

Changes in resting-state functional connectivity in children with prenatal alcohol exposure

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INTRODUCTION

- Resting-state fMRI (rs-fMRI) has rarely been studied in children.
- Only two rs-fMRI studies have been conducted in children [1,2] with fetal alcohol spectrum disorders (FASD); one in adults [3] with FASD.
- Previous rs-fMRI FASD studies have only examined the default mode network (DMN) and only used seed-based correlation, and none of these studies used independent component analysis (ICA).
- This study is the first to assess multiple resting state networks in children with varying severity of FASD compared to healthy controls using dual regression based on group ICA [4].

METHODOLOGY

- Participants: 30 right-handed children (mean \pm sd age: 11.1 \pm 0.8 yr) from the Cape Town Longitudinal Study [5]:
 - 10 with full or partial fetal alcohol syndrome (FAS/PFAS);
 - 10 non-syndromal heavily exposed (HE);
 - 10 non- or minimally-exposed controls (Ctl).
- Record of maternal alcohol consumption: Timeline follow-back interviews [5] were conducted with the mother to record her alcohol consumption during pregnancy. Two interviews were administered during pregnancy and one at 1 month postpartum.
- FASD group criteria: Mothers consumed at least 14 standard drinks/week or engaged in binge drinking (≥ 5 drinks/occasion) during pregnancy.
- Control group criteria: Mothers abstained or drank < 1 drink/month and did not binge drink during pregnancy.
- FASD diagnosis: All of the children were evaluated for FAS facial dysmorphism and growth at 5 years of age by two U.S.-based expert FAS dysmorphologists following the revised Institute of Medicine criteria [6].
- Scanning protocol: Scans were performed on a 3T Allegra MRI (Siemens, Erlangen, Germany) using a gradient echo EPI sequence (TR=2000 ms, TE=30 ms, flip angle=90°, FOV=200 mm, voxel size 3.125 \times 3.125 \times 3.0 mm³). T1-weighted structural images were acquired using a 3D EPI-navigated multiecho MPRAGE sequence [7].
- Pre-processing: Preprocessing was conducted using afni_proc in AFNI and included the following standard procedures: motion correction, realignment, regression and blurring. All images were registered to a 3x3x3 mm³ Talairach-Tournoux (TT) standard space.
- Analyses: Dual regression was performed in FSL. We report regions of interest (ROIs) that survive cluster size correction of 81mm³ [8] at a family-wise $p < 0.05$.

RESULTS

- Compared to healthy controls, reductions of resting-state functional connectivity (RSFC) in children with FASD have been found in four networks (DMN, left executive control, visual, and attention) within five regions (right posterior parietal lobe, left primary motor cortex, right prefrontal lobe, left lateral occipital lobe, and right occipital temporal).

Table 1. Cluster sizes and peak coordinates (in TT standard space) of regions in different resting state networks where connectivity differs between children with FASD compared to controls.

Networks	Groups	Size (mm ³)	Peak coordinates (mm)			Peak coordinate location
			X	Y	Z	
DMN	FAS/PFAS	621	24	-69	38	R Posterior parietal lobe
		189	-52	-9	41	L Primary motor cortex
	HE	216	42	34	2	R Prefrontal lobe
L executive control	FAS/PFAS	405	-40	-6	29	L Primary motor cortex
		324	-13	-84	23	L Lateral occipital lobe
	HE	135	-37	-9	41	L Primary motor cortex
	HE	108	-10	-87	26	L Lateral occipital lobe
Visual	FAS/PFAS	621	30	-72	-14	R Occipital-temporal region
Attention	FAS/PFAS	81	15	-78	38	R Posterior parietal lobe

