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A Manual Segmentation Protocol for Cortical Gyri

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Introduction

This protocol provides a guideline for outlining the superior frontal gyrus (SFG), the supramarginal gyrus (SMG) and the cingulate gyrus (CG). While protocols do exist for these particular gyri, they tend to lack the ability to precisely identify the gyral borders[1].

The guideline is based on a thorough revision of 2 atlases: (1) the Duvernoy atlas[2], a magnetic resonance imaging (MRI) and 3-dimensional sectional anatomical atlas with annotations in the axial, sagittal, and coronal views, and (2) the Ono atlas[3], a single subject anatomical atlas that identifies sulcal patterns and variability. Although highly revered by the brain research community, when used independently, these atlases are incomplete: the first points to gyri but overlooks their demarcation and any mention of anatomical variability; the second focuses on sulcal patterns and variability with limited mention of gyri. By combining the 2 atlases' strengths, however, we have now formed a comprehensive and reliable protocol. It accurately and consistently locates and outlines regions of interest (ROIs), while incorporating the encountered anatomical variations.

While the borders of the 3-dimensional ROIs defined below may not always be anatomically accurate, the protocol clearly and systematically highlights the cut-off slices, or ROI edges. This facilitates and ensures consistency, accuracy, repeatability and reproducibility of manual drawings which serve as the critical ground truth.

For additional support with the segmentation, we have released a dataset[4] of 60 ROIs (SFGs, CGs, and SMGs) derived following this protocol. The ROIs were drawn in both the right and left hemispheres of 10 healthy middle-aged subjects.

Methods

Preparatory Steps

1. For accurate gyral segmentation, it is recommended that all drawings are made on the difference volume 'T1w_bfc-T2w' derived as follows:

1st: the T1 weighted (T1w) MRI volume is bias field corrected (producing output volume T1w_bfc)

2nd: the T2 weighted (T2w) MRI volume is subtracted from the T1w MRI volume, yielding the difference volume 'T1w_bfc - T2w'

The difference volume 'T1w_bfc – T2w' has better grey matter-white matter (GM-WM) contrast than T1w or T2w MRI volumes on their own, making it easier to use for manual gyral segmentation. This volume is used in all figures and instructions from here on.

2. Download and install the latest version of the drawing tool 'MRIcron' along with its user guide from https://www.nitrc.org/projects/mricron. Alternative drawing tools can be used, however this is the one we chose to demonstrate our manual segmentation protocol.

3. Generally speaking, each region of interest (ROI) can be represented by 2 open paired curves, or masks, representing the outer grey matter (GM) and inner white matter (WM) curves (Figure 1). However, due to the folding nature of the cortical surface and the need to accurately represent them and consecutively measure their metrics (e.g., volume, thickness, and surface area), it is essential to break down the curves into as many segments as necessary. For example, consider using separate segments for:

- discontinuities in an ROI, creating one segment per discontinuity. Sample discontinuities can be seen in Figure 1a in cyan, yellow and navy.
- every rise and drop in a gyral fold, particularly when these 2 parts are very close to one another and the voxels of the opposing sides are almost touching (Figure 1a-c).

