Reduction of functional connectivity in adolescents prenatally exposed to alcohol

Bing Ji[1,2], Zhihao Li[1,3], Claire Coles[4], Julie A Kable[4], Renjie Zhang[2], and Xiaoping Hu[1]

[1]*Biomedical Engineering, Emory University & Georgia Institute of Technology, Atlanta, GA, United States,* [2]*School of Optical Electrical and Computer Engineering, University of Shanghai for Science & Technology, Shanghai, Shanghai, China,* [3]*Institute of affective and Social Neuroscience, Shenzhen University, Shenzhen, Guangdong, China,* [4]*Psychiatry and behavioral Science, Emory University, Atlanta, GA, United States*

TARGET AUDIENCE Researchers interested in resting-state functional connectivity and/or neurodevelopmental effects of prenatal substance exposure.

PURPOSE Prenatal alcohol exposure (PAE) is associated with a wide range of cognitive and behavioral deficits [1]. Traditional neuroimaging studies of PAE typically took "regional" approaches that only focus on a few brain regions or neural pathways despite evidences that the teratogenic impact is widespread [2]. Since a network-dysconnecitivity hypothesis that examines the entire brain is valid and desirable for further neuroimaging investigations in this population [3], the present study examined PAE associated alterations of functional connectivity in 7 brain networks.

METHOD Resting-state (eye closed) fMRI data were acquired from 15 control (8M7F, Age=13.1±2.9) and 15 PAE (9M6F, Age=12.7±3.7) adolescents (3T Siemens, EPI-BOLD, TR/TE/FA/FOV=2000ms/30ms/75°/220cm, volume=180, 33 axial slices, thickness/gap=4mm/1mm, matrix=64×64). AFNI (http://afni.nimh.nih.gov) was used for data preprocess which included slice timing correction, volume registration, band-pass filtering (0.009 Hz < f < 0.08 Hz), and spatial smoothing (FWHM = 4 mm). After these preprocessing steps, individual's 4D fMRI datasets were transformed into the MNI space for independent component (IC) decomposition using FSL (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/MELODIC). In the resultant ICs, we specifically focused on 7 resting-state functional networks, including the default mode network (DMN), the left frontal-parietal network (LFPN), the right frontal-parietal network (RFPN), the primary motor network (PMN), the primary visual network (PVN), the extra-striate visual network (ESVN), and the salient network (SN). These networks have been found to exhibit robust correspondence between functional and structural connectivity [4], thus are relatively consistent across subjects and easily identified. With these network ICs individually identified, a voxel-wise group comparison (PAE vs. control) was performed for each of these networks and all resultant statistical maps were corrected for multiple comparison with a combined threshold of $p<0.05$/voxel and 736 mm^3 cluster (corrected $p<0.05$).

RESULTS The ICA identified all 7 functional networks in each individual subject. Particularly, the PVN mainly covered the calcarine areas while the ESVN extended downwards into ventral and lateral temporal cortex. As shown in Fig.1, significant reduction of functional connectivity was observed in 6 out of the 7 networks (except salient network) in the exposed group, demonstrating a long-term and large-scale alteration of network connected due to PAE.

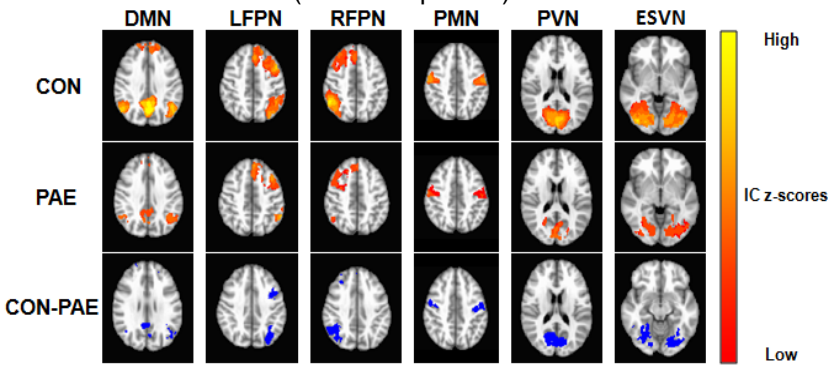

Fig.1. PAE associated reduction of functional connectivity in default mode (DMN), left prefrontal/parietal (LPFN), right prefrontal/parietal (RPFN), primary motor (PMN), primary visual (PVN), and extra striate visual (ESVN) networks. Blue regions are voxels with a significant connectivity reduction in the PAE group.

DISCUSSION AND CONCLUSION The current results of DMN are consistent with a previous study reporting a PAE effect in an older sample [5]. Together with the reduced functional connectivity in LFPN and RFPN, these results underscore the cognitive and attention deficits regularly seen in PAE population [1]. Specifically, visual attention deficits is one of the frequently reported behavioral problems in individuals with PAE. Since visual attention requires functional support from both the "top" regions of prefrontal-parietal network and "down" regions of visual network, behavioral deficits could reflect neurobiological underpinnings from both ends. While previous research has put an emphasis on the role of "top" regions [2] for visual attention deficits, the present study reveals impairment from both sides. In addition, connectivity reductions shown here in the ESVN complements previous reports of PAE associated alterations of functional activation and neuroanatomy in the same region [6]. In the PMN, the reduced connectivity also explains gross motor deficits in children with PAE [7]. In summary, the present results support the general hypothesis of PAE associated large-scale network-dysconnectivity thus motivating whole brain connectivity based profiling.

REFERENCES [1] Mattson et al., 2011. Neuropsychol Rev. 21:81. [2] Riley et al., 2011. Neuropsychol Rev. 21:73. [3] Coles et al., 2011. Neuropsychol Rev. 21:119. [4] van den Heuvel et al., 2009. Hum Brain Mapp. 30:3127. [5]. Santhanam et al., 2011. Psychiatry Res. 194:354. Li et al., 2008. Brain Imaging Behav. 2:39. [7] Lucas et al., 2014.Pediatrics. 134:e192

This work was supported by: Georgia Research Alliance and NIH grant RO1 DA033393,UO1 AA017122-06