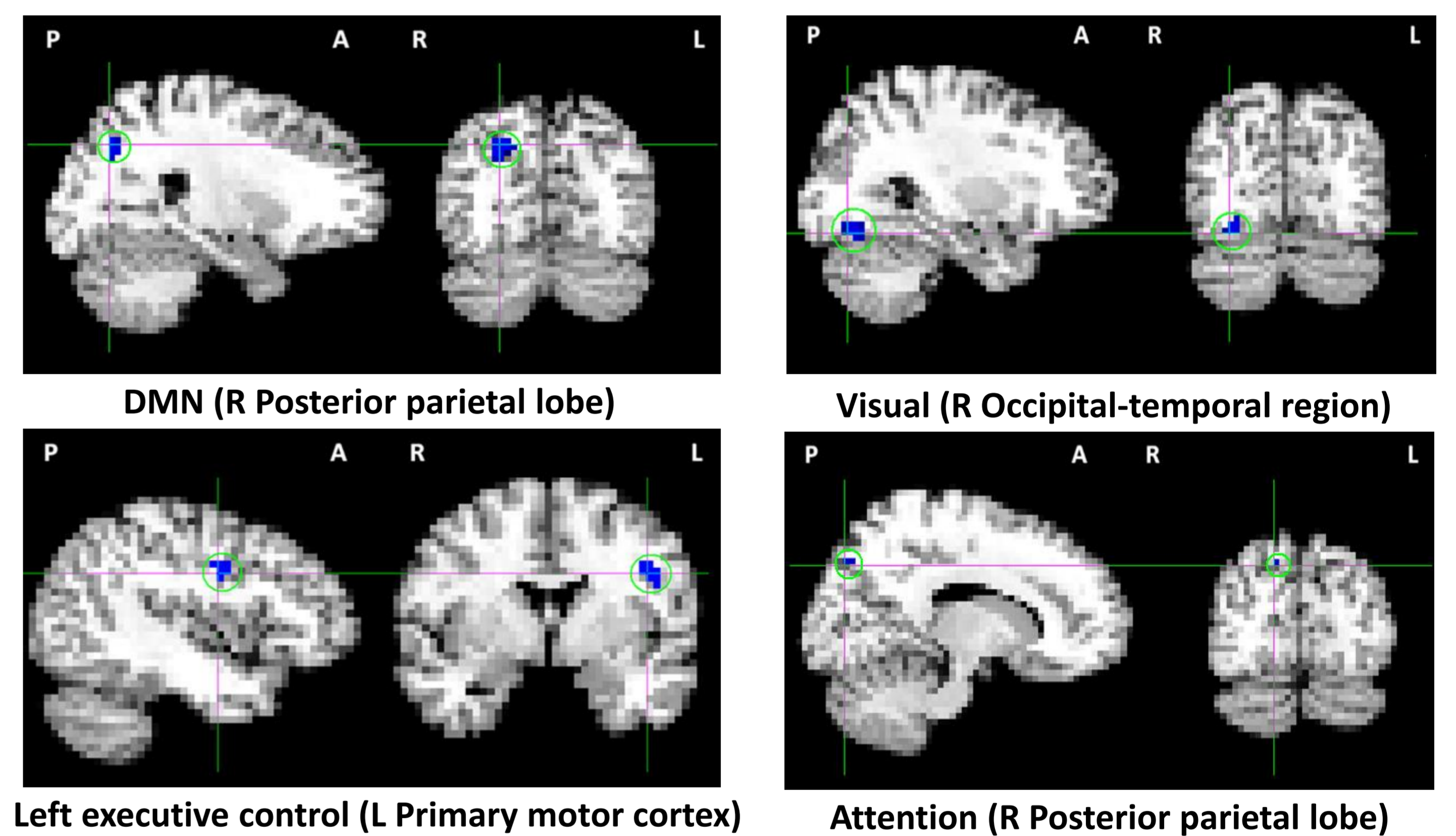


Figure 1. Regions in four different resting state networks where connectivity in children with either FAS or PFAS is significantly reduced compared to controls

CONCLUSIONS

- Compared to healthy controls, significant changes in RSFC within 5 regions in 4 networks were found in children with FASD.
- Reduction in connectivity in the DMN in alcohol-exposed children is consistent with a previous adult study [3]. Deficits in executive function and visual attention have consistently been reported in children with FASD using behavioural performance, fMRI, and event-related potential measures [9-13].
- The regions where most of the connectivity differences were found in this study (frontal and parietal) are also consistent with areas where shape abnormalities related to behavioural deficits have been previously reported by a structural MRI study [14].

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