1) Newborn infants subjects  
- 11 prenatally alcohol exposed (PAE): -6 female/5 male; postconception age range 36-44 wk, median 42 wk;  
- 9 healthy controls (HC): -3 female/6 male; postconception age range 38-44 wk, median 42 wk.

<table>
<thead>
<tr>
<th>Table 1: Summary of sample characteristics</th>
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<tr>
<td>Alcohol-exposed (n=11)</td>
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<td>------------------------</td>
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<tr>
<td>Age since conception</td>
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<tr>
<td>Maternal age at delivery</td>
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2) DTI + structural parameters  
- Diffusion tensor imaging (DTI):  
  - fractional anisotropy (FA); mean, axial and radial diffusivity (MD, AD, RD).  
- Structural: proton density (PD) and physical T1  
- ROI volume (scaled by whole brain)  

3) Tractography  
- AFNI-FATCAT used to estimate and delineate similar white matter (WM) ROIs across all subjects.  
- Probabilistic tracking in 5 networks (Figure below, left panel):  
  A) Transcallosal: corpus callosum and corona radiata (CCCR);  
  B) Corticospinal: L and R projection (PROJ) fibers;  
  C) Corticocortical: L and R association (ASSOC) fibers.

4) Subject recruitment  
Data from three timeline follow-back interviews were combined to provide continuous measures of drinking during pregnancy. Infant exclusionary criteria were major chromosomal anomalies, neural tube defects, multiple births, very low birthweight (< 1500 g), gestational age <32 wks, seizures and major drug usage.

Human subjects approval was obtained from the Wayne State University and University of Cape Town institutional review boards. Informed consent was obtained both at time of recruitment and at time of scan. All women who reported drinking during pregnancy were advised to stop or reduce their intake and were offered referrals for treatment.

5) Data acquisition and processing  
No infants were sedated (feeding and swaddling ensured sleep and reduced motion).  
Scanning: 3T Siemens Allegra using a custom-built, 170.9 mm (inner diameter) circularly polarized birdcage RF coil.  
Two DWI sets were acquired (each: 4 b=0 and 30 b=1000 s mm⁻² images) with opposite phase encoding (AP/PA) using a twice-refocused SE-EPI sequence (2 mm isotropic voxels). Processing included motion correction using FSL, susceptibility-distortion correction, and outlier rejection.  
Anatomical imaging (1 mm isotropic) was performed using a multiecho FLASH sequence, and T1 and PD maps reconstructed using FreeSurfer's mri_ms_fitparms.

6) WM networks: analysis and statistics  
- Tracking connections:  
  - many found in all subjects (dark blue, Figure right);  
  - used in analyses;  
  - many found in >80% of both groups (light blue);  
  - few found only in >80% of single group (orange).  
- Network level alcohol-structure relations (Table below):  
  - calculated with multivariate GLM (using R package afex).  
  - accounted for confounds: infant age and sex; maternal age and cigarettes.  
  - no significant relation with FA or ROI volume in any network;  
  - AD (axial diffusivity) showed significant relations (decrease with increasing alcohol) in most networks (even after multiple comparison correction).

| Table 2: Network level alcohol-structure relations (Table below):  
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<tr>
<td>Week</td>
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<tr>
<td>0.05</td>
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<td>≥0.10</td>
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7) Intranetwork statistics for AD relations  
- Follow-up, per WM ROI alcohol-structure relations (graphs below):  
  - investigate where in networks most significant AD-alcohol relations occur.  
  - accounted for confounds: infant age and sex; maternal age and cigarettes.  
  - β plots show several ROIs with significant AD-alcohol relation (green)  
  - strongest relations were observed in medial and inferior WM.

8) Take home conclusions  
- PAE in newborns is associated with structural WM changes.  
- Changes occur across transcallosal, corticospinal and corticocortical networks  
- FA showed no significant alcohol relations  
- AD shows significant decrease with increased alcohol exposure in WM networks  
- Strongest AD-alcohol relations were seen in medial+inferior WM (likely locations of early maturation).

9) References  