

Mapping Cortical Morphology in the Human and Non-Human Primate Brain and Relations to Function

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Symposium

Pioneering investigations in the 19th and early 20th centuries identified the major folds of the human cerebral cortex using post-mortem brains (e.g., Retzius, 1896; Cunningham, 1905; Eberstaller, 1890). Many of these studies demonstrated strong correlations between the location of certain cortical folds and regions of cortex involved in specific functions (e.g., Smith, 1907; Brodmann, 1909; Economo and Koskinas, 1925; Penfield and Boldrey, 1937). For example, the central sulcus is a defining morphological landmark of the primary motor cortex, which occupies its anterior bank, and the primary somatosensory cortex, which can be found on its posterior bank. Some of these anatomo-functional relationships are conserved across the primate lineage (Bailey and Bonin, 1950).

With the advent of neuroimaging techniques, our understanding of the morphology of the cerebral cortex has expanded beyond these early studies, which were limited to post-mortem dissections and, often, to small sample sizes. Using MRI, researchers have been able to map the three-dimensional extent of cortical folds and quantify their spatial variability across individuals at large scale. Furthermore, functional brain imaging has allowed for the investigation of additional anatomo-functional relationships.

The present symposium will provide an overview of some of the cutting-edge research on cortical morphology, research that is valuable to the entire neuroimaging community as it has provided an anatomical framework with which to study the functional organization of the cortex. Studies presented here will provide examples of morphology-to-function relationships that are valuable for analyses that aim to capture individual patterns of brain organization at the single subject level. The comparative anatomical studies of non-human primates provide compelling insight into the evolution of the cerebral cortex and the emergence of higher cognitive processes.

Objective

- to learn about diverse approaches to study cortical morphology
- to understand the anatomo-functional relationships of certain cortical folds and the value of using these folds as morphological landmarks to interpret results of functional imaging studies
- to gain insight into the evolution of the human cerebral cortex from comparative anatomical studies of homologous cortical folds in non-human primate brains

Target Audience

The proposed symposium will be of value to all researchers using neuroimaging, in particular those who aim to characterize the functional organization of the cerebral cortex and those employing individual subject level analyses. This symposium will also benefit those who are investigating the evolution of the cerebral cortex.

Presentations

Investigations of Sulcal Morphology in the Human Brain and Relations to Specific Aspects of Functional Processing

Classic studies in the late 19th and early 20th centuries demonstrated certain reliable anatomo-functional relationships in the human cerebral cortex. For example, it was established that the primary motor cortex occupies the anterior bank of the central sulcus, while the primary somatosensory cortex occupies the posterior bank(1). Nevertheless, it was widely believed that such strong structure-to-function relations exist only for primary sulci, which are the first to form in utero and which maintain a reliable morphology across individuals. It was thought that the variability in the morphology of sulci in so-called higher cortical regions prevents any attempt to characterize their morphology and relate it to function. The Petrides laboratory has since examined many sulci in these higher cortical regions, such as in the anterior frontal cortex, the posterior parietal cortex, and the temporal cortex. The results of this research has led to the realization that, although variable, these sulci can be reliably identified across individuals. This, in turn, has led to the creation of a detailed map of the sulci of the human cerebral cortex and the naming of many of these sulci for the first time(2). Furthermore, using fMRI, the Petrides laboratory has established anatomo-functional relationships for many of these sulci by conducting analysis at the individual-subject level. The purpose of this presentation is to provide an overview of some of this research. Sprung-Much and Petrides (2018, 2020), for example, characterized the morphology of specific sulci of the inferior frontal gyrus and quantified, for the first time, the spatial variability of these sulci in a standard stereotaxic space(3,4). Segal and Petrides (2013) investigated how the caudal branches of the superior temporal sulcus (STS), which occupy the region of the angular gyrus, relate to functional activation peaks generated during reading-related activity(5). The results demonstrated that these peaks were consistently located between the central and posterior branches of the caudal STS(5). In another study, Huntgeburth and colleagues (2017) examined the relationship between the collateral sulcus that defines the parahippocampal cortex in the medial temporal region and brain activity evoked by navigation information retrieved from a previously established cognitive map(6). It was shown that the sulci that comprise the collateral sulcal complex provide an accurate localization of the activation foci along the parahippocampal cortex in individual subjects and clearly discriminate this activity from the nearby entorhinal cortex and the cortex of the fusiform gyrus(6). The above investigations are examples of valuable studies of cortical morphology that have contributed to the field's understanding of the structural and functional organization of the human cerebral cortex. 1. Brodmann, K. (1909). *Vergleichende Localisationslehre der Grosshirnrinde in ihren Principien Dargestellt auf Grund des Zellenbaues*. Leipzig, Barth. 2. Petrides, M. (2012). *The human cerebral cortex. An MRI atlas of the sulci and gyri in MNI stereotaxic space*. New York, Academic Press. 3. Sprung-Much, T. and Petrides, M. (2020). Morphology and spatial probability maps of the horizontal ascending ramus of the lateral fissure. *Cerebral Cortex*, 30, 1586-1602. 4. Sprung-Much, T. and Petrides, M. (2018). Morphological patterns and spatial probability maps of two defining sulci of the posterior ventrolateral frontal cortex of the human brain: the sulcus diagonalis and the anterior ascending ramus of the lateral fissure. *Brain Structure and Function*, 223, 4125-4152. 5. Segal, E. & Petrides, M. (2013). Functional activation during reading in relation to the sulci of the angular gyrus region. *European Journal of Neuroscience*, 38, 2793-2801. 6. Huntgeburth, S.C. et al. (2017). Local morphology informs location of activation during navigation within the parahippocampal region of the human brain. *Brain Structure and Function*, 222, 1581-1596.

