**Poorer Recruitment of Intraparietal Sulcus in Number Processing in Children with Fetal Alcohol Spectrum Disorders**


### Introduction

Among the broad range of cognitive outcomes affected by prenatal alcohol exposure, number processing is particularly sensitive to prenatal exposure [1,4,9] and is consistently more impaired than reading or spelling on academic achievement tests. In a meta-analysis, Dehaene and colleagues [2] identified five parietal regions critical to number processing: bilateral horizontal intraparietal sulcus (HIPS), bilateral posterior superior parietal lobes (PSPL), and left angular gyrus (AG). The HIPS is activated in tasks involving nonverbal abstract representation of numerical quantity [3]; left AG, during manipulation of numbers in a verbal format [2]; and PSPL supports orienting attention. We investigated the effect of prenatal alcohol exposure on brain activation in these regions during number processing.

### Methods

59 right-handed Cape Coloured children (7.9 to 13.4 years; median=10.4; 35, no. 3, pp. 431-442). 14 fetal alcohol syndrome (FAS) or partial FAS (PFAS), 21 non-exposed controls were included. Outliers were identified using a timeline follow-back method in the second trimester. Prenatal alcohol exposure in this Cape Town community, which is among the highest in the world [8], was assessed by interviewing the mothers about their drinking during pregnancy using a timeline follow-back interview [7,6]. Measures included oz absolute alcohol (AA)/day averaged across pregnancy and AA/drinking occasion. AA/day was log transformed to reduce skewness. fMRI data were acquired during exact addition (EA) (e.g., "2+3=5 or 67"), proximity judgment (PJ) (e.g., "Is 5 closer to 4 or 7?"), and a control task (Greek letter matching) [9]. Data of runs for which children scored <66% were excluded from further analyses.

fMRI analyses were performed using BrainVoyager QX (Brain Innovation). Preprocessing included correction for different slice acquisition times and linear trends, temporal smoothing, and motion correction.

### Regions of interest (ROIs)

Regions of interest (ROIs) were defined as spheres, radius 5mm around the centres of the five parietal number processing regions derived from Dehaene et al.’s [2] meta-analysis.

Random effects analysis of variance was performed on the average signal in each ROI using a general linear model. Beta values were used to estimate % signal change during the numeric task compared to the control task. Outliers in differences in % signal change (>2 SD from mean) were removed. Differences were examined both in relation to FASD diagnostic group and as a function of degree of prenatal alcohol exposure based on maternal report of alcohol consumption during pregnancy.

### For the EA task, data from 9 FAS/PFAS, 13 HE, and 17 control children were included. For PJ, data from 11 FAS/PFAS, 18 HE, and 18 control children were used.

### Results

Increased AA/day was associated with decreased activation in the right HIPS during both Exact Addition ($r = -0.50, p < 0.01$) and Proximity Judgment ($r = -0.37, p < 0.51$). Similarly, increased AA/drinking occasion was associated with decreased activation in the right HIPS during both Exact Addition ($r = -0.47, p < 0.003$) and Proximity Judgment ($r = -0.39, p < 0.007$).

### Conclusions

The association of prenatal alcohol exposure with reduced activation in the right HIPS in both number processing tasks is consistent with behavioral evidence from studies in both Detroit [4] and Cape Town [5] suggesting a specific fetal alcohol-related deficit in the ability to represent and manipulate quantity, which has been repeatedly localized to the HIPS [2,3]. The finding of greater activation of the left angular gyrus in the PJ task in the FAS/PFAS group suggests that children in this group may have been more likely to use a verbal arithmetic strategy to perform simple PJ magnitude comparisons that were performed more automatically by the other groups. The greater activation in the left PSPL by the children who performed the PJ task more slowly suggests increased attention possibly to compensate for reduced facility in magnitude representation. Consistent with previous findings, the continuous prenatal alcohol measures were more sensitive to these deficits in neural activation than the clinical diagnoses.

### References


Admission

Supported by grants from the NIH Fogarty International Center (RO3-TW007530); NASA RO3 AA-16785; National Research Foundation of South Africa (2002/04/08/0024); South African Research Chairs Initiative of the Department of Science and Technology and National Research Foundation of South Africa; and seed money grants from the University of Cape Town, Wayne State University, and the Joseph Young, Sr., Fund, State of Michigan. The FAS clinical diagnostic assessments were supported by grants awarded in conjunction with the NIAAA Collaborative Initiative on FASD (U01-DA014790). We thank H.E. Heye, L.K. Robinson, and N. Khale, who conducted the dysmorphology assessments; our UCT and WSU research staff, M. Pareira, M. September, R. Sun, and N. Dodge; and G. Adams, J. Heyne, N. Samuels, K. Selle, and N. Solomor, the MRI technicians at Groote Schuur Hospital.