*Using tertiary sulci to map the “cognitive globe”
of prefrontal cortex*

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Keywords: prefrontal cortex, functional neuroanatomy, morphology, gradients, brain mapping, higher-order cognition

ABSTRACT

Stuss considered the human prefrontal cortex (PFC) as a “cognitive globe” (Stuss and Benson, 1984) on which functions of the frontal lobe could be mapped. Here, we discuss classic and recent findings regarding the evolution, development, function, and cognitive role of shallow indentations, or tertiary sulci, in PFC with the goal of using tertiary sulci to map the “cognitive globe” of PFC. First, we discuss lateral PFC (LPFC) tertiary sulci in classical anatomy and modern neuroimaging, as well as their development, with a focus on those within the middle frontal gyrus (MFG). Second, we discuss tertiary sulci in comparative neuroanatomy, focusing on primates. Third, we summarize recent findings showing the utility of tertiary sulci for understanding structural-functional relationships with functional network insights in ventromedial PFC and LPFC. Fourth, we revisit and update unresolved theoretical perspectives considered by Vogt and Vogt (1919) and Sanides (1964) that tertiary sulci serve as landmarks for cortical gradients. Together, the consideration of these classic and recent findings indicate that tertiary sulci are situated in a unique position within the complexity of the “cognitive globe” of PFC: they are the smallest and shallowest of sulci in PFC, yet can offer insights that bridge spatial scales (microns to networks), modalities (functional connectivity to behavior), and species. As such, the map of tertiary sulci within each individual participant serves as a coordinate system specific to that individual on which functions may be further mapped. We conclude with new theoretical and methodological questions that if answered in future research, will likely lead to mechanistic insight regarding the structure and function of human LPFC.

INTRODUCTION

“The anatomy of the frontal lobe and its connections suggests a possible cognitive globe on which our knowledge of frontal lobe functions may be mapped” (Stuss and Benson, 1984).

Understanding how anatomical structures of the brain support functional networks underlying human-specific aspects of cognition is a major goal in cognitive neuroscience. Of the many anatomical structures to study, prefrontal cortex (PFC) is particularly important given its central role in cognitive control and goal-directed behavior (Goldman-Rakic, 1995; E. K. Miller & Cohen, 2001; Stuss, 2011; Stuss & Alexander, 2000; Stuss & Knight, 2012). Throughout his career, Don Stuss used maps of lesion damage to begin parcellating the PFC into the component pieces of a “cognitive globe” as he described in the above quote (Stuss & Alexander, 2000; Stuss & Benson, 1984; Stuss & Knight, 2012). The composition of Stuss’ “cognitive globe” argued against the notion of PFC as a general “central executive” (Stuss, 2011)¹. Instead, Stuss’ “cognitive globe” within the frontal lobe consisted of several, interacting regions:

“The frontal lobes (in anatomical terms) or the supervisory system (in cognitive terms) do not function (in physiological terms) as a simple (inexplicable) homunculus...Because of their extensive reciprocal connections with virtually all other brain regions, the frontal lobes may be unique in the quality of the processes that have evolved, and perhaps in the level of processing which might be labeled “executive” or supervisory. The different regions of the frontal lobes provide multiple interacting processes.” (Stuss et al., 1995, pg. 206)

In the decades since Stuss’ original proposal, functional maps and parcellations of the PFC at the scale of several centimeters have been developed across many cognitive domains using a

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¹ Specifically, Stuss (2011) wrote: “There is no central executive. There are, instead, numerous domain general processes discretely distributed across several frontal regions that act in concert to accomplish control” (Stuss, 2011, pg. 759)

variety of neuroimaging techniques. For example, modern neuroimaging research shows widespread support for a hierarchical functional gradient organized along the rostral-caudal axis of lateral PFC (LPFC; (Badre & D'Esposito, 2009; Demirtas et al., 2019; Koechlin, Ody, & Kouneiher, 2003; Koechlin & Summerfield, 2007; Nee & D'Esposito, 2016; Reid et al., 2016)). Additionally, several different anatomical, functional, and multimodal approaches have further parcellated human LPFC into dozens of different areas (Eickhoff, Yeo, & Genon, 2018; Glasser et al., 2016; Goulas, Uylings, & Stiers, 2012; Kong et al., 2018; Sallet et al., 2013). Despite this progress, we still lack fundamental neuroanatomical details of the functional maps and parcellations within LPFC largely for two main reasons. First, invasive methods commonly used to uncover the neuroanatomical details of cortical networks in animal models cannot be used in humans. This is not a new issue and over three decades ago was summarized as the “backwardness of human neuroanatomy” (Crick & Jones, 1993). Second, human and non-human hominoid brains contain neuroanatomical structures that other primate brains lack. For instance, association cortices in hominoid brains contain shallow indentations known as tertiary sulci that are missing in the more lissencephalic brains of other species widely studied in cognitive neuroscience such as mice, marmosets, and macaques (Armstrong, Schleicher, Heyder, Maria, & Zilles, 1995; Petrides, 2019; Sanides, 1962; Welker, 1990).

Here, we propose that identifying and studying tertiary sulci contribute a *forwardness* to human neuroanatomy as this approach offers an opportunity to examine neuroanatomical-functional relationships in humans that cannot be conducted in other animal models – even non-human hominoids. Specifically, we cannot map non-human hominoid brains in the way that we can map the human brain due to ethical reasons. As such, examining the relationship among tertiary sulci and different types of functional and neuroanatomical maps across spatial scales is a

unique opportunity specific to the human brain. Consideration of tertiary sulci allows the “cognitive globe” of LPFC to be mapped within individuals without relying on an average cortical surface or template across individuals within which tertiary sulci commonly disappear (**Fig. 1**). Consistent with Stuss’ approach to conduct neuropsychological and lesion mapping studies “within the frontal lobes with finer anatomical and experimental precision” (Stuss et al., 2005) than had been conducted previously, in this paper, we discuss recent research showing that tertiary sulci are useful for improving the scale of precision in anatomical-functional mapping in neuroimaging with translational and comparative applications with a particular emphasis on PFC. Specifically, we propose that tertiary sulci in the human cerebral cortex serve as a meso-scale coordinate map for linking neuroanatomical and functional properties of the human brain across spatial scales and modalities. The map of tertiary sulci within each individual participant serves as a coordinate system specific to that individual on which functions and additional anatomical features may be further mapped. That is, instead of a canonical atlas that typically uses an x,y,z coordinate system implemented in group analyses, in our suggested approach, tertiary sulci within each individual participant serve as a coordinate system specific to that individual in association cortices that often perform computations associated with human-specific aspects of cognition.

identification of the middle frontal sulci (*pmfs*) within individuals

Figure 1. Tertiary sulci in LPFC disappear on averaged cortical surface reconstructions from anatomical MRIs. *Top:* three individually labeled left hemispheres with tertiary sulci in the middle frontal gyrus (MFG) outlined in white. The superior and inferior frontal sulci (*sfs*, *ifs*) are labeled for reference above and below the MFG, respectively. *Bottom:* average cortical surfaces show much smaller tertiary sulci compared to individual participants. As more participants are included in the averaged cortical surface, tertiary sulci within the MFG disappear almost entirely, which is inconsistent with their prominence in individual hemispheres. Modified with permission from Miller et al., 2021.

