Regional cortical thinning in children with increased prenatal alcohol exposure

Frances C. Robertson[1,2], Katherine L. Narr[3], Christopher D. Molteno[4], Joseph L. Jacobson[2,4,5], Sandra W. Jacobson[2,4,5], Ernesta M. Meintjes[1,2]

[1]MRC/UCT Medical Imaging Research Unit, University of Cape Town, South Africa [2]Department of Human Biology, University of Cape Town, South Africa [3]Laboratory of Neuro Imaging, UCLA School of Medicine, Los Angeles, Los Angeles, CA [4]Department of Psychiatry, University of Cape Town, South Africa [5]Department of Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine, Detroit, MI

INTRODUCTION

- Fetal alcohol spectrum disorders (FASD) have been linked to thicker cerebral cortex in frontal and temporal brain regions[6,9]. This finding has been attributed to a delay or absence of the age-related cortical thinning that occurs in normally developing children.
- However, one recent study has shown thinner cortex in frontal, parietal, temporal and occipital regions in youth with FASD[10].
- All previous studies have included subjects spanning a broad age range and none have considered effects of the extent of prenatal alcohol exposure or of different forms of FASD on cortical thickness at different developmental stages.
- This study investigates the relation of *in utero* alcohol exposure to cortical thickness in FASD children and controls across a narrow age range.

METHODS

Participants

- Participants were 10 children with fetal alcohol syndrome (FAS), 18 with partial FAS, 29 heavily exposed (HE) nonsyndromal children, and 22 controls from the Cape Coloured (mixed ancestry) community (44 male, mean age 10.7 – 0.6 yr.), who are taking part in the Cape Town Longitudinal FASD Study.
- Women were recruited during pregnancy at their first antenatal clinic visit. The mothers of exposed children reported consuming ≥14 drinks/week or ≥5 drinks/occasion during pregnancy. These women consumed 3.1 - 25.2 drinks/occasion (median = 6.8).
- All but one of the mothers of the 21 control children abstained during pregnancy; 1 drank 2 drinks on 3 occasions.
- The amount of alcohol consumed during pregnancy was determined using timeline follow-back interviews[4] conducted at recruitment, during a follow-up antenatal visit, and at 1 month postpartum, and converted to average oz. absolute alcohol (AA) consumed/day and AA/drinking occasion around time of conception and across pregnancy.

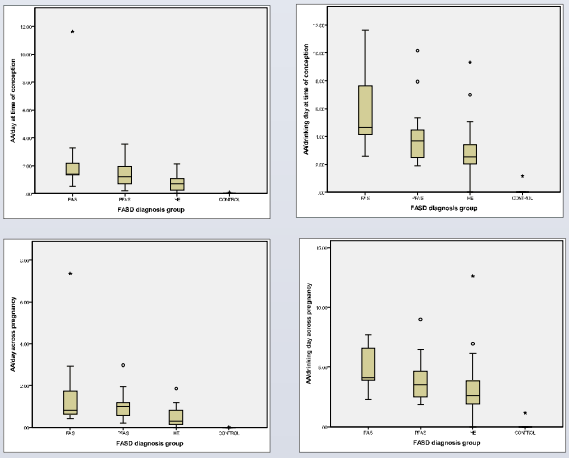

Fig 1. Boxplots of the 4 alcohol exposure measures for each diagnostic group. One child with FAS was excluded as an extreme outlier (>3 times the interquartile range above the median) on AA/day at conception and across pregnancy and one HE subject was excluded as an outlier on AA/drinking day across pregnancy.

Imaging

- High-resolution motion-corrected multi-echo MPRAGE images[7,8] were acquired on a 3T Siemens Allegra scanner.

Analysis

- FreeSurfer 5.1.0 processing streams that include automated segmentation and extraction of pial, gray and white matter surfaces with manual error correction, were used to estimate cortical thickness.
- Thickness maps were smoothed with a 10mm FWHM kernel. General linear model analyses across the whole brain were performed with cortical thickness as the dependent variable and diagnostic group and alcohol exposure as independent variables.
- Results were thresholded at $p<0.05$ and cluster-size correction for multiple comparisons was performed using Monte Carlo simulation.

RESULTS

- No significant differences in cortical thickness were found between diagnostic groups.
- After multiple comparison correction, there were no significant clusters in analyses relating cortical thickness to alcohol exposure at conception.
- AA/drinking day across pregnancy was inversely related to cortical thickness in 3 regions: right cuneus/pericalcarine/superior parietal lobe, fusiform/lingual gyrus, and supramarginal/postcentral gyrus.

