< Accepted Version >

Title

Individual differences, missing sulci, and nomenclature: A comment on “On presentation of the human cerebral sulci from inside the cerebrum”

Authors and affiliations

Ethan H. Willbrand[1,2], Benjamin J. Parker[1], Kevin S. Weiner[1,2]

[1]Helen Wills Neuroscience Institute, [2]Department of Psychology, University of California, Berkeley, Berkeley, CA, USA

Corresponding author: Kevin S. Weiner (kweiner@berkeley.edu)

Conflict of Interest: The authors declare no competing financial interests.

Acknowledgments: This letter was supported by NSF CAREER Award 2042251.

Text

Nowinski (2023) proposes a methodology and brain atlas utilizing the inner cortical surface to visualize human cerebral sulci in three dimensions, which allows improved visualization of sulcal relationships. For example, sulci located on the medial portion of the brain can be viewed simultaneously relative to sulci located on the lateral surface of the brain. This is in contrast to most software packages and brain atlases that require separate views of the brain to visualize sulci on the medial and lateral surfaces (Figure 1). Given that sulcal morphology has cognitive and clinical implications (Cachia *et al.*, 2021), this atlas and tool together show promise to have “educational value” as proposed by Nowinski (2023). Nevertheless, in this Letter, we highlight that the present work is also limited in that it (i) overlooks individual differences in cortical folds, (ii) is missing sulci, and (iii) only includes one sulcal nomenclature.

First, in terms of individual differences of cortical folds, prominent sulci that are often depicted as one long, deep structure in atlases can be broken up into variable “complexes” in an individual hemisphere in which this variability is functionally meaningful. Complexes refers to the fact that annectant gyri, or *pli de passage*, “break up” the sulcus into multiple pieces (Mangin *et al.*, 2019). Often, this morphological variability is related to individual differences in functional brain organization and/or cognitive performance. For example, while the long, deep, and prominent central sulcus (CS) is shown as a single, continuous cortical fold in the present work, it can be separated into as many as five separate segments in a given hemisphere based on the presence of buried gyri (Eichert *et al.*, 2021). This variability across individuals corresponds with variability in functional organization related to motor movement (Germann *et al.*, 2020). The relationship between variability in sulcal morphology and individual differences in functional

organization is not specific to the CS but also extends to other sulci: the pre- (PRCS) and post-central (POCS) sulci (Zlatkina, Amiez and Petrides, 2016; Germann and Petrides, 2020) and superior frontal sulcus (SFS; Amiez and Petrides, 2018) are just three additional examples due to space limitations of this Letter (Figure 1A).

Second, if the present atlas is to be used as an educational tool, readers and students should be aware that this example brain is missing sulci. That is, not every sulcus is present in every hemisphere. Though many variable sulci excluded in the present work are small and shallow (outlined in Figure 1), which are not the focus of the present work, some are prominent. For example, the paracingulate sulcus (PCGS) is absent in the proposed educational tool/atlas. The PCGS is a prominent longitudinal sulcus parallel to the cingulate sulcus (CGS; Figure 1B) that is identifiable in ~70% of hemispheres (Amiez *et al.*, 2021). The presence of the PCGS is cytoarchitecturally, functionally, cognitively, and clinically relevant, as well as is a hominoid-specific structure (Amiez and Petrides, 2014; Amiez *et al.*, 2021; Cachia *et al.*, 2021).

Third, it is important for readers of the journal who may be unfamiliar with brain anatomy and students who may use this atlas to be aware that there are many names for the same sulcus or gyrus. This issue stems all the way back to one of the first atlases to begin to collate the many names proposed by different anatomists (Ecker, 1869) and is an issue that continues to the present day (Weiner and Zilles, 2016; ten Donkelaar *et al.*, 2018; Willbrand *et al.*, 2022). One such example is the “superior occipital sulcus” labeled in the present work that is now commonly referred to as the paroccipital sulcus (Petrides, 2019), which was labeled as such by Wilder (1886).

Of course, the three issues raised in this Letter are not only relevant for providing the most accurate research tools for educating future neuroanatomists, but also for future neurosurgeons as sulci are used as “corridors,” or entry points, in neurosurgery (Ribas *et al.*, 2006; Tomaiuolo and Giordano, 2016). Finally, these three issues are not limited to the present work and reflect ongoing issues in the broader neuroanatomical field that require further discussions among neuroanatomists moving forward.