In order to link Stuss' classic ideas with recent anatomical-functional findings, this review is divided into four main sections. First, we discuss LPFC tertiary sulci in classical anatomy and modern neuroimaging with a focus on those within the middle frontal gyrus (MFG). Second, we discuss tertiary sulci in development and comparative neuroanatomy, focusing on primates. Third, we summarize recent findings showing the utility of tertiary sulci for understanding structural-functional relationships in LPFC and likely in association cortices more broadly. Fourth, we revisit unresolved theoretical perspectives that tertiary sulci can serve as landmarks for cortical gradients. We conclude with new theoretical and methodological questions that if answered in future research, will likely lead to mechanistic insight regarding the structure and function of LPFC.

a Principle characteristics of tertiary sulci

extended developmental trajectory

shallower cortical depth

smaller surface area

b Historical ambiguity over labeling tertiary sulci in MFG

omission of sulci

same label for multiple structures

splitting sulci into subcomponents

numerical labels for sulcal branches

different names for same structure

Figure 2. Characteristics of tertiary sulci in LPFC and their historical identification. (a) Principle characteristics distinguishing tertiary sulci from larger primary sulci include later emergence in gestation and extended developmental trajectory (*left*), shallower sulcal depth (*middle*), and smaller surface area (*right*). Nissl stain (*middle*) downloaded from the Allen Human Brain Atlas (<http://human.brain-map.org/>), while developmental images (*left*) are adapted from Welker (1990). (b) We use the tertiary sulci in the posterior *middle frontal gyrus* (MFG) as an example to outline the main types of ambiguity across post-mortem studies leading to the neglect of some tertiary sulci in LPFC. *Top and bottom left*: Sulci in the MFG were depicted, but often left unlabeled (arrow) in official schematics as in Eberstaller (1890) and Connolly (1950). *Top middle*: Cunningham (1892) differentiated the “Fronto-marginal sulcus of Wernicke” (*w*) from the “Sulcus frontalis medius of Eberstaller” (*f.m.*), in which the *f.m.* label included all tertiary sulci in the posterior MFG. *Bottom middle*: Tertiary sulci were identified and assigned letters, while sulcal branches were assigned numbers. Neither were given any distinguishing acronyms or labels in brain sections or schematics (Bailey and Bonin, 1951). *Top right*: Separate labels were applied to different tertiary sulci within the posterior MFG. Retzius (1896) acknowledged a posterior transverse component (*fmt*) that was often distinct from the rest of the middle frontal sulcus. Ariens-Kappers (1928, 1929, 1936) also acknowledged three components of the middle frontal sulcus (**Appendix**) largely consistent with the most modern and thorough schematic of sulcal morphology (Petrides, 2019), which identifies three components of the *posterior middle frontal sulcus* (*pmfs*): an *anterior*, *intermediate*, and *posterior* (Petrides, 2019). *Bottom right*: Sulci within the MFG have been referred to using different labels such as the *medifrontal sulcus*, *frontomarginal sulcus*, *intermediate frontal sulcus*, *middle frontal sulcus*, and *posterior middle frontal sulcus*, among others (see **Appendix**).

I: LPFC tertiary sulci in classic anatomy and modern neuroimaging: Clarity vs. Ambiguity

It is widely accepted that LPFC is “phylogenetically novel” (Stuss & Benson, 1984) and is expanded in the human brain relative to non-human primate species commonly used in neuroscience research, such as rhesus macaques (Amiez, Kostopoulos, Champod, & Petrides, 2006; Amiez & Petrides, 2009; Barrett et al., 2020; Croxson et al., 2005; Petrides, 2005; Petrides & Pandya, 1999; Petrides, Tomaiuolo, Yeterian, & Pandya, 2012). This “phylogenetically novel” LPFC includes additional anatomical structures such as tertiary sulci that are lacking in brains that are phylogenetically older. Tertiary sulci are so named for their developmental ordering, as they are the last sulci to emerge in gestation after the larger and deeper primary and secondary sulci (**Fig. 2a**). It is also worth highlighting that there is a clear correlation among i) the temporal emergence of a sulcus in gestation, ii) the surface area of a sulcus, and iii) the depth of a sulcus: primary sulci emerge first and are largest/deepest, while tertiary sulci emerge last and are smallest/shallowest (Bailey & Bonin, 1951; Bailey, Bonin, & McCulloch, 1950; Chi, Dooling, & Gilles, 1977; Connolly, 1950; Cunningham, 1892; J. A. Miller et al., 2020; Petrides, 2019; Retzius,

1896; Sanides, 1962, 1964; Turner, 1948; Weiner, 2019; Weiner et al., 2014; Weiner & Zilles, 2016; Welker, 1990).

Ongoing research attempts to better understand the function of these evolutionarily new structures, some of which are likely unique to the human cerebral cortex. Specifically, large, freely available multi-modal datasets have provided the ability to finally assess typical variations in tertiary sulcal morphology and functional organization within individuals that was not possible in classical studies of post-mortem brains. Indeed, tertiary sulci were often excluded from classic neuroanatomical atlases because anatomists could not discriminate tertiary sulci from indentations produced by veins and arteries on the outer surface of the cerebrum in post-mortem tissue, which is considered the gold standard of anatomical research (Weiner, Natu, & Grill-Spector, 2018). Consequently, the patterning of tertiary sulci within LPFC has a contentious history (Petrides, 2019; Petrides & Pandya, 2012), whereby tertiary sulci in LPFC were often undefined in classic atlases or contained different combinations of sulcal-label mappings (**Fig. 2a; Appendix**).

We highlight that modern neuroimaging methods contribute either clarity or ambiguity depending on the methods used for definitions of tertiary sulci. In terms of clarity, defining tertiary sulci in cortical surface reconstructions of MRI data within individual participants produces an accurate representation of tertiary sulci because cortical surface reconstructions from MRI scans are made from the inner surface at the boundary between gray and white matter. As such, the definitions of tertiary sulci are clear and are not confusable with indentations produced by veins and arteries as in postmortem tissue. In terms of ambiguity, many researchers today analyze MRI data on cortical surfaces averaged across individuals (e.g. *fsaverage*, *MNI152*, and other cortical surface templates) that often do not accurately depict the patterning or location of tertiary sulci (Coalson, Van Essen, & Glasser, 2018; Dale, Fischl, & Sereno, 1999; Fischl, Sereno, & Dale,

1999; Fischl, Sereno, Tootell, & Dale, 1999). For example, our recent work shows that even though a tertiary sulcus is present within every individual studied (J. A. Miller, Voorhies, Lurie, D’Esposito, & Weiner, 2021), it may shrink or disappear when cortical surfaces are averaged together because LPFC tertiary sulci are more variable in location and much smaller compared to primary and secondary sulci (**Fig. 1**). For instance, the *posterior middle frontal sulcus*, a tertiary sulcus in LPFC discussed throughout this review, is about five times smaller (in terms of surface area) and about half as deep as the primary central sulcus. Nevertheless, in other cortical expanses, such as ventral temporal cortex, tertiary sulci are preserved on average cortical surfaces (J. A. Miller et al., 2020; Weiner, 2019; Weiner et al., 2018). Thus, future studies will shed light on what anatomical and functional factors contribute to the variability and consistency of tertiary sulci in a given cortical expanse. Taken together, tertiary sulci have an unclear history for methodological reasons, which can be corrected with methods that instead preserve neuroanatomical structures and take individual anatomical organization into consideration.

II: Developmental trajectory of LPFC tertiary sulci

Despite these historical and modern issues contributing to our lack of understanding of tertiary sulci within LPFC (**Fig. 2a; Appendix**), classic and modern studies seem to agree on the developmental trajectory of these sulcal components. That is, tertiary sulci emerge last in development, but not in a temporally uniform fashion across the cerebral cortex (Chi et al., 1977; Welker, 1990). Instead, they emerge at different timepoints depending on the lobe they are in and also their topological positioning within that lobe. For the MFG, classic anatomists agreed that the *fronto-marginal* and *middle frontal* sulcal components emerged from anterior to posterior (**Fig. 3a; Appendix**). Between 16-24 weeks, the most anterior fronto-marginal components appear

(Cunningham, 1892; Retzius, 1896; Turner, 1948), while between 24 and 36 weeks, the rest of the sulci emerge in the middle and posterior portions of the MFG, respectively.

