Quantitative Analysis of Human White Matter Brain Curvature: Perspectives on Folding From Neonate to Adult

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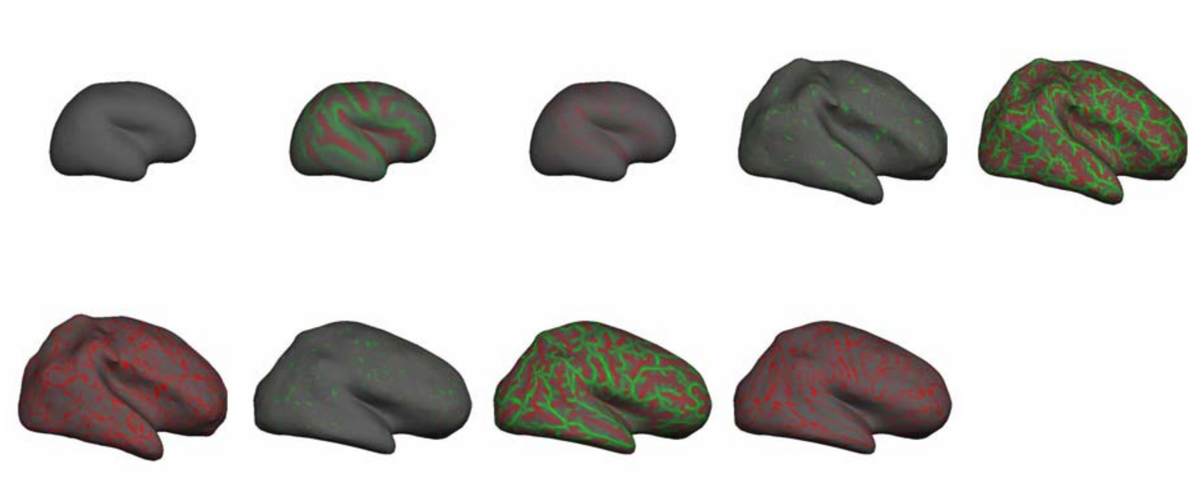
Introduction: Although widely accepted that increased gyral folding complexity is a measure of early brain development, few methods currently exist to quantify gyral folding or analyze how it develops with age. Most existing techniques rely on qualitative visual assessments and are often performed on axial 2D images that do not account for the 3D complexity of folding. This paper presents: (1) a method for creating topologically correct white matter surfaces for neonatal subjects based on segmented volumetric T1 images; (2) a method for analyzing the reconstructed surfaces to extract useful global and regional curvature measures.

Methods: This preliminary study reports results for 9 neonatal subjects ranging from 30.4 weeks corrected Gestational Age (wcGA) through 40.3 wcGA; three pediatric subjects of 2, 3, and 7 years; and a 39 year old male adult subject. All subjects are neurologically normal. T1 weighted axial or coronal 3D SPGR images were collected on a 1.5T (GE, Milwaukee) scanner, with TR/TE=30/8, flip angle=25 to 30, matrix=256x192, FOV=220x165mm or 200x150mm with a slice thickness of 1.2 to 1.5mm. Neonatal subjects were manually segmented (others auto-segmented) in a slice-by-slice fashion with tissue being classed as either "cortex" (cortical gray matter), "non-cortex" (white matter, ventricles, and deep cortical gray), or subarachnoid "CSF" (cerebrospinal-fluid). T1 contrast inversion necessary for "FreeSurfer" processing of the neonatal subjects was achieved with a custom filter that re-colored the segmented tissue classes to adult-normal contrast values. A volumetric analysis was performed and gray/white surface meshes were reconstructed using "FreeSurfer". Volumetric-derived results included volumes of cortical and non-cortical brain matter, as well as a modified gyral folding index (GI – the ratio of the gray-white surface area to the "exterior" cortical-CSF surface area) and gray-white junction folding (GWF – the ratio of the gray-white surface area to the 2/3 power of the non-cortex volume) in 3D. Reconstructed surfaces allowed determination of principle curvatures (maximal curvature k_1, minimal curvature k_2) at each point in the surface mesh, as well as mean curvature, $H=(k_1+k_2)/2$, "Curvedness" $C=\mathrm{sqrt}(k_1^2+k_2^2)$, "Sharpness" of curves, $S=(k_1-k_2)^2$ and Gaussian curvature $K=k_1k_2$. The Gaussian curvature is the only measure intrinsic to the surface. K does not change as the surface buckles and folds as long as no stretches, tears or sharp folds result. If K=0 the surface is isometric to a plane, if positive, to a sphere and if negative, to a saddle. S emphasizes regions where k_1 and k_2 are maximally different and therefore where cylindrical folding dominates. C also weighs lower amplitude folding.

Volumetric Results: Cortical gray matter (GM) growth exceeded non-cortical white matter (WM) growth across neonates: initially GM volume was smaller than WM volume. However from ~38 weeks cGA to adult, GM volume was >50% brain volume. Both the GI and GWF increased rapidly through the neonates to term, showing a general slow decline post term to adult. **Reconstructed Surface Results:**. In general, k_1 is perpendicular to the long axis of gyri ($k_1<0$ with "outward" folds) and sulci ($k_1>0$ with "inward" folds). Neonates have a higher % of -ve k_1 values (dominant outward brain curvature with sharply ridged gyral peaks). In pediatric cases, $k_1>0$ dominates, suggesting sharper ridged sulci and flatter gyri. In the adult, k_1 was balanced suggesting neither gyral nor sulcal ridges dominated. By definition $k_2 < k_1$ and typically describes the small amplitude low frequency undulations along the main axis of gyri and sulci. There is a close balance of negative and positive k_2 values while the mean absolute value increased to term and decreased with age thereafter. H increases in general with age until term with little change in the three children but declining again in the adult mean. S highlights crests of gyri and depths of sulci, while C shows less obvious folding along sulcal banks. At birth K ~ 0 everywhere with small positive and negative undulations indicating that the 30 week brain can be unfolded into a flat sheet with very few wrinkles. As the brain develops more gyri, smalls regions of higher K with alternating outward and inward undulations develop primarily along gyral crests with outward undulations dominating. In the figure below we see various principle curvature functions projected onto a reconstructed 31.1 wcGA neonate surface, a term 40.3 wcGA, and an adult. From left in the first row, K-31.1 wcGA, k_1-31.1 wcGA, S-31.1 wcGA, K-40.3 wcGA, k_1-40.3 wcGA; second row from left S-40.3 wcGA, K-adult, k_1-adult, S-adult. Note how S detects gyral and sulcal ridges.



Conclusions: To the best of our knowledge, this is the first study analyzing reconstructed 2D neonatal gray-white matter surfaces in 3D. Most curvature (and hence folding) measures peak around term and decline as the brain matures. In general the majority of the brain is isometric to a plane but deviations also peak at term. The underlying mechanisms are unknown but we postulate that post term myelination and neuronal pruning attenuate the initial folding pattern.