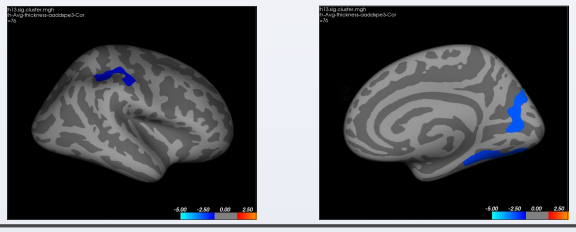

Fig 2. Clusters in right cuneus/pericalcarine, fusiform/lingual gyrus, and supramarginal/postcentral gyrus showing inverse relation between absolute alcohol per drinking day across pregnancy and cortical thickness (n= 78, $p<0.05$ cluster-size correction for multiple comparisons applied).

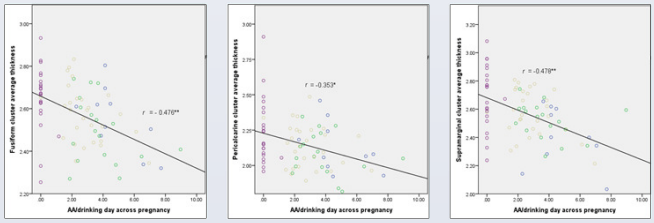

Fig 3. Relation of absolute alcohol per drinking day across pregnancy to average cortical thickness in fusiform (r = -0.48), pericalcarine (r = -0.35) and supramarginal (r = -0.48) clusters (* $p<0.005$,** $p<0.001$).

CONCLUSIONS

- These data from a homogeneous prepubertal cohort support a fetal alcohol-related reduction in regional cortical thickness in middle childhood.
- Our results are most compatible with those of Zhou et al., which demonstrated FASD-related reductions in cortical thickness in similar parietal, temporal and occipital association areas.
- Notably, a continuous measure of maternal alcohol consumption was more sensitive in predicting cortical thinning than FASD diagnosis. This effect was most evident in relation to average alcohol dose consumed/occasion.

REFERENCES

1. Dale, A.M. (1999), 'Cortical surface-based analysis. I. Segmentation and surface reconstruction', Neuroimage, vol. 9, pp. 179-194.
2. Fischl, B. (1999), 'Cortical surface-based analysis. II: Inflation, flattening, and a surface-based coordinate system', Neuroimage, vol. 9, pp. 195-207.
3. Fischl, B. (2000), 'Measuring the Thickness of the Human Cerebral Cortex from Magnetic Resonance Images', Proceedings of the National Academy of Sciences, vol. 97, pp 11044-11049.
4. Jacobson, S.W. (2002), 'Validity of maternal report of prenatal alcohol, cocaine, and smoking in relation to neurobehavioral outcome', Pediatrics, vol. 109, pp. 815-825.
5. Jacobson, S.W. (2008), 'Impaired eyeblink conditioning in children with fetal alcohol syndrome', Alcoholism: Clinical and Experimental Research, vol. 32, pp.365-372.
6. Sowell E.R. (2008), 'Abnormal cortical thickness and brain-behavior correlation patterns in individuals with heavy prenatal alcohol exposure', Cerebral Cortex, vol. 18, no. 1, pp.136-44.
7. Tisdall, M.D. (2012), 'Volumetric navigators for prospective motion correction and selective reacquisition in neuroanatomical MRI', Magnetic Resonance in Medicine, vol. 68, pp. 389-399.
8. Van der Kouwe, A.J. (2008), 'Brain morphometry with multiecho MPRAGE', Neuroimage, vol. 40, pp.559-569.
9. Yang Y. (2012), 'Abnormal cortical thickness alterations in fetal alcohol spectrum disorders and their relationships with facial dysmorphology', Cerebral Cortex, vol. 22, no. 5, pp. 1170-9
10. Zhou D. (2011), 'Developmental cortical thinning in fetal alcohol spectrum disorders', Neuroimage vol. 58, no. 1, pp. 16-25

ACKNOWLEDGEMENTS

NIH grants R01AA016781, R21AA017410, U01-AA014790; South African Research Chairs Initiative of the Department of Science and Technology and National Research Foundation of South Africa; Medical Research Council of South Africa; Fulbright South Africa Research/Scholar Award; Joseph Young, Sr., Fund, State of Michigan; Ellison Medical Foundation.

We thank Bruce Spottiswoode, Ph.D., the CUBIC radiographers Marie-Louise de Villiers and Nailah Maroof, and our UCT and WSU research staff Nicolette Hamman, Mariska Pienaar, Maggie September, Emma Makin, Renee Sun and Neil Dodge.

www.PosterPresentations.com