Developmental and Genetic Factors Underlying the Complexity and Variability of Cortical Convolutions

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Abstract.
The convolutions of human cerebral cortex are remarkable for their complexity and their variability from one individual to the next. Recent methodological and experimental advances in neuroimaging have yielded valuable insights regarding the pattern of cortical convolutions, how they vary in health and disease, and how they form during development. Cerebral cortex forms early in development as a completely smooth sheet; convolutions arise and mature during the extended period over which long-distance cortico-cortical connections are established. An attractive hypothesis is that mechanical tension along these long-distance connections drives the formation of cortical folds and determines their specific arrangement. This hypothesis can simultaneously account for (i) the consistency of folding patterns in regions that are dominated by connections among a few relatively large cortical areas and (ii) the highly variable folding of regions that contain numerous small 'balkanized' areas. Moreover, genetic factors that affect the sizes of cortical areas and the patterns of connectivity may contribute to abnormal cortical folding in specific disease conditions as well as normal variability in a genetically heterogeneous population.

Surface-based approaches have proven invaluable for systematically analyzing cortical folding patterns and their variability. Surface-based atlases provide a flexible and powerful way to visualize and analyze vast amounts of data obtained from large numbers of individuals after registration to a common spatial framework. Until recently, a drawback to the surface-based approach was the necessity of choosing a single individual brain as a target atlas, because this introduces biases associated with whichever brain is chosen as the target. To address this problem, the Population-Average Landmark-and Surface-based (PALS) human cortical atlas was generated, along with a landmark-based registration strategy for mapping data from individuals to the atlas (Van Essen, 2005). Within-group and between-group comparisons of shape characteristics can be made using maps of 'sulcal depth' (distance from the cerebral hull) computed for each individual hemisphere and registered to the PALS atlas. This strategy has been used to analyze shape characteristics in normal humans and in multiple disease conditions. In one such analysis, hemispheric asymmetries and gender differences were evaluated in a population of 72 normal human subjects. Between-group comparisons of average sulcal depth revealed eight localized regions of significant hemispheric asymmetry in temporal, parietal, and frontal cortex, but no significant gender differences. However, there was a highly significant gender difference, insofar as men are more variable in shape in the right hemisphere.

Comparison of individuals with Williams Syndrome (WS) to normal controls revealed 35 folding abnormalities distributed across a broad swath of cortex involving all lobes and arranged in a strikingly symmetric pattern in the two hemispheres. The abnormalities included a significantly shallower olfactory sulcus in WS compared to controls. A possible mechanistic/developmental explanation for this folding abnormality is that two cortical areas occupying most of the olfactory sulcus (areas 13b and 13m) may be smaller in size or have abnormal connection patterns in WS. Comparison of individuals with autistic spectrum disorder (ASD) compared to age-matched controls revealed several folding abnormalities in young but not older autistic individuals. The folding abnormalities differ across ASD subtypes; the most prominent abnormalities are in the left frontal operculum of low-functioning autistic individuals.

Altogether, shape characteristics of human cerebral cortex vary across hemisphere, gender, and disease condition, and these differences can be profitably explored using a surface-based approach.

Reference.
Van Essen, DC (2005) NeuroImage 28: 635-662