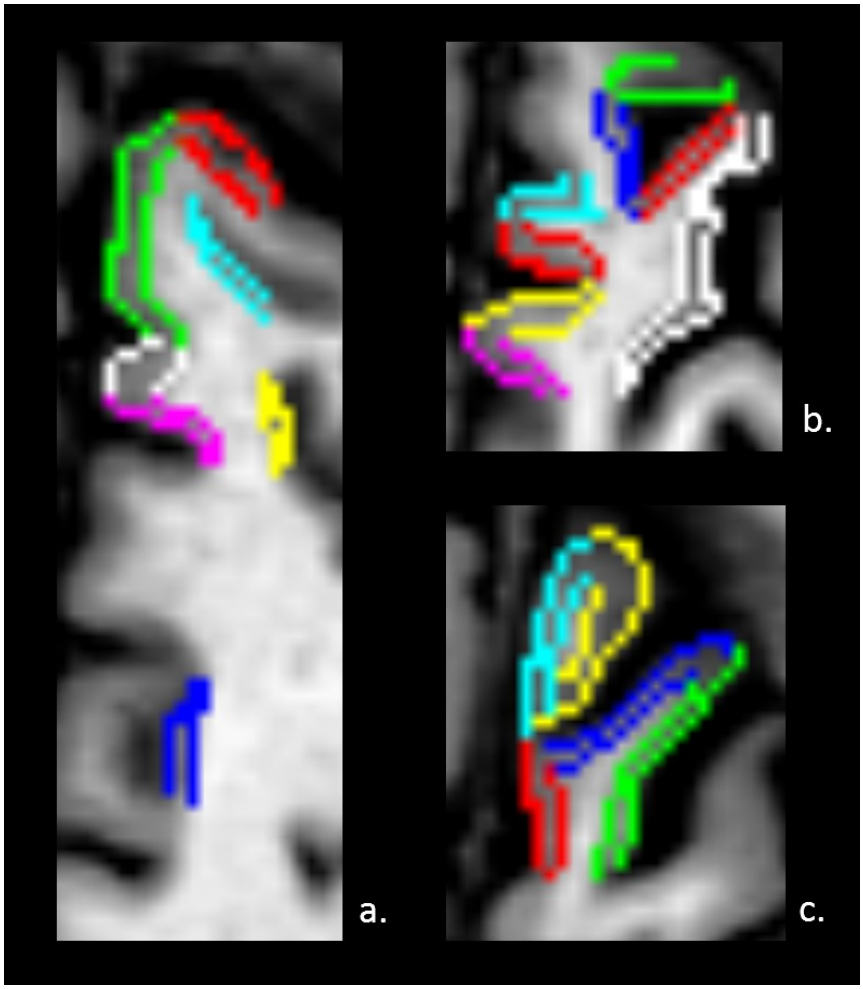

Figure 1. *Examples of segmentation of a single ROI (here SFG) using numerous segments to address discontinuities (a,c) and sharp changes in curvature (a-c). Each of the outer GM curves, or masks, has a corresponding inner WM mask. The paired masks in this figure are represented by the same colour.*

Notes to the User

1. Every GM mask should have a corresponding WM mask, so the number of GM and WM masks is the same. Use nomenclature of the form 'subj#_roi_r/l_gmsegment#.nii' and 'subj#_roi_r/l_wmsegment#.nii' for each GM and WM segment, respectively. For example, the first segment of subject 1's left SFG can be drawn using the paired masks '1_sfg_l_gm1.nii' and '1_sfg_l_wm1.nii'; their second segment can be drawn using '1_sfg_l_gm2.nii' and '1_sfg_l_wm2.nii', and so on.

2. Corresponding GM and WM masks should start and end at the same place, on the respective GM and WM layers, as illustrated in Figure 1.

3. The protocol starts by identifying all bordering aspects (whether anterior, posterior, medial, lateral, superior, inferior, rostral or caudal) of a gyrus, usually sulci, which consequently enables the user to segment the gyrus contained within them. The sulci can be deleted at the end.

4. Start by drawing the GM segments for the entire ROI. Then go back and draw all corresponding WM segments in such a way that their endpoints that would be the intersection of the GM-WM layer with the imaginary normals drawn from the GM endpoints.

5. To avoid unnecessary repetition, from here-on we shall reference pages in the Ono atlas[3] with braces ({ }), and in the Duvernoy atlas[2] with brackets ([ ]).

6. In the event that a bordering sulcus includes side branches ({28-32}), do not include the latter, and limit your segmentation to the main branch, unless otherwise stated.

7. In the event of sulcal interruptions ({17-19}), ensure that all main sulcal segments are drawn. Note the possibility of connections to other sulci ({20-27}) and avoid segmenting the latter.

8. Use as many, yet an equal number of, GM and WM segments or masks as necessary to accommodate for sulcal interruptions, gyral folding, etc.

9. Following segmentation, morphometric tools such as Masks2Metrics[5] (at https://github.com/Edinburgh-Imaging/Masks2Metrics) can be run to derive ROI metrics including gyral volume, gyral thickness, and white matter (WM) surface area.

10. We have made public a sample dataset of ROIs drawn following this protocol[4] which can be accessed for detailed examples. All figures in this protocol are taken from this dataset.