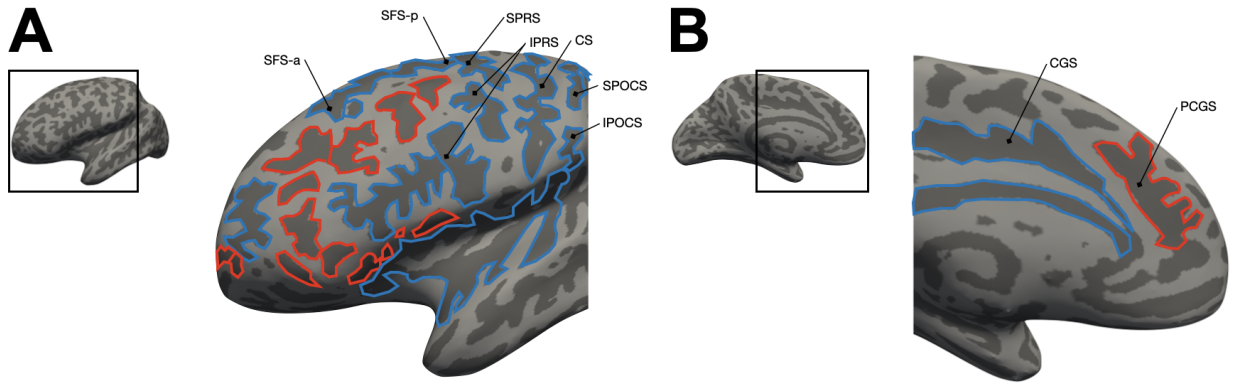

Figure 1. Visualizing sulci on the outer (lateral) and inner (medial) surface of the cerebral cortex, but what about missing sulci?

A. Left hemisphere FreeSurfer *inflated* cortical reconstruction (gyri: light gray, sulci: dark gray) from an example Human Connectome Project participant (neuroimaging data from https://db.humanconnectome.org/) focused on the lateral prefrontal cortex (LPFC; inset for the location of the zoomed portion). LPFC sulci have been manually defined (outlined) based on the most recent atlas (Petrides, 2019) and published previously in this individual (Miller *et al.*, 2021; Willbrand *et al.*, 2023). Red sulci are those excluded from the present tool, whereas blue sulci are those included. **B.** Same format as A, but for a medial PFC view. Note that two separate views are necessary to visualize sulci on the lateral and medial sides of the cerebral cortex in FreeSurfer, while Nowinski's method allows the visualization of both simultaneously. Nevertheless, as an educational tool, this atlas does not address individual differences in prominent sulci such as the central sulcus (CS), precentral sulcus (PRS), postcentral sulcus (POCS), and superior frontal sulcus (SFS; see text), or the fact that some sulci can be present in one hemisphere and not in another—even in the same individual. For example, only ~70% of hemispheres have a present or prominent paracingulate sulcus (PCGS; red) that is located above the cingulate sulcus (CGS; blue; Amiez *et al.*, 2021).

References

Amiez, C. *et al.* (2021) 'Chimpanzee histology and functional brain imaging show that the paracingulate sulcus is not human-specific', *Communications biology*, 4(1), p. 54. Available at: https://doi.org/10.1038/s42003-020-01571-3.

Amiez, C. and Petrides, M. (2014) 'Neuroimaging evidence of the anatomo-functional organization of the human cingulate motor areas', *Cerebral cortex* , 24(3), pp. 563–578. Available at: https://doi.org/10.1093/cercor/bhs329.

Amiez, C. and Petrides, M. (2018) 'Functional rostro-caudal gradient in the human posterior lateral frontal cortex', *Brain structure & function*, 223(3), pp. 1487–1499. Available at: https://doi.org/10.1007/s00429-017-1567-z.

Cachia, A. *et al.* (2021) 'Towards Deciphering the Fetal Foundation of Normal Cognition and Cognitive Symptoms From Sulcation of the Cortex', *Frontiers in neuroanatomy*, 15, p. 712862. Available at: https://doi.org/10.3389/fnana.2021.712862.

ten Donkelaar, H.J.T. *et al.* (2018) 'Toward a Common Terminology for the Gyri and Sulci of the Human Cerebral Cortex', *Frontiers in Neuroanatomy*. Available at: https://doi.org/10.3389/fnana.2018.00093.