With modern neuroimaging tools, the temporal emergence and continued development of tertiary sulci can be revisited. Recent findings examining the development of cortical folding in pre-term infants using MRI shows feasibility of this comparison. As illustrated in **Fig. 3b**, shallow tertiary sulci begin to emerge at 30 weeks and then deepen at 38 weeks. Additionally, the location in LPFC that expanded the most during fetal development was in the vicinity of the posterior component of the *pmfs* (**Fig. 3b**, bottom), which is consistent with the developmental timeline from anterior (early) to posterior (late) identified by classic neuroanatomists. These findings provide new evidence for the developmental trajectory of macroanatomical structures in LPFC and suggest a link between cortical folding patterns and the cognitive abilities supported by LPFC. That is, just as prolonged myelination is a hallmark of association cortex development (D. J. Miller *et al.*, 2012), tertiary sulcal development in LPFC may be an important marker for a complex array of genetic and environmental factors related to variations in human cognitive abilities.

Figure 3. Sulci within the MFG likely emerge and develop along an anterior-posterior axis. (a) *Top to bottom:* Images from classic atlases and papers depicting the emergence of sulci during 16-24 weeks (Cunningham, 1892), 24-28 weeks (Turner, 1948), 28-32 weeks (Retzius, 1896), and 32-36 weeks (Retzius, 1896). Despite contentions regarding sulcal definitions within the MFG discussed in the main text and the **Appendix**, anatomists commonly agreed that sulci in the anterior MFG emerged first, while sulci in the posterior MFG emerged last *in utero* and continued to develop after birth (**Appendix**). **(b)** *Top to bottom:* MRI images depicting average cortical surfaces across pre-term infants during different developmental time periods (PMA: postmenstrual age) in gestation (Garcia et al., 2018). Consistent with the classic images in **(a)** and as specified in the **Appendix**, tertiary sulci within the MFG become prominent during the 7th and 8th month in gestation. Black lines outline the MFG, and asterisks show correspondence with the approximate location of the posterior *pmfs* component (*pmfs-p*) based on the shading of the cortical surface. *Bottom:* An average cortical surface map comparing the relative expansion across development.

III. Tertiary sulci in comparative neuroanatomy and primate evolution

Among primates, the level of cortical folding (or gyrification index) tracks with evolutionary complexity, suggesting that sulcal structures are at the bare minimum markers of primate evolution (Zilles, Palomero-Gallagher, & Amunts, 2013). Classic and recent research findings indicate that some primate species display tertiary sulci that are likely homologous to human tertiary sulci in these cortical expanses. For example, Amiez and colleagues compared the sulcal morphology of vmPFC using anatomical MRI from human, chimpanzee, baboon, and macaque brains. Across the four analyzed primate species, the majority of tertiary sulci in the vmPFC were only identifiable in *hominoids* (humans and chimpanzees) and a subset were human-specific (**Fig. 4a**). For example, the *dorsomedial polar sulcus* (*dmfs*) was identified as a hominoid-specific marker present in most human brains and ~50% of chimpanzee brains, while the *ventromedial polar sulcus* (*vmfs*) was present in most individual human brains (64%), but entirely absent in chimpanzees and other primate brains. Interestingly, while the presence of major cytoarchitectonic areas is largely conserved across species in vmPFC, what are considered the most expanded areas (BA 9 and 10) were the locations for the identified tertiary sulci (Amiez et al., 2019).

In LPFC, consistent with Amiez and colleagues (2019), it is likely that some, but not all chimpanzees have all three *pmfs* components as in humans. Two different chimpanzee brains with and without tertiary sulci in the MFG are shown in **Fig. 4b**, in contrast to an example human brain, in which tertiary sulci are always present within the MFG. Future studies performing morphological comparisons of tertiary sulci between chimpanzees and humans will further quantify these observations. This homology may be important since the *pmfs* appears to delineate borders or transitional zones for cytoarchitectonic areas in both humans and chimpanzees. For

example, the seminal papers of Rajkowska and Goldman-Rakic (1995a, 1995b) analyzed the cytoarchitecture of the LPFC within nine post-mortem human brains. In the presented coronal sections of cytoarchitectonic areas 9 and 46 (**Fig. 4c**), a common trend appears that the *posterior middle frontal sulcus* (or MFS, as it was labeled) delineates a transitional zone between areas 9 and 46 (Rajkowska & Goldman-Rakic, 1995a, 1995b). The characteristics of areas 9 and 46 are different enough (area 9 with a more prominent layer 3, area 46 with more prominent deeper layers) that Petrides coined area 9/46d to describe this transitional zone (Petrides, 2005; Petrides & Pandya, 1999). We posit that this transitional zone is tightly coupled to the *pmfs* and may point to a mechanistic association between granular cortex and tertiary sulci in primates, with a specific expansion of middle cortical layers. For example, recent support for this hypothesis is evident from re-examining cytoarchitectonic studies of chimpanzees showing that the *pmfs* also appears to mark cytoarchitectonic transitions between granular regions FD and FDΔ in chimpanzee brains differing in the extent of granular cell proliferation in layer 3 (Bailey & Bonin, 1951; Bailey et al., 1950). These observations suggest that tertiary sulci could serve as an organizing framework to study PFC evolution and to compare with the evolution of cytoarchitecture and connectivity patterns across species. They further lead to potential mechanistic links relating tertiary sulci to the expansion of granular cortex and white matter across primate evolution (Donahue, Glasser, Preuss, Rilling, & Van Essen, 2018; Garcia-Cabezas, Zikopoulos, & Barbas, 2019; Van Essen et al., 2019).

As tertiary sulci are identified as important landmarks in functional areas especially within association cortices in humans, comparing tertiary sulci among primate species also leads to questions about whether sulci would serve as trait-level behavioral markers within and across species. Is variability in sulcal morphology in macaques, baboons, and chimpanzees associated with behavioral traits? Do animals with more “human-like” sulcal morphology (e.g. a chimpanzee

with a *dmfs* or *pmfs*) exhibit cognitive control or other behaviors closer to human-level performance? As more cognitive paradigms from the human literature are adapted for non-human primates (Badre, Frank, & Moore, 2015), these anatomical-behavioral relationships can begin to shed light on PFC structural-functional relationships across evolutionary timescales.

Figure 4. Tertiary sulci across primate PFC. (a) The sulcal morphology of the medial PFC and anterior cingulate cortex shown in example sagittal MRI sections of human and chimpanzee brains. The *vmfs* (top) is a human-specific tertiary sulcus, while the *dmfs* (bottom) is found in humans and over half of the chimpanzee hemispheres examined. Figure adapted from Amiez et al. (2019). (b) *Top*: Cortical surface (left hemisphere) from the NIH macaque brain template (<https://afni.nimh.nih.gov/NMT>) in which the principal and arcuate sulci are labeled. *Middle*: Two chimpanzee cortical surface reconstructions showing variability in the presence or absence of a *pmfs* (outlined in white) within the MFG (National Chimpanzee Brain Resource: <https://www.chimpanzeebrain.org/>; (Hopkins, Li, Crow, & Roberts, 2017; Keller, Roberts, & Hopkins, 2009)). The inset shows the *pmfs* (then labeled as “*fm*”) as the boundary between areas FD and FDA. (adapted from Bailey, Bonin, & McCulloch, 1950). *Bottom*: An example human left hemisphere cortical surface reconstruction in which the prominent three *pmfs* components are outlined in white. (c) Schematic of a post-mortem coronal section with the *pmfs* (labeled then as the *middle frontal sulcus*, *MFS*) indicating a transitional zone between cytoarchitectonic areas 9 and 46. Inlets show Nissl stained histological sections revealing the cytoarchitectural organization in areas 9, 46, and transitional area 9/46d. Figures adapted from Rajkowska & Goldman-Rakic (1995) and Petrides & Pandya (1999). Additionally, a recent cytoarchitectonic atlas shows that the *pmfs-a* identifies a transition between 9/46v and 9/46d (Petrides, 2019).