Drawing Instructions for Regions of Interest

Superior Frontal Gyrus (SFG)

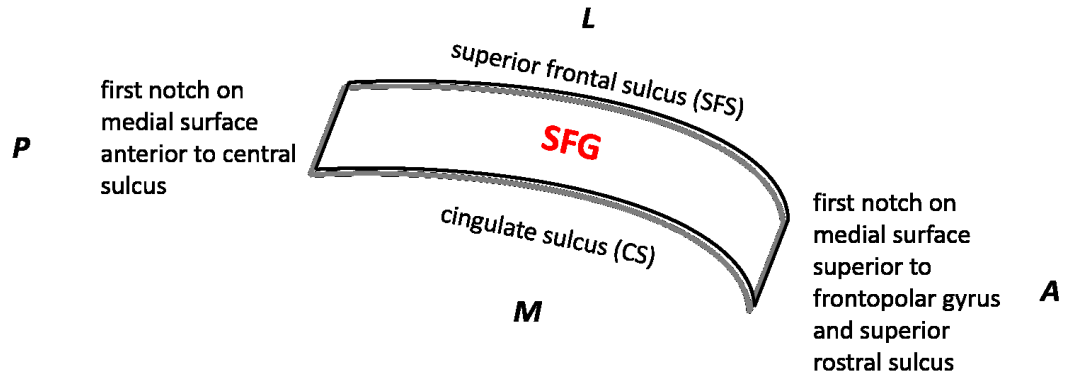

***Figure 2**. Anterior (A), posterior (P), medial (M) and lateral (L) borders of the superior frontal gyrus (SFG).*

The Superior frontal gyrus (SFG, Figure 2) is situated in the superior-most portion of the frontal lobe, and runs in the anteroposterior direction, spreading across both medial and lateral surfaces. The gyrus is to be drawn continuously along the axial direction as follows:

1. Starting at the superior-most axial slices (Figure 3), and traversing the volume in the inferior direction, first identify and demarcate the anterior and lateral borders of the SFG, the superior frontal sulcus (SFS), while roughly guided by sample axial sections indicating the location of this sulcus on pages ([382 (superior-most slice)-428 (inferior-most slice)]). Start at the SFS's superior-most slice and work your way backwards to its inferior-most slice. Refer to ({49-53}) for SFS patterns and variations.

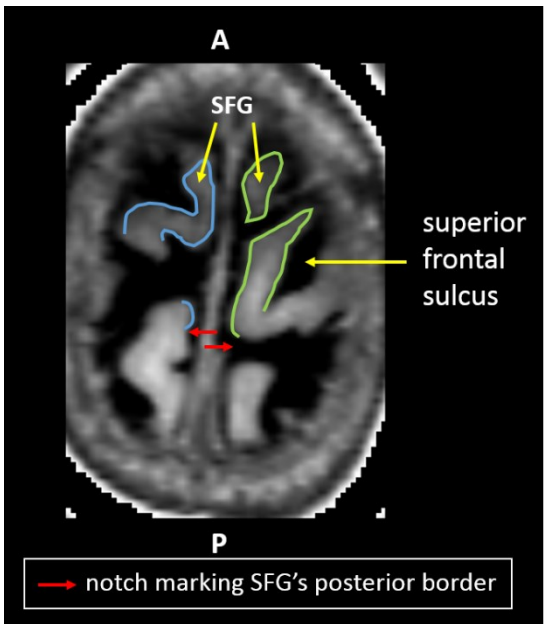

***Figure 3**. Identify the SFG in the superior-most axial slices as the anterior-most gyrus, bound by the SFS laterally.*

2. The SFG's posterior border on the medial surface is unclear and differs from protocol to protocol. To ensure consistency, we propose a fixed and easily identifiable landmark seen in the superior-most axial slices: the first notch or indentation on the medial surface that is anterior to the (superior-most portion of the) central sulcus. Several examples are shown in Figure 4. Identify and mark this

indentation as it will serve as the posterior border on the SFG's medial surface. All the anatomy anterior to it and medial to the SFS belongs to the SFG, with the exception of the cingulate gyrus which may or may not appear in the inferior-most slices. Segment this portion of the SFG in axial view.