Presenter

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Sulcal Organization in the Medial Frontal Cortex Provides Insights into Primate Brain Evolution

Although the relative expansion of the frontal cortex in primate evolution is generally accepted, the nature of its scaling and inter-species anatomic-functional comparisons of the frontal areas remain controversial. For this symposium, I will present novel results showing how the Medial Frontal Cortical (MFC) sulcal organization has evolved through the primate order. This region has been neglected by evolutionary studies, despite its key role in cognitive functions often thought to be uniquely human, such as mentalizing or counterfactual thinking. Our between-species comparison of sulcal morphology using magnetic resonance imaging (MRI) provides evidence for a novel interpretation of the evolution of the MFC from Old-world monkeys (80 macaques and 88 baboons) to Hominoidea (225 chimpanzees and 197 humans). To start, we found that chimpanzees do possess a paracingulate sulcus (PCGS), a feature previously thought to be unique to the human brain(1,2). Both the cytoarchitectonic and the functional organization of the PCGS at the level of the mid-cingulate cortex (MCC) are similar in chimpanzee and in human(3). However, we did observe species differences regarding the probability of occurrence of this sulcus and its lateralization across the two hemispheres. Additionally, these two species differed with regard to the organization of the MFC rostral to the genu of the corpus callosum. There is no evidence from cytoarchitectonic(4) and neuroimaging(5) studies that these changes are associated with new cortical areas, suggesting instead a differential expansion of the rostral MFC and the medial frontopolar cortex, two brain regions that have been considered important for high-order socio-cognitive processing, and the ventral-medial frontal cortex, which is implicated in value-based decisions. In Old-world monkeys, the organization of the MFC posterior to the genu of the corpus callosum (i.e. the MCC) has all the basic features of the human sulcal organization and reaches a similar organization across Hominoidea. Specifically, Old-world monkeys display precursors of the four vertical sulci of this region. Importantly, these sulci appear to be located at specific anatomical landmarks that are common to all primates. These results, in combination with functional imaging data that I will present, provide evidence that the MCC is comparable, anatomically and functionally, from macaque to human(6). The above results demonstrate an evolutionarily conserved organizational principle from Old-world monkeys to Hominoidea species, providing a new framework to compare sulcal morphology, cytoarchitectonic areal distribution, connectivity, and function across the primate order. The data presented here can be used to generate clear predictions about how other primate brains might be anatomic-functionally organized(7). 1. Cole, M. et al. (2009). Cingulate cortex: Diverging data from humans and monkeys. *Trends in Neurosciences*, 32, 566-574. 2. Vogt, B. A. (2016). Midcingulate cortex: Structure, connections, homologies, functions and diseases. *Journal of Chemical Neuroanatomy*, 74, 28-46. 3. Amiez C. et al. (in press). Chimpanzee histology and functional brain imaging show that the paracingulate sulcus is not human specific. *Communication Biology*. 4. Petrides, M. et al. (2012). The prefrontal cortex: Comparative architectonic organization in the human and the macaque monkey brains. *Cortex*, 48, 46-57. 5. Sallet, J. et al. (2013). The organization of dorsal frontal cortex in humans and macaques. *Journal of Neuroscience*, 33, 12255-12274. 6. Procyk, E. et al. (2016). Midcingulate motor map and feedback detection: Converging data from humans and monkeys. *Cerebral Cortex*, 26, 467-476. 7. Amiez, C. et al. (2019). Sulcal organization in the medial frontal cortex provides insights into primate brain evolution. *Nature Communications*, 10, 3437. <https://doi.org/10.1038/s41467-019-11347-x>.

Presenter

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Morphological Features of Sulci and Their Relationship to Function And Connectivity