IV: Tertiary sulci as markers of structural-functional relationships in PFC: Network insight from neuroanatomical precision

One of Stuss' research goals was to understand brain networks from improved neuroanatomical precision in lesion-behavioral studies. Many of Stuss' studies examined the relationship between neuroanatomical damage and behavioral performance in order to determine brain-behavioral relationships (Stuss, 2011; Stuss & Alexander, 2000; Stuss & Levine, 2002). For these studies, Stuss and colleagues generated methods (Stuss *et al.*, 2005; Stuss & Levine, 2002) to examine lesion location relative to cytoarchitectonic parcellations of cortex beyond Brodmann - specifically from Petrides and Pandya (1994). Such an approach not only provided cytoarchitectonic links to the lesion location, but also functional properties of that cytoarchitectonic region. As Stuss writes:

“The location of the lesions provides the clues to dissociating processes.” Stuss, 2011, pg. 760

Often, if a researcher strives for improved anatomical detail regarding either the cortical location of a lesion or a functional region (or both), it is assumed that the researcher favors a modular versus distributed theory of how information is represented in cortex. Or, that improved anatomical insight in general is just a type of “modern phrenology,” without relation to fundamental properties of neuronal functioning. On the contrary, Stuss was very clear about how his approach was a preliminary attempt to use improved anatomical precision in lesion research to gain insight into functional brain networks. Stuss wrote:

“Our research on the effect of focal frontal lobe lesions on separable cognitive and noncognitive processes revealed distinct roles for different regions of the frontal lobes. Careful reading of the results leads to the conclusion that this is not a modern phrenology but a preliminary effort in the

use of lesion research to understand integrated neural networks. Converging evidence from multiple methodologies compellingly argues for the regulatory role of the frontal lobes in networks involving posterior regions.” (Stuss et al., 2002 pgs. 400-401)

We echo Stuss’ clarity and emphasize that zooming in to tertiary sulci in PFC forms a foundation for understanding how these largely overlooked neuroanatomical structures contribute to typical brain function and cognition. Using modern multi-modal neuroimaging datasets, two recent parallel lines of work show that meticulously labeling tertiary sulci within individuals uncovers new structural-functional relationships within PFC at the network level. In a recent study, the sulcal morphology of the ventral medial PFC (vmPFC) was carefully divided into four distinct patterns across individuals and the superior rostral sulcus (*ros-s*), a tertiary sulcus, was found to co-localize with a hub of the default mode network (Lopez-Persem, Verhagen, Amiez, Petrides, & Sallet, 2019). Further, the presence or absence of nearby tertiary sulci shifted the functional organization within vmPFC. For example, the presence or absence of the tertiary *inferior rostral sulcus* (*ros-i*) shifted the location of the vmPFC peak of the default mode network superiorly (**Fig. 5a**). Moreover, individual differences showed higher connectivity strength of the vmPFC with the rest of the default-mode network in individuals with an *ros-i* (64.04%) compared to those without an *ros-i*. These results indicate a relationship between sulcal variability and functional variability within vmPFC as well as other cortical locations. For instance, the presence of the *ros-i* also resulted in a functional cluster in posterior cingulate cortex (PCC) that was not present in individuals lacking an *ros-i*.

A second line of modern neuroimaging evidence comes from our recent work characterizing the *pmfs* in LPFC. We applied a recently proposed labeling scheme of tertiary sulci in LPFC (Petrides, 2019) to test whether these sulci could be defined in the LPFC of individual

participants *in-vivo*. Consistent with Petrides' (2019) proposal, we identified the *pmfs* as a prominent tertiary sulcal structure that consists of three distinct components along an anterior-posterior axis within each of 72 individual hemispheres. While the *pmfs* was present within each individual, its location was the most variable across hemispheres of all sulci examined in LPFC. This variability likely contributed to the historical ambiguity of its identification (**Fig. 1**), as well as contributes to its disappearance in commonly used average cortical surfaces (J. A. Miller et al., 2021). To determine if *pmfs* components have distinct functional network organization, we analyzed multi-modal data from the Human Connectome Project (HCP) after manual labeling of sulci in LPFC. The three *pmfs* components were dissociable based on myelin content, resting-state functional connectivity profiles, and task activations across a meta-analysis of 83 cognitive tasks (**Fig. 5b**). Together, these results show that each *pmfs* component has a different network *fingerprint* (**Fig. 5b**).

In combination with recent findings, these results show the utility of using tertiary sulci to study functional organization and properties at the level of areas and networks in the cerebral cortex (Amiez et al., 2006; Amiez et al., 2013; Amiez & Petrides, 2009; Lorenz et al., 2017; Weiner et al., 2014; Weiner et al., 2018). Because tertiary sulci are prominent within individuals, they can serve as a scaffolding to link microanatomical and functional features of the cerebral cortex (Weiner, 2019; Weiner et al., 2014; Weiner et al., 2018), as well as allow for communication and replication between research groups that is more accurate than average cortical surface reconstructions or stereotaxic coordinates. In terms of the latter, depending on the cortical expanse, tertiary sulci can nearly disappear entirely on average cortical surface templates, which is a direct consequence of their variability when aligned to stereotaxic space (J. A. Miller et al., 2021; Weiner et al., 2014). As such, average *x, y, z* stereotaxic coordinates likely will not accurately predict the

location of tertiary sulci as previously shown (Weiner et al., 2014). Instead, until computational methods are developed to precisely identify tertiary sulci automatically (expanded further in the next section), the manual definition of tertiary sulci within each individual participant will continue to serve as a personalized coordinate system for each individual that is also generalizable across individuals. That is, *personalized* in the sense that the location (or coordinates) of tertiary sulci will likely be specific to that individual and *generalizable* in the sense that once tertiary sulci are defined in a given hemisphere, sulcal-functional or sulcal-behavioral relationships can be compared among many individuals rather than relying on coordinates that miss the location of small, shallow tertiary sulci entirely. Once precisely defined, individual differences in the morphology of tertiary sulci within and across individuals can then be leveraged to discover important relationships with the functional properties of cortical areas and ultimately, a host of cognitive processes. For example, across individuals, tertiary sulci show extensive individual differences in depth, length, shape, and location (Amiez et al., 2019; Armstrong et al., 1995; Bailey & Bonin, 1951; Bailey et al., 1950; Borne, Riviere, Mancip, & Mangin, 2020; Chi et al., 1977; Connolly, 1950; Cunningham, 1892; Garrison et al., 2015; Lopez-Persem et al., 2019; J. A. Miller et al., 2021; J. A. Miller et al., 2020; Paus et al., 1996; Retzius, 1896; Sanides, 1962, 1964; Turner, 1948; Weiner, 2019; Weiner et al., 2014; Weiner & Zilles, 2016; Welker, 1990). Often this variability corresponds with functional and/or microanatomical organization in the cerebral cortex or behavioral performance. For instance, tertiary sulcal morphology in ventral temporal cortex (VTC), predicts the delineation of functional and microarchitectonic boundaries (Grill-Spector & Weiner, 2014; Weiner, 2019; Weiner et al., 2014; Weiner & Zilles, 2016) and even perceptual abilities across individuals (Parker et al., 2020). Additionally, i) medial PFC and cingulate areas also show distinct functional organization based on the presence of certain tertiary sulci (**Fig. 5**),

and ii) recent studies show that individual differences in sulcal morphology in PFC are related to individual differences in cognition (Amiez, Wilson, & Procyk, 2018; Brun et al., 2016; Voorhies, Miller, Yao, Bunge, & Weiner, 2020).