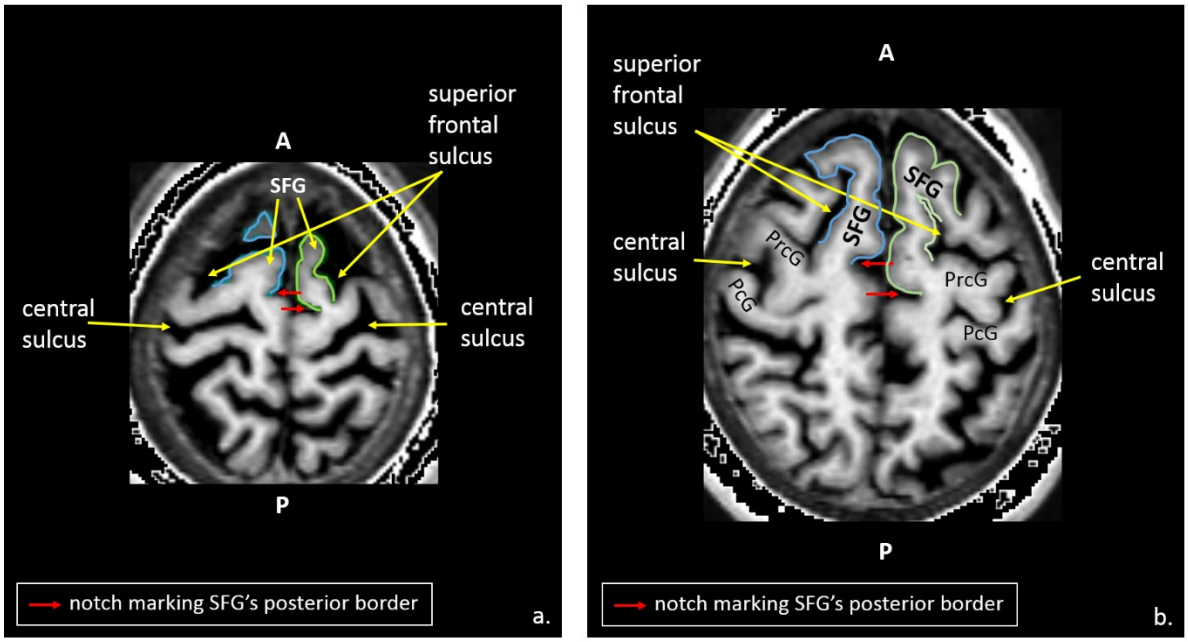

Figure 4. *Segment the SFG in the axial view, while travelling in the inferior direction, and continuing to end it laterally at the superior frontal sulcus, and medially at the notch on the medial surface (red arrow), immediately anterior to the central sulcus. Figure a is more superior than b. PrcG: precentral gyrus, PcG: postcentral gyrus.*

3. Once the indentation identified in step 2 is no longer visible in the axial view when traversing the volume from the superior to inferior direction), the cingulate sulcus (CS, {112-118}) becomes the posterior border of the SFG. Identify and mark this border in the sagittal view, starting from the mid-sagittal and traversing laterally. Ensure that the cingulate gyrus is omitted from the segmentation (Figure 5a). The CS also serves as the SFG's medial border. In the event of a double cingulate sulcus, the superior one is the border; the volume inferior to that belongs to the cingulate gyrus. Now resume posterior SFG segmentation in the axial view using this marked border.

