ATLAS METHODS

The following paragraphs describe the methods that were used on the different version(s) of the Fetal Brain Atlas.

Fetal Brain Atlas

Image preprocessing

The native DICOM imaging data were converted to NIFTI and Analyze formats using FreeSurfer's MRI convert module. Intensity inhomogeneity correction was applied to all converted data using the N3 algorithm. Both the data conversion and bias field correction were implemented as Pipeline workflows. Our attempts to automatically skull strip the fetal brain volumes using SSMA and BET were unsuccessful. Manual removal of the non-brain tissue for every individual brain was performed using BrainSuite software. The LPBA protocol was used for manually removing extra cerebral tissue -- both cerebellum and brainstem were included (Shattuck et al., 2008).

Template building

Optimal template construction function of ANTS (version 1.9) was used. ANTS has been demonstrated to be among the most accurate intensity-based normalization method among fourteen different methods. The script buildtemplateparallel.sh was run for all specimen within each gestational week, using the default settings except for an additional option '-r 1' to turn on rigid-body registration. Following the ANTS recommendations, we used symmetric diffeomorphic mapping (SyN) energy terms, which measure image similarity and diffeomorphism lengths for the diffeomorphic transformations. The ANTS-SyN approach is defined by the minimum shape and appearance distance image. It uses symmetric pair-wise mapping, symmetrically optimizes the two terms in normalization methods (geometry and appearance) across the population and is unbiased; that is, it does not prefer any specific image input by the user or specific guess for the initial template. Instead, the template should be derived completely from the database of n images. The procedure first optimizes the mappings with a fixed template, then, optimizes the template appearance with fixed shape and mappings, and, finally, optimizes the template shape. The process then repeats.

Temporal modeling of anatomical deformations

The growth-related changes in the size and shape of the fetal brain are captured by the components of the affine scaling and the displacement fields estimated during the diffeomorphic registration. For each symmetric pairwise mapping, an Affine and Warp transformation files were computed for each subject. Using the ANTS script ComposeMultiTransform.sh, the affine and warp files were composed to one deformation file, and the two deformation files of the two steps during the template build were also composed into one total deformation field. This total deformation field was used to calculate the Jacobian (with ANTS script: ANTSJacobian.sh), which reflected the non-linear deformation field of temporal changes at each voxel location. Using FSLStats module in LONI Pipeline, we obtain the mean and standard deviation (as univariate measures) of Jacobian field at each voxel location.

Fetal Brain Atlas continued

Tensor based morphometry (TBM)
Tensor-based morphometry (TBM) is a method enabling the mapping of structural changes between groups in time or space to identify anatomical differences using 3D non-linear volumetric warping. For instance, TBM analysis may be employed to investigate structural brain changes due to prenatal exposure to methamphetamine alcohol exposure, traumatic brain injury , or voxel-wise genome-wide association study. Regional structural differences of deformation fields (tensors) are represented as TBM maps and identify the relative positions of different brain structures.
The first step in TBM analysis is the non-affine spatial normalization of all structural images into a common anatomical space. This facilities the localized quantitative characterization of the population differences using 3x3 Jacobian matrices representing the magnitude of the gradient of the displacement vector fields. After generating a brain template for each GW, each subject's brain is warped to the corresponding template and the determinant of the Jacobian of this transformation is computed. At each voxel, this Jacobian map represents a univariate measure of relative volume change caused by the spatial deformation. The Jacobian determinants are interpreted as volume loss ($\det|J|<1$), volume gain ($\det|J|>1$), or no change ($\det|J|=1$) (Brun et al., 2011).

Global measurement and surface analysis
Using the skull-stripped brain volumes for each subject, BrainSuite's surface extraction tool was used to obtain topologically correct cortical surface models (triangulated 2-manifolds). For each cortex, 6 complementary global shape metrics were computed using LONI ShapeTools pipeline library - surface area, fractal dimension, shape index, curvedness, shape-index and volume. These were added to the subject demographics as derived imaging biomarkers, along with the overall (global) Jacobian value obtained from linearly registering the template to each individual subject?s brain.

The local shape analysis (LSA) pipeline workflow was employed to obtain local shape metrics (displacement-field, radial-distance), per vertex in the triangulated surface representations. The displacement fieldand the radial distance measures were computed by surface registration of the template cortical model to each individual cortical surface using a diffeomorphic algorithm. The displacement feature is computed by applying a (volume-preserving) rigid transformation spatially normalizing each shape to the population-wide mean shape. In placing each surface into the template?s space, the magnitude of the displacement field is computed at each vertex point on the surface. The radial distance , on the other hand, measures the distance from each surface point to the central core of the shape (point of gravitational balance). This metric index captures local expansions or contractions of the developing cortical surface. These two local shape measures were used as covariates to generate brain maps representing the associations between derived shape morphometric and GW at each cortical location. The captured surface development patterns will be helpful to discover the growth direction of fetal brain. The growth direction specifies the surface that is changing (e.g. anterior aspect of the brain) which may be different from the growth in an orthogonal direction (e.g. A-P axis).