These findings also lead to new questions regarding the emergence of tertiary sulci and the development of anatomical and functional cortical connectivity patterns across individuals. For example, does the emergence of the *ros-i* in development precede the detection of a default mode network? Promising new lines of infant fMRI scanning may be able to reveal how the developmental trajectory of tertiary sulci in gestation relates to the layout and functioning of whole-brain functional networks (Ellis & Turk-Browne, 2018). Long-range (Schilling et al., 2018; Van Essen et al., 2014; Welker, 1990) and short-range (Reveley et al., 2015) connectivity differ between gyri and sulci, and early-life anatomical and functional data open a new array of research tools and questions for structural-functional relationships in PFC.

Figure 5. Network insights from identifying tertiary sulci. (a) The *superior rostral sulcus* (*ros-s*) serves as a landmark for default-mode network connectivity strength and organization. *Top left:* Sulcal organization in vmPFC showing the *inferior rostral sulcus* (*ros-i*). *Bottom Left:* The location of peak functional connectivity to the default-mode network within the vmPFC is consistently highest at the anterior tip of the *ros-s*. *Right:* Individuals with versus without an *ros-i* show a shift in the peak location of default-mode network connectivity in the vmPFC. Specifically, both the peak location of default-mode network connectivity and the *ros-s* are shifted superiorly when an *ros-i* is present. Figures adapted from Lopez-Persem et al. (2019). (b) *Left:* The three components of the *posterior middle frontal sulcus* (*pmfs*) in the MFG outlined in white on five individual cortical surfaces (left hemispheres). *Right:* The three *pmfs* components exhibit different patterns of network connectivity along an anterior-posterior gradient. Modified with permission from Miller et al., 2021.

V: Tertiary sulci as landmarks in association cortices: unresolved theoretical perspectives and future directions

The potential importance of tertiary sulci as landmarks in human association cortices was championed by the Vogts (Vogt & Vogt, 1919) and further refined by Sanides (1962, 1964). Sanides proposed “gradations” or “streams” which matched the directions of neocortical development during brain evolution (Henssen *et al.*, 2016; Sanides, 1964). Consistent with observations by the Vogts, Sanides noted that tertiary sulci often served as boundaries for cortical gradations in the myeloarchitecture of PFC sections (for a detailed description of Sanides’ methods and ideas, see Henssen *et al.*, 2016).

More recent work in the functional neuroimaging and neurology literature seem to also support this correspondence. For example, examining the relationship between the *pmfs* components and the recent whole-brain multimodal parcellation from Glasser and colleagues (2016) suggests that 1) the *pmfs-p* and *pmfs-i* likely identify boundaries between area *8Av* superiorly from *8C* inferiorly, 2) the *pmfs-i* likely identifies a boundary between a posterior cluster containing areas *8Av* and *8c* and a more anterior cluster containing areas *46* and *p9/46v*, and 3) the *pmfs-a* likely identifies the boundary between areas *46* and *p9/46v*. As this is a parcellation derived from averaging brain data across individuals, future studies can explore if tertiary sulci correspond to transitions between multimodal areas in individual participants.

Additionally, identifying the location of the *pmfs* components in previously published images from Stuss’ work shows that lesions superior to these components likely result in response time deficits (**Fig. 6**, left). Functional and behavioral links are not limited to the location of *pmfs* components, but also other nearby sulci in LPFC. For instance, the intermediate frontal sulcus (*imfs*), which is anterior to the *pmfs*, seems to identify a functional activation for the monitoring

(or manipulation) of working memory content ((Amiez & Petrides, 2007); **Fig. 6**, right). Finally, a functional region preferentially activated during higher-order, temporal control appears to co-localize with the three *pmfs* components, while the *imfs* seems to co-localize with a functional region preferentially activated during contextual control (Nee, 2020; Nee & D’Esposito, 2016). The combination of these interpretations of previously published data demonstrates the utility of tertiary sulci to situate functional maps across findings from different research groups and to ground functional maps to evolutionary new anatomical features of the cerebral cortex.

When considering these anatomical-functional correspondences in the context of future research, it is important to also consider the limitations of examining the functional role of tertiary sulcal patterns and individual differences in i) any portion of the cerebral cortex and ii) any relevant behavior or cognitive process associated with a given cortical expanse. The main limitation is that there is often no causal inference when examining the anatomical-functional relationship between tertiary sulci and functional regions (**Fig. 5**). Nevertheless, previous research in VTC does show a causal relationship among the location of functional regions relative to tertiary sulci and perception (Parvizi et al., 2012; Rangarajan et al., 2014; Schrouff et al., 2020). Thus, an immediate open question is whether the anatomical-functional relationships emphasized here for PFC also have causal implications, which can be addressed in future research. Additionally, as cortical morphology changes with age, it would be especially useful for future studies to quantify how much unique variance is explained by morphological features of tertiary sulci above and beyond age, as well as over and beyond other aspects of gyrification that change with age such as cortical thickness. Ongoing work in a developmental cohort using a model-based approach does just this and shows that the depths of a subset of tertiary LPFC sulci explain reasoning ability in both discovery and replication cohorts above and beyond age, as well as beyond the variance explained

by cortical thickness (Voorhies et al., 2020). Thus, ongoing work suggests that considering tertiary sulcal morphology explains cognition well beyond incremental predictive validity in LPFC. Future work in freely available, large, multi-modal datasets such as the HCP and UK BioBank are needed to systematically relate variability in these tertiary sulci to a wider array of cognitive domains. Nevertheless, increasing evidence from classic and recent studies suggests that some tertiary sulci serve as landmarks that bridge spatial scales (microns to networks), modalities (functional connectivity to behavior), and even species.

In addition to this ongoing and future work, we emphasize that examining the relationship between tertiary sulci and other types of data presently requires accurate, validated, and manually defined sulci in individual participants. For example, in our work, we manually defined 936 sulci in 72 hemispheres. While 72 is a large sample size compared to other labor-intensive anatomical studies in which 20 hemispheres was considered sufficient to encapsulate individual differences (Amunts & Zilles, 2015), 2400 hemispheres are available just from the HCP dataset alone (Glasser et al., 2013). Defining tertiary sulci in only the LPFC of every HCP participant would require ~26,400 manual definitions, while defining all tertiary sulci in the entire HCP dataset would require over a quarter of a million (~256,800) manual definitions. Consequently, manual identification of tertiary sulci will continue to limit sample sizes until new automated methods are generated. Uncovering structural-functional relationships in PFC will be advanced by leveraging anatomical expertise to develop computational approaches to neuroanatomy such as deep learning algorithms. Indeed, recent work using deep learning algorithms and expanded training shows improvements in the ability to identify tertiary sulci automatically in LPFC (Borne et al., 2020; Klein et al., 2017; Lyu et al., 2020). As such, it is most likely that LPFC tertiary sulci can “survive” normalization of individual brain images given these advanced computational techniques. This

work is especially important as individual-level data has been increasingly recognized as important for basic and clinical human research, in which it is critical to understand within-participant native anatomy, function, and behavior (Fisher, Medaglia, & Jeronimus, 2018; Gordon et al., 2017; Seitzman et al., 2019; Stuss, 2016)

