## BACKGROUND
Autopsy and MRI studies have consistently demonstrated disproportionately smaller corpus callosum in children and adults with a history of prenatal alcohol exposure (PAE). Incidence of partial or complete corpus callosum agenesis among children with PAE may be as high as 6.8%, as compared to a normal population rate of 0.3% and a developmentally delayed population rate of 2.3%. Imaging studies in children and adults have documented:
- Reduced callosal size
- Callosal shape abnormalities
- Anterior and inferior displacement of the posterior CC regions
- Reduced CC thickness

Alterations in the antenatal growth of CC and other brain structures as a consequence of PAE may result in profound effects on subsequent integration of neural activity.

Only a few studies have implemented MRI segmentation techniques for cerebral volume measurements. Baseline magnetic resonance imaging (MRI) was performed on 43 pregnant mothers and their infants. Fetal MRI was acquired using the same protocol (Siemens, Erlangen, Germany) for all subjects. Examinations were performed on a 3T Allegra MR scanner using a head coil and were not sedated. The following structural protocol was used:
- Multiplanar FLASH (MEF) 30° 3D encoding: 144 x 144 matrix on 144 mm isotropic resolution, TR 20 ms, 8 echoes with TE = 1.46 ms + n*1.68 ms where n = 0, 1, 2, 651 Hz/pa, non-selective excitation with flip angle 30°, T2* 6 min 9 s.
- Multiplanar FLASH 5° (same as above with flip angle 5°).

Fetal MRI scans were obtained, and both 3D and MEF sequences were performed. The MEF sequence was used to acquire the neonatal MRI data without use of sedation.

### METHODS

#### DATA ACQUISITION
- No sedation was used.
- Scanned using 3T Allegra MR Scanner (Siemens, Erlangen, Germany).
- A custom-built 170.9 mm (inner diameter) circularly polarized birdcage radiofrequency coil (designed by L. Wald, Ph.D., Director MR Core, Martinos Center, Radiology, MGH, built by A. Hess, Ph.D.) was used.
- T1 scans were acquired at two different flip angles, allowing the images to be segmented with different relative T1 vs. proton density weightings to optimize contrast across boundaries of adjacent structures (to facilitate manual tracing).

The following structural protocol was used:
- MEF = 0°, bandwidth 651 Hz/pa,
- MEF = 30°, bandwidth 144 Hz/pa,
- Bandwidths were matched across MEF and had high values so that distortions (due to B0 inhomogeneities) were small and matched across scans. These are true physical parameters of the scanned tissue in the 3 T Field and not simply weighted intensities that vary with the scanning sequence and system.

#### IMAGE PROCESSING
- CC was independently traced by 2 graduate research assistants (NML and FW).
- Both initially trained at the MGH Martinos Center and subsequently supervised by a senior neuroradiologist (CW) at UCT.
- Each neonatal CC was hand-segmented (using FreeView software) on an AC-PC aligned T1-weighted image.
- Median interobserver Dice Index $S_0 = 0.85$.
- Average of the 2 tracings used as CC area measure in the analyses.

### RESULTS

#### Characterization of PAE Exposed Infants

The following characteristics were associated with PAE exposure:
- Maternal age at delivery: $r = -0.35$, $p < 0.05$.
- Frequency of maternal alcohol consumption: $r = -0.36$, $p = 0.05$.
- Maternal education: $r = -0.37$, $p < 0.01$.

#### Effect of prenatal alcohol exposure to newborn corpus callosum area controlling for other prenatal exposures (N=43)

<table>
<thead>
<tr>
<th>Variable</th>
<th>CC (mean/SD)</th>
<th>PAE (mean/SD)</th>
<th>$r$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age at birth</td>
<td>202.6/19.5</td>
<td>203.5/20.6</td>
<td>-0.1</td>
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<tr>
<td>Age at scan</td>
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<td>Prenatal exposure</td>
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<td>-0.39</td>
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<tr>
<td>Cigarettes</td>
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<tr>
<td>Marijuana</td>
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<td>-0.31</td>
<td>0.1</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>-0.31</td>
<td>-0.32</td>
<td>0.1</td>
</tr>
</tbody>
</table>

#### Correlation of newborns characteristics and other prenatal exposures to corpus callosum area ($N=43$)

The following variables were correlated with CC area:
- Maternal education: $r = -0.36$, $p < 0.01$.
- Frequency of maternal alcohol consumption: $r = -0.35$, $p < 0.01$.

### CONCLUSIONS

Given the rapid and heterochronous nature of early brain growth, volumetric measures based on MRI in the first weeks of life may provide a more sensitive index of future neurological outcome than standard newborn behavioral or neurological examinations.

Because the craniofacial dysmorphic features that characterize FAS are difficult to detect in infancy, early indicators of effect are needed that will contribute to understanding the ontogeny of impairment as it unfolds across development.

### FUNDING

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