Cortical folds, or sulci, are the main visible features when observing the cortex at a macroscopic scale and, as such, they are often used to define locations on the surface of the cortex and, to some extent, describe macroscopic cortical organization. The current presentation will describe how sulcal morphology can be used to define functionally relevant landmarks within specific folds. Starting with the central sulcus (CS), I will first define the sulcal profile, a morphological curve that quantifies the antero-posterior variations in shape of the CS along its dorso-ventral axis. The sulcal profile of the CS can be used to locate automatically the well-known hand-knob, a morphological landmark in the CS that has been associated with the primary motor area of the hand(1). Functional data will be presented that show a strong relationship between the location of this motor area and that of features extracted from the sulcal profile(2). Sulcal depth is another feature that has been used to characterize cortical shape, and it will be demonstrated that variations in sulcal depth can be used to describe morphology and localize function. Specifically, evidence will be provided for how inter-hemispheric depth asymmetries within the superior temporal sulcus (STS) can be used to localize temporal voice areas(3), that is, functional areas that respond specifically to vocal sounds. Studies have shown strong relationships between morphology and function at the group level, but sulcal patterns show topological and geometrical variations that often make it difficult to establish inter-subject correspondences. Therefore, the group average is not representative of individual sulcal morphology. It has been proposed that morphological features called 'annectant gyri' or 'plis-de-passage' (PdP) can explain inter-individual variations in sulcal patterns(4). Studies will be presented that suggest that PdPs are related to specific short-range U-shape white matter connectivity(5,6). More specifically, PdPs appear to occur at the location of a denser connectivity between the two opposite banks of a sulcus, which in some cases might explain the link between specific PdPs and functional areas(7). To conclude, the above research demonstrates the value of studying morphological features of sulci. Despite the existence of inter-subject variability in sulcal patterns, morphological features, such as sulcal depth, can provide insight into the functional organization of the cerebral cortex and its local short-range white matter connectivity. 1. Yousry, T.A. et al. (1997). Localization of the motor hand area to a knob on the precentral gyrus. A new landmark. *Brain*, 120, 141-157. 2. Coulon, O. et al. (2011). Two new stable anatomical landmarks on the central sulcus: Definition, automatic detection, and their relationship with primary motor functions of the hand, in *IEEE EMBC 2011*, pp.7795-7798, Boston, USA. 3. Bodin, C. et al. (2018). Anatomic-functional correspondence in the superior temporal sulcus. *Brain Structure and Function*, 223, 221-232. 4. Ochiai, T. et al. (2004). Sulcal pattern and morphology of the superior temporal sulcus. *NeuroImage*, 22, 706-719. 5. Pron, A. et al. (2020). U-shape short-range extrinsic connectivity organisation around the human central sulcus. *Brain Structure and Function*. doi:10.1007/s00429-020-02177-5 6. Bodin, C. et al. (2020). Plis de passage in the superior temporal sulcus: Morphology and local connectivity. *NeuroImage*, 117513. doi:10.1016/j.neuroimage.2020.117513 7. Boling, W. et al. (1999). Localization of hand motor activation in Broca's pli de passage moyen. *Journal of Neurosurgery*, 91, 903-910.

Presenter

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Mechanical Morphogenesis and the Development and Evolution of Primate Cortical Folding

Cortical folding is a defining characteristic of large mammalian brains. The degree of folding increases steeply with brain volume, and these folds follow a conserved pattern, distinctive of each species. Furthermore, the geometry of cortical folds has been shown to correspond with their cytoarchitectonic, connective, and functional organisation(1,2). In recent years, the idea that cortical folding is produced by mechanical instability triggered by cortical expansion has become increasingly recognised(3). However, folding patterns are still believed to be genetically encoded(4). In this presentation, I will discuss to what extent mechanical morphogenesis influences the development and evolution of the primate cortex. Our analyses made use of cortical reconstructions of 34 primate species, obtained from MRI, in combination with phylogenetic comparative methods to explore different evolutionary hypotheses(5). The Brownian Motion model, which assumes that phenotypes change randomly along the phylogenetic tree, provided the best fit to the data. We estimated ancestral phenotypes for various neuroanatomical measurements: brain volume, gyrification index, sulcal depth, and sulcal width. While we observed large changes in brain volume and surface area, sulcal width was surprisingly stable. These results support the mechanical folding hypothesis, in which fold width is determined by cortical thickness, which varies little across primates(3). We also used phylogenetic tree data to study the relationship between genetic similarity and folding pattern. If folding patterns are genetically encoded, phylogenetically closer primate species should be more similar in folding patterns than those farther apart on the tree. We described folding patterns using graphs for which edges represented gyri, and nodes represented the connection of several gyri. We compared the fold graphs using graph edit distance and observed that their similarity was more strongly driven by volume than by phylogenetic distance(6). Even in species stemming from a lissencephalic ancestor, evolutionary increases in brain volume led to the emergence of a similar folding pattern. These results suggest that folding patterns result from mechanical and geometric constraints: similar initial geometry and cortical expansion lead to similar folding patterns. In addition to global shape, global expansion gradients should influence mechanical morphogenetic processes, which then lead to the formation of folding patterns(3). We recently studied these gradients using a non-linear surface deformation algorithm to create homologies between species. The resulting evolutionary expansion trajectory, going from small lemurs towards great apes, illustrated a striking continuity, such that folding patterns were similar among species with a comparable brain volume, despite their position in the phylogenetic tree. These studies suggest that mechanical morphogenesis may provide a sort of mechanical canalisation, able to produce robust, polygenic modules – cortical folds – with a stereotypical shape and pattern. These modules are associated with large-scale gradients of mechanical stress that influence cell proliferation, cell death, cell fate, and connectivity(7,8), thereby having a causal role on the development and evolution of brain organisation.

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