Resting State Analysis of Function in the Moving Fetal Brain?

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Introduction: Motion corrected fetal brain imaging has recently emerged as an active area of work [1], with MRI providing a valuable new insight into early structural brain growth. However, functional imaging has been limited to the analysis of stimulus correlated BOLD fluctuations in the small fraction of cases where motion is not occurring [2-4]. Recent pioneering work [5] has shown the first application of resting state fetal fMRI by selecting a subset of subjects that are relatively motion free and applying conventional volume motion correction to account for gross changes in head position between time frames, assuming no motion within each slice stack. In work presented here, we specifically account for motion between individual slices during a resting state analysis of the moving fetal head using full slice motion correction of multi-slice EPI data, with the aim of providing a more generally applicable tool to study early brain function. We develop a framework that incorporates motion correction (volume and slice correction), density based weighting to account for under-sampling due to motion, and ICA to extract the functional network architecture.

Materials and Methods: Our current database consists of healthy fetuses (ages of 31 and 36 wks), scanned 1-2 times using a 1.5T GE Scanner. Each scan is a multishot EPI consisting of 60-160 frames, acquired with a 2-interleave, flip angle=80, TE=40-50, TR=2000. Large scale volume motion estimation of each frame to the first frame is carried out by maximization of NMI with respect to the 6 rigid transformation parameters, using an age specific head mask synthesized from a spatio-temporal model of the fetal brain [7]. Individual slice transformation parameters are then estimated by iterative minimization of intensity differences between an "average" 3D volume (using current slice motion estimates) and each slice using a two step reconstruction-matching based iterative scheme [6]. Data is then reconstructed into a regularly sampled 3D volume at each time frame using scattered data interpolation (Fig. 1). To account for varying sample density supporting each reconstructed voxel we then use the slice profiles of the individually aligned slices to form a slice density map for each frame. This density function is then explicitly incorporated to create a frame weighting for the voxel correlation analysis by counting the brain voxels that have densities falling below a given threshold. Spatial and temporal smoothing is then applied and weighted ICA analysis is performed on each subject dataset. All development was carried out in C++. The ITPP FastICA library was used for ICA analysis.

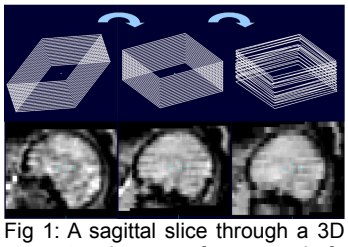

Fig 1: A sagittal slice through a 3D reconstruction from Left: Uncorrected Data, Middle: Volume Motion Correction, Right: Volume and Slice Correction

Results: We performed experiments on 3 subjects: Subject 1 (36 weeks) contained very little motion whereas Subject 2 (34.5 weeks) and Subject 3 (32.5 weeks) contained more motion. In order to demonstrate the significance of slice correction, we applied ICA to data from Subject 3 after applying volume correction only. Of the resulting ICA components, only two did not appear to be motion artifacts (Fig. 1). Next, we applied slice correction and extracted ICA components on the same subject (bottom row, Fig. 2), and by comparison this analysis yielded several plausible components localized within the brain. We then separately applied the pipeline to the other two subjects. Fig. 2 shows 8 ICA components extracted for these three subjects; we obtained 5 similar network patterns across subjects. Consistencies between the ICA components extracted across subjects and adherence to anatomical boundaries, both suggest these are functional networks rather than artifactual components. Here, we tested new methods for removing motion artifacts and weighting data densities in spatial and temporal domains, and have achieved an encouraging result. The method we have developed may provide an essential new framework for successful management of movement related effects. We believe this key in order to achieve full detailed mapping of the developmental trajectory of the fetal brain, without bias toward studying select cases where motion is reduced.

References: [1] Studholme C., *Ann Rev Bio Eng*, 13:345-368 (2011) [2] Hykin J. et al, *Lancet* 354:645-46 (1999) [3] Fulford J. et al, *HBM* 20:239-45 (2003) [4] Born P. et al, *Pediatr. Res.* 44:578-83 (1998) [5] Schöpf V. et al, *IJDN*, Oct. 2011 [6]Rousseau F. et al, *Acad Rad*, 13:1072-1081 (2006) [7] Habas P. et al, *NeuroImage* 53(2):460-70(2010)

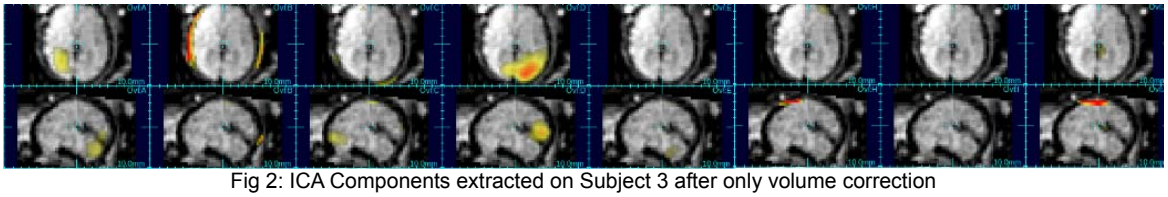

Fig 2: ICA Components extracted on Subject 3 after only volume correction

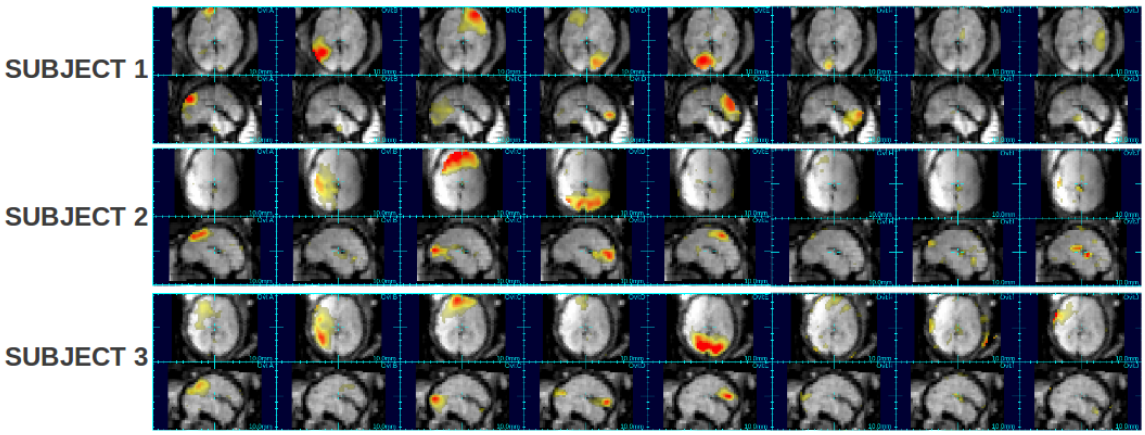

Fig 3: 8 ICA components extracted on 3 different subjects after slice correction. Each row contains an axial and sagittal view of the brain, with the ICA components. Top row: Subject 1, Middle row: Subject 2, Bottom row: Subject 3