a multi-modal parcellation

c functional neuroimaging

b PFC lesions

hierarchical cognitive control processes

Nee, 2020

Figure 6. Tertiary sulci are useful for building an understanding of LPFC across scales of organization. (a) Maximum probability maps (thresholded at 33% overlap across participants; white outlines) for the *pmfs-p*, *pmfs-i*, and *pmfs-a* on the FreeSurfer average template (left hemisphere) relative to four areas from a multi-modal cortical parcellation based on structural and functional MRI data (Glasser et al., 2016). If and how the different *pmfs* components serve as areal boundaries in individual participants can be tested in future research. Modified with permission from Miller et al., 2021. (b) A schematic illustration of a lateral view of a left hemisphere from Picton and colleagues (Picton, Stuss, Shallice, Alexander, & Gillingham, 2006). The location of lesions that produced a significant ($p < .05$) deterioration in behavioral performance are illustrated in black. Yellow: Approximate location of the three *pmfs* components discussed in this paper that could serve as putative lesion borders. (c) *Top*: While we emphasize *pmfs* components in the present paper, we recognize that identifying other sulci in individual participants could also provide anatomical-functional insight. For example, previous work indicates that the intermediate frontal sulcus (*imfs*) co-localizes with a functional region that is crucial for monitoring during working memory. *Bottom*: Recent research at the group level (Nee, 2020; Nee & D’Esposito, 2016) indicates that *pmfs* components likely couple with functional activations associated with temporal control, while functional activations associated with contextual control likely couple with the *imfs* – both of which can be tested further at the level of individual participants in future studies. Altogether, future research can examine if/how tertiary sulci serve as relevant boundaries, or landmarks, across scales of LPFC organization. Figures adapted from listed studies.

Open questions

- How many of the ~75 tertiary sulci in the human cerebral cortex serve as anatomical, functional, or multimodal landmarks?
- How does the emergence of tertiary sulci in development relate to the development of functional networks?
- Is there a relationship between the expansion of granular cortex and tertiary sulci?
- Can tertiary sulci serve as individual-level biomarkers in cognitive and behavioral disorders?
- In order to accurately define tertiary sulci in large datasets (n=1,000+), can learning algorithms be developed to automatically define tertiary sulci within individual hemispheres with a level of precision that approaches manual definitions?

Box 1. Open questions for future investigations regarding tertiary sulci and the anatomical and functional organization of the PFC and other association cortices.

Concluding remarks

Motivated by Stuss' provocative concept of considering PFC as a "cognitive globe," we have discussed classic and recent findings regarding the development, evolution, function, and cognitive role of PFC tertiary sulci with a particular focus on vmPFC and LPFC. Tertiary sulci are situated in a unique position within the complexity of this cognitive globe as they are the smallest and shallowest of sulci in PFC, yet can offer insights that bridge spatial scales (microns to networks), modalities (functional connectivity to behavior), and species. The unique position of tertiary sulci generates innumerable open questions, some that we have included in the main text and five of which we highlight in **Box 1**. Future research will continue to shed light on the unique position of tertiary sulci not only in PFC, but also in other association cortices.

References

- Amiez, C., Kostopoulos, P., Champod, A. S., & Petrides, M. (2006). Local morphology predicts functional organization of the dorsal premotor region in the human brain. *J Neurosci*, 26(10), 2724-2731.
- Amiez, C., Neveu, R., Warrot, D., Petrides, M., Knoblauch, K., & Procyk, E. (2013). The location of feedback-related activity in the midcingulate cortex is predicted by local morphology. *J Neurosci*, 33(5), 2217-2228.
- Amiez, C., & Petrides, M. (2007). Selective involvement of the mid-dorsolateral prefrontal cortex in the coding of the serial order of visual stimuli in working memory. *Proc Natl Acad Sci U S A*, 104(34), 13786-13791.
- Amiez, C., & Petrides, M. (2009). Anatomical organization of the eye fields in the human and non-human primate frontal cortex. *Prog Neurobiol*, 89(2), 220-230.
- Amiez, C., Sallet, J., Hopkins, W. D., Meguerditchian, A., Hadj-Bouziane, F., Ben Hamed, S., et al. (2019). Sulcal organization in the medial frontal cortex provides insights into primate brain evolution. *Nat Commun*, 10(1), 3437.
- Amiez, C., Wilson, C. R. E., & Procyk, E. (2018). Variations of cingulate sulcal organization and link with cognitive performance. *Sci Rep*, 8(1), 13988.
- Amunts, K., & Zilles, K. (2015). Architectonic Mapping of the Human Brain beyond Brodmann. *Neuron*, 88(6), 1086-1107.
- Armstrong, E., Schleicher, A., Heyder, O., Maria, C., & Zilles, K. (1995). The Ontogeny of Human Gyrification. *Cereb Cortex*, 5(1).
- Badre, D., & D'Esposito, M. (2009). Is the rostro-caudal axis of the frontal lobe hierarchical? *Nat Rev Neurosci*, 10(9), 659-669.
- Badre, D., Frank, M. J., & Moore, C. I. (2015). Interactionist Neuroscience. *Neuron*, 88(5), 855-860.
- Bailey, P., & Bonin, G. V. (1951). *The Isocortex of Man* (Vol. 1). Urbana: University of Illinois Press.
- Bailey, P., Bonin, G. V., & McCulloch, W. S. (1950). *The isocortex of the chimpanzee*. Urbana, IL: University of Illinois Press.
- Barrett, R. L. C., Dawson, M., Dyrby, T. B., Krug, K., Ptito, M., D'Arceuil, H., et al. (2020). Differences in Frontal Network Anatomy Across Primate Species. *J Neurosci*, 40(10), 2094-2107.
- Borne, L., Riviere, D., Mancip, M., & Mangin, J. F. (2020). Automatic labeling of cortical sulci using patch- or CNN-based segmentation techniques combined with bottom-up geometric constraints. *Med Image Anal*, 62, 101651.
- Brun, L., Auzias, G., Viellard, M., Villeneuve, N., Girard, N., Poinso, F., et al. (2016). Localized Misfolding Within Broca's Area as a Distinctive Feature of Autistic Disorder. *Biol Psychiatry Cogn Neurosci Neuroimaging*, 1(2), 160-168.
- Chi, J. G., Dooling, E. C., & Gilles, F. H. (1977). Gyral development of the human brain. *Ann Neurol*, 1(1), 86-93.
- Coalson, T. S., Van Essen, D. C., & Glasser, M. F. (2018). The impact of traditional neuroimaging methods on the spatial localization of cortical areas. *Proc Natl Acad Sci U S A*, 115(27), E6356-E6365.
- Connolly, C. (1950). *External Morphology of the Primate Brain*. Springfield.
- Crick, F., & Jones, E. (1993). Backwardness of human neuroanatomy. *Nature*, 361, 109-110.
- Croxson, P. L., Johansen-Berg, H., Behrens, T. E., Robson, M. D., Pinski, M. A., Gross, C. G., et al. (2005). Quantitative investigation of connections of the prefrontal cortex in the human and macaque using probabilistic diffusion tractography. *J Neurosci*, 25(39), 8854-8866.
- Cunningham, D. J. (1892). *Contribution to the surface anatomy of the cerebral hemispheres*. Dublin: Academy House.
- Dale, A. M., Fischl, B., & Sereno, M. I. (1999). Cortical surface-based analysis. I. Segmentation and surface reconstruction. *Neuroimage*, 9(2), 179-194.

