurements in the fetus may therefore allow for developmental brain activity monitoring and provide important impact on the understanding of neuronal processes.

References:
Power, J. D.; Fair, D. A.; Schlaggar, B. L. & Petersen, S. E.
The development of human functional brain networks.
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