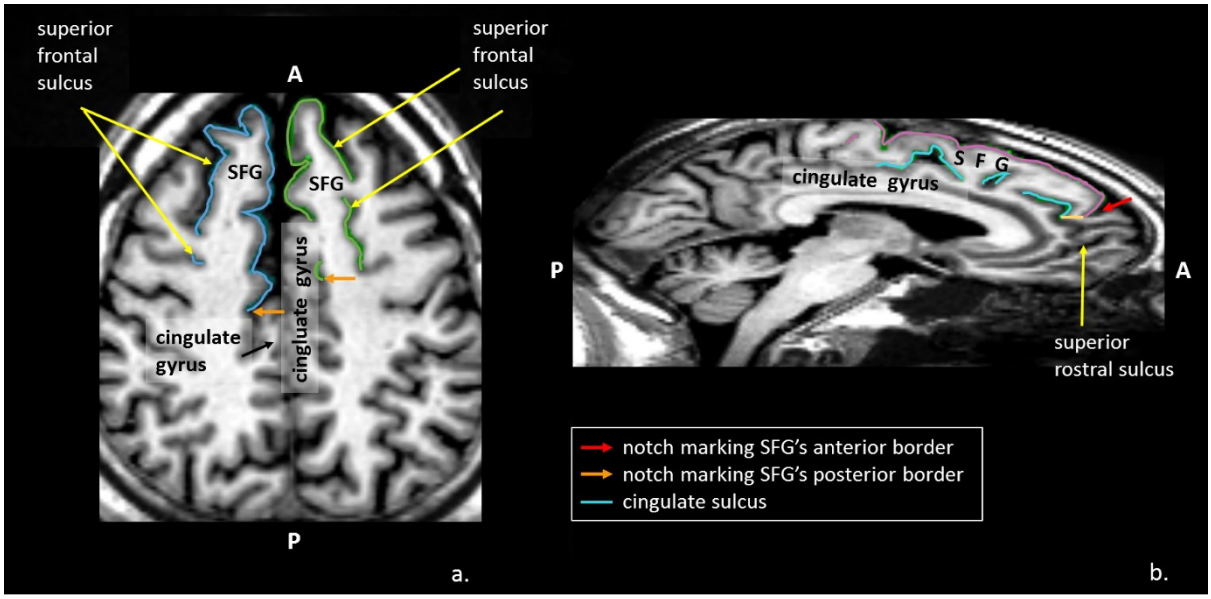

Figure 5. *The SFG in (a) axial and (b) mid-sagittal views, bound by 2 notches (marked in red anteriorly and orange posteriorly), and excluding the cingulate gyrus.*

4. Return to the sagittal view at the brain midline and mark the notch on the cortical surface situated immediately above the superior frontopolar gyrus and superior rostral sulcus, best seen in Figures 5b and 6. This landmark defines the SFG's rostral border at the midline. Proceed with rostral SFG segmentation (with the CS as the posterior border) in axial view, in all slices in which this indentation appears. It is easiest done by starting at the superior-most slice of this notch and ending at its inferior-most slice.

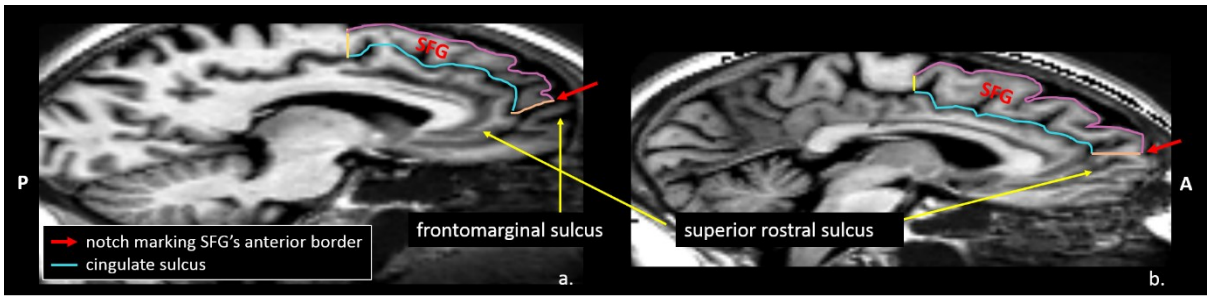

Figure 6. *The SFG's outline in mid-sagittal view for 2 subjects. Anteriorly, it is bound by the notch on the cortical surface superior to the superior rostral sulcus (a,b). Inferiorly, it is bound by the cingulate sulcus, and in the event of the double cingulate sulcus (as in a), the superior one is used.*

5. Now that all SFG borders and extremities have been marked, finalize ROI segmentation (GM and WM) in the axial view, from superior-most to inferior-most slice, by connecting all aspects not yet connected but within the pre-marked borders.

Cingulate Gyrus (CG)