Ecker, A. (1869) *Die Hirnwindungen des Menschen*. Braunschweig: F. Vieweg u. Sohn.

Eichert, N. *et al.* (2021) 'Morphological and functional variability in central and subcentral motor cortex of the human brain', *Brain structure & function*, 226(1), pp. 263–279. Available at: https://doi.org/10.1007/s00429-020-02180-w.

Germann, J. *et al.* (2020) 'Tight Coupling between Morphological Features of the Central Sulcus and Somatomotor Body Representations: A Combined Anatomical and Functional MRI Study', *Cerebral cortex* , 30(3), pp. 1843–1854. Available at: https://doi.org/10.1093/cercor/bhz208.

Germann, J. and Petrides, M. (2020) 'Area 8A within the Posterior Middle Frontal Gyrus Underlies Cognitive Selection between Competing Visual Targets', *eNeuro*, 7(5). Available at: https://doi.org/10.1523/ENEURO.0102-20.2020.

Mangin, J.-F. *et al.* (2019) '"Plis de passage" Deserve a Role in Models of the Cortical Folding Process', *Brain topography*, 32(6), pp. 1035–1048. Available at: https://doi.org/10.1007/s10548-019-00734-8.

Miller, J.A. *et al.* (2021) 'Overlooked Tertiary Sulci Serve as a Meso-Scale Link between Microstructural and Functional Properties of Human Lateral Prefrontal Cortex', *The Journal of neuroscience: the official journal of the Society for Neuroscience*, 41(10), pp. 2229–2244. Available at: https://doi.org/10.1523/JNEUROSCI.2362-20.2021.

Nowinski, W.L. (2023) 'On presentation of the human cerebral sulci from inside of the cerebrum', *Journal of anatomy* [Preprint]. Available at: https://doi.org/10.1111/joa.13880.

Petrides, M. (2019) *Atlas of the Morphology of the Human Cerebral Cortex on the Average MNI Brain*. Academic Press. Available at: https://play.google.com/store/books/details?id=qeWcBAAAQBAJ.

Ribas, G.C. *et al.* (2006) 'Surgical anatomy of microneurosurgical sulcal key points', *Neurosurgery*, 59(4 Suppl 2), pp. ONS177–210; discussion ONS210–1. Available at: https://doi.org/10.1227/01.NEU.0000240682.28616.b2.

Tomaiuolo, F. and Giordano, F. (2016) 'Cerebal sulci and gyri are intrinsic landmarks for brain navigation in individual subjects: an instrument to assist neurosurgeons in preserving cognitive function in brain tumour surgery (Commentary on Zlatkina et al.)', *The European journal of neuroscience*, pp. 1266–1267. Available at: https://doi.org/10.1111/ejn.13072.

Weiner, K.S. and Zilles, K. (2016) 'The anatomical and functional specialization of the fusiform gyrus', *Neuropsychologia*, 83, pp. 48–62. Available at: https://doi.org/10.1016/j.neuropsychologia.2015.06.033.

Wilder, B.G. (1886) *Human Cerebral Fissures: Their Relations and Names and the Methods of Studying Them*. Press of McCalla & Stavely, Phil.

Willbrand, E.H. *et al.* (2022) 'Uncovering a tripartite landmark in posterior cingulate cortex', *Science Advances*, 8(36), p. eabn9516. Available at: https://doi.org/10.1126/sciadv.abn9516.

Willbrand, E.H. *et al.* (2023) 'Development of Human Lateral Prefrontal Sulcal Morphology and Its Relation to Reasoning Performance', *The Journal of neuroscience: the official journal of the Society for Neuroscience*, 43(14), pp. 2552–2567. Available at: https://doi.org/10.1523/JNEUROSCI.1745-22.2023.

Zlatkina, V., Amiez, C. and Petrides, M. (2016) 'The postcentral sulcal complex and the transverse postcentral sulcus and their relation to sensorimotor functional organization', *The European journal of neuroscience*, 43(10), pp. 1268–1283. Available at: https://doi.org/10.1111/ejn.13049.