- Demirtas, M., Burt, J. B., Helmer, M., Ji, J. L., Adkinson, B. D., Glasser, M. F., et al. (2019). Hierarchical Heterogeneity across Human Cortex Shapes Large-Scale Neural Dynamics. *Neuron*, 101(6), 1181-1194 e1113.
- Donahue, C. J., Glasser, M. F., Preuss, T. M., Rilling, J. K., & Van Essen, D. C. (2018). Quantitative assessment of prefrontal cortex in humans relative to nonhuman primates. *Proc Natl Acad Sci U S A*.
- Eickhoff, S. B., Yeo, B. T. T., & Genon, S. (2018). Imaging-based parcellations of the human brain. *Nat Rev Neurosci*, 19(11), 672-686.
- Ellis, C. T., & Turk-Browne, N. B. (2018). Infant fMRI: A Model System for Cognitive Neuroscience. *Trends Cogn Sci*, 22(5), 375-387.
- Fischl, B., Sereno, M. I., & Dale, A. M. (1999). Cortical surface-based analysis. II: Inflation, flattening, and a surface-based coordinate system. *Neuroimage*, 9(2), 195-207.
- Fischl, B., Sereno, M. I., Tootell, R. B. H., & Dale, A. M. (1999). High-Resolution Intersubject Averaging and a Coordinate System for the Cortical Surface. *Human Brain Mapping*, 8, 272-284.
- Fisher, A. J., Medaglia, J. D., & Jeronimus, B. F. (2018). Lack of group-to-individual generalizability is a threat to human subjects research. *Proc Natl Acad Sci U S A*, 115(27), E6106-E6115.
- Garcia, K. E., Robinson, E. C., Alexopoulos, D., Dierker, D. L., Glasser, M. F., Coalson, T. S., et al. (2018). Dynamic patterns of cortical expansion during folding of the preterm human brain. *Proc Natl Acad Sci U S A*, 115(12), 3156-3161.
- Garcia-Cabezas, M. A., Zikopoulos, B., & Barbas, H. (2019). The Structural Model: a theory linking connections, plasticity, pathology, development and evolution of the cerebral cortex. *Brain Struct Funct*.
- Garrison, J. R., Fernyhough, C., McCarthy-Jones, S., Haggard, M., Australian Schizophrenia Research, B., & Simons, J. S. (2015). Paracingulate sulcus morphology is associated with hallucinations in the human brain. *Nat Commun*, 6, 8956.
- Glasser, M. F., Coalson, T. S., Robinson, E. C., Hacker, C. D., Harwell, J., Yacoub, E., et al. (2016). A multi-modal parcellation of human cerebral cortex. *Nature*, 536(7615), 171-178.
- Glasser, M. F., Sotiropoulos, S. N., Wilson, J. A., Coalson, T. S., Fischl, B., Andersson, J. L., et al. (2013). The minimal preprocessing pipelines for the Human Connectome Project. *Neuroimage*, 80, 105-124.
- Goldman-Rakic, P. S. (1995). Cellular Basis of Working Memory. *Neuron*, 14, 477-485.
- Gordon, E. M., Laumann, T. O., Gilmore, A. W., Newbold, D. J., Greene, D. J., Berg, J. J., et al. (2017). Precision Functional Mapping of Individual Human Brains. *Neuron*.
- Goulas, A., Uylings, H. B., & Stiers, P. (2012). Unravelling the intrinsic functional organization of the human lateral frontal cortex: a parcellation scheme based on resting state fMRI. *J Neurosci*, 32(30), 10238-10252.
- Grill-Spector, K., & Weiner, K. S. (2014). The functional architecture of the ventral temporal cortex and its role in categorization. *Nat Rev Neurosci*, 15(8), 536-548.
- Henssen, A., Zilles, K., Palomero-Gallagher, N., Schleicher, A., Mohlberg, H., Gerboga, F., et al. (2016). Cytoarchitecture and probability maps of the human medial orbitofrontal cortex. *Cortex*, 75, 87-112.
- Hopkins, W. D., Li, X., Crow, T., & Roberts, N. (2017). Vertex- and atlas-based comparisons in measures of cortical thickness, gyrification and white matter volume between humans and chimpanzees. *Brain Struct Funct*, 222(1), 229-245.
- Keller, S. S., Roberts, N., & Hopkins, W. (2009). A comparative magnetic resonance imaging study of the anatomy, variability, and asymmetry of Broca's area in the human and chimpanzee brain. *J Neurosci*, 29(46), 14607-14616.
- Klein, A., Ghosh, S. S., Bao, F. S., Giard, J., Hame, Y., Stavsky, E., et al. (2017). Mindboggling morphometry of human brains. *PLoS Comput Biol*, 13(2), e1005350.
- Koechlin, E., Ody, C., & Kouneiher, F. (2003). The architecture of cognitive control in the human prefrontal cortex. *Science*, 302(5648), 1181-1185.

- Koechlin, E., & Summerfield, C. (2007). An information theoretical approach to prefrontal executive function. *Trends Cogn Sci*, 11(6), 229-235.
- Kong, R., Li, J., Orban, C., Sabuncu, M. R., Liu, H., Schaefer, A., et al. (2018). Spatial Topography of Individual-Specific Cortical Networks Predicts Human Cognition, Personality, and Emotion. *Cereb Cortex*.
- Lopez-Persem, A., Verhagen, L., Amiez, C., Petrides, M., & Sallet, J. (2019). The Human Ventromedial Prefrontal Cortex: Sulcal Morphology and Its Influence on Functional Organization. *J Neurosci*, 39(19), 3627-3639.
- Lorenz, S., Weiner, K. S., Caspers, J., Mohlberg, H., Schleicher, A., Bludau, S., et al. (2017). Two New Cytoarchitectonic Areas on the Human Mid-Fusiform Gyrus. *Cereb Cortex*, 27(1), 373-385.
- Lyu, I., Bao, S., Hao, L., Yao, J., Miller, J. A., Voorhies, W., et al. (2020). Labeling Lateral Prefrontal Sulci using Spherical Data Augmentation and Context-aware Training. *Neuroimage (in revision)*.
- Miller, D. J., Duka, T., Stimpson, C. D., Schapiro, S. J., Baze, W. B., McArthur, M. J., et al. (2012). Prolonged myelination in human neocortical evolution. *Proc Natl Acad Sci U S A*, 109(41), 16480-16485.
- Miller, E. K., & Cohen, J. D. (2001). AN INTEGRATIVE THEORY OF PREFRONTAL CORTEX FUNCTION. *Annu Rev Neurosci*, 24, 167-202.
- Miller, J. A., Voorhies, W., Lurie, D. J., D'Esposito, M., & Weiner, K. S. (2021). Overlooked tertiary sulci serve as a meso-scale link between microstructural and functional properties of human lateral prefrontal cortex. *The Journal of Neuroscience*.
- Miller, J. A., Voorhies, W. I., Li, X., Raghuram, I., Palomero-Gallagher, N., Zilles, K., et al. (2020). Sulcal morphology of ventral temporal cortex is shared between humans and other hominoids. *Sci Rep*, 10(1), 17132.
- Nee, D. E. (2020). Integrative Frontal-Parietal Dynamics Supporting Cognitive Control. *bioRxiv*.
- Nee, D. E., & D'Esposito, M. (2016). The hierarchical organization of the lateral prefrontal cortex. *eLife*, 5.
- Parker, B. J., Voorhies, W., Gomez, J., Jiahui, G., Furl, N., Garrido, L., et al. (2020). On the Role of Tertiary Sulci in Developmental Prosopagnosia. *The FASEB Journal*, 34(S1), 1-1.
- Parvizi, J., Jacques, C., Foster, B. L., Witthoft, N., Rangarajan, V., Weiner, K. S., et al. (2012). Electrical stimulation of human fusiform face-selective regions distorts face perception. *J Neurosci*, 32(43), 14915-14920.
- Paus, T., Otaky, N., Caramanos, Z., Macdonald, D., Zijdenbos, A., D'Avirro, D., et al. (1996). In Vivo Morphometry of the Intrasulcal Gray Matter in the Human Cingulate, Paracingulate, and Superior-Rostral Sulci: Hemispheric Asymmetries, Gender Differences and Probability Maps. *The Journal of Comparative Neurology*, 376, 664-673.
- Petrides, M. (2005). Lateral prefrontal cortex: architectonic and functional organization. *Philos Trans R Soc Lond B Biol Sci*, 360(1456), 781-795.
- Petrides, M. (2019). *Atlas of the Morphology of the Human Cerebral Cortex on the Average MNI Brain* (1 ed.). London, UK: Elsevier.
- Petrides, M., & Pandya, D. N. (1999). Dorsolateral prefrontal cortex: comparative cytoarchitectonic analysis in the human and the macaque brain and corticocortical connection patterns. *Eur J Neurosci*, 11, 1101-1036.
- Petrides, M., & Pandya, D. N. (2012). The-Frontal-Cortex. In J. Mai & G. Paxinos (Eds.), *The Human Nervous System* (pp. 988-1011): Elsevier.
- Petrides, M., Tomaiuolo, F., Yeterian, E. H., & Pandya, D. N. (2012). The prefrontal cortex: comparative architectonic organization in the human and the macaque monkey brains. *Cortex*, 48(1), 46-57.
- Picton, T. W., Stuss, D. T., Shallice, T., Alexander, M. P., & Gillingham, S. (2006). Keeping time: effects of focal frontal lesions. *Neuropsychologia*, 44(7), 1195-1209.
- Rajkowska, G., & Goldman-Rakic, P. S. (1995a). Cytoarchitectonic definition of prefrontal areas in the normal human cortex: I. Remapping of areas 9 and 46 using quantitative criteria. *Cereb Cortex*, 5(4), 307-322.

- Rajkowska, G., & Goldman-Rakic, P. S. (1995b). Cytoarchitectonic Definition of Prefrontal areas in the Normal Human Cortex: II. Variability in Locations of Areas 9 and 46 and Relationship to the Talairach Coordinate System. *Cereb Cortex*, 5.
- Rangarajan, V., Hermes, D., Foster, B. L., Weiner, K. S., Jacques, C., Grill-Spector, K., et al. (2014). Electrical stimulation of the left and right human fusiform gyrus causes different effects in conscious face perception. *J Neurosci*, 34(38), 12828-12836.
- Reid, A. T., Bzdok, D., Langner, R., Fox, P. T., Laird, A. R., Amunts, K., et al. (2016). Multimodal connectivity mapping of the human left anterior and posterior lateral prefrontal cortex. *Brain Struct Funct*, 221(5), 2589-2605.
- Retzius, G. (1896). *Das Menschenhirn*. Stockholm, Sweden: Norstedt and Soener.
- Reveley, C., Seth, A. K., Pierpaoli, C., Silva, A. C., Yu, D., Saunders, R. C., et al. (2015). Superficial white matter fiber systems impede detection of long-range cortical connections in diffusion MR tractography. *Proc Natl Acad Sci U S A*, 112(21), E2820-2828.
- Sallet, J., Mars, R. B., Noonan, M. P., Neubert, F. X., Jbabdi, S., O'Reilly, J. X., et al. (2013). The organization of dorsal frontal cortex in humans and macaques. *J Neurosci*, 33(30), 12255-12274.
- Sanides, F. (1962). Die Architektur Des Menschlichen Stirnhirns Zugleich Eine Darstellung Der Prin. In M. Muller, H. Spatz & P. Vogel (Eds.), *Monographien aus dem Gesamtgebiete der Neurologie und Psychiatrie* (Vol. 98, pp. 176-190). Berlin: Springer Berlin Heidelberg.
- Sanides, F. (1964). STRUCTURE AND FUNCTION OF THE HUMAN FRONTAL LOBE. *Neuropsychologia*, 2, 209-219.
- Schilling, K., Gao, Y., Janve, V., Stepniewska, I., Landman, B. A., & Anderson, A. W. (2018). Confirmation of a gyral bias in diffusion MRI fiber tractography. *Hum Brain Mapp*, 39(3), 1449-1466.
- Schrouff, J., Raccach, O., Baek, S., Rangarajan, V., Salehi, S., Mourao-Miranda, J., et al. (2020). Fast temporal dynamics and causal relevance of face processing in the human temporal cortex. *Nat Commun*, 11(1), 656.
- Seitzman, B. A., Gratton, C., Laumann, T. O., Gordon, E. M., Adeyemo, B., Dworesky, A., et al. (2019). Trait-like variants in human functional brain networks. *Proc Natl Acad Sci U S A*, 116(45), 22851-22861.
- Stuss, D. T. (2011). Functions of the frontal lobes: relation to executive functions. *J Int Neuropsychol Soc*, 17(5), 759-765.
- Stuss, D. T. (2016). A career of harnessing group variability. *Can J Exp Psychol*, 70(4), 279-287.
- Stuss, D. T., & Alexander, M. P. (2000). Executive functions and the frontal lobes: a conceptual view. *Psychol Res*, 63, 289-298.
- Stuss, D. T., Alexander, M. P., Shallice, T., Picton, T. W., Binns, M. A., Macdonald, R., et al. (2005). Multiple frontal systems controlling response speed. *Neuropsychologia*, 43(3), 396-417.
- Stuss, D. T., & Benson, D. F. (1984). Neuropsychological Studies of the Frontal Lobes. *Psychological Bulletin*, 95(1), 3-28.
- Stuss, D. T., & Knight, R. T. (2012). *Principles of Frontal Lobe Function* (2 ed.). Oxford: Oxford University Press.
- Stuss, D. T., & Levine, B. (2002). Adult clinical neuropsychology: lessons from studies of the frontal lobes. *Annu Rev Psychol*, 53, 401-433.
- Turner, O. A. (1948). Growth and development of the cerebral cortical pattern in man. *Arch Neurol Psychiatry*, 59(1).
- Van Essen, D. C., Donahue, C. J., Coalson, T. S., Kennedy, H., Hayashi, T., & Glasser, M. F. (2019). Cerebral cortical folding, parcellation, and connectivity in humans, nonhuman primates, and mice. *Proc Natl Acad Sci U S A*.
- Van Essen, D. C., Jbabdi, S., Sotiropoulos, S. N., Chen, C., Dikranian, K., Coalson, T. S., et al. (2014). Mapping Connections in Humans and Non-Human Primates. In *Diffusion MRI* (pp. 337-358).
- Vogt, C., & Vogt, O. (1919). Allgemeinerere ergebnisse unserer hirnforschung. *J. Psychol. Neurol.*, 25, 279-462.

- Voorhies, W., Miller, J. A., Yao, J., Bunge, S. A., & Weiner, K. S. (2020). Cognitive insights from evolutionarily new brain structures in prefrontal cortex. *bioRxiv*.
- Weiner, K. S. (2019). The Mid-Fusiform Sulcus (sulcus sagittalis gyri fusiformis). *Anat Rec (Hoboken)*, 302(9), 1491-1503.
- Weiner, K. S., Golarai, G., Caspers, J., Chuapoco, M. R., Mohlberg, H., Zilles, K., et al. (2014). The mid-fusiform sulcus: a landmark identifying both cytoarchitectonic and functional divisions of human ventral temporal cortex. *Neuroimage*, 84, 453-465.
- Weiner, K. S., Natu, V. S., & Grill-Spector, K. (2018). On object selectivity and the anatomy of the human fusiform gyrus. *Neuroimage*, 173, 604-609.
- Weiner, K. S., & Zilles, K. (2016). The anatomical and functional specialization of the fusiform gyrus. *Neuropsychologia*, 83, 48-62.
- Welker, W. (1990). Why does cerebral cortex fissure and fold? A review of determinants of gyri and sulci. In A. Peters & E. G. Jones (Eds.), (pp. 3-136). New York: Plenum Press.
- Zilles, K., Palomero-Gallagher, N., & Amunts, K. (2013). Development of cortical folding during evolution and ontogeny. *Trends Neurosci*, 36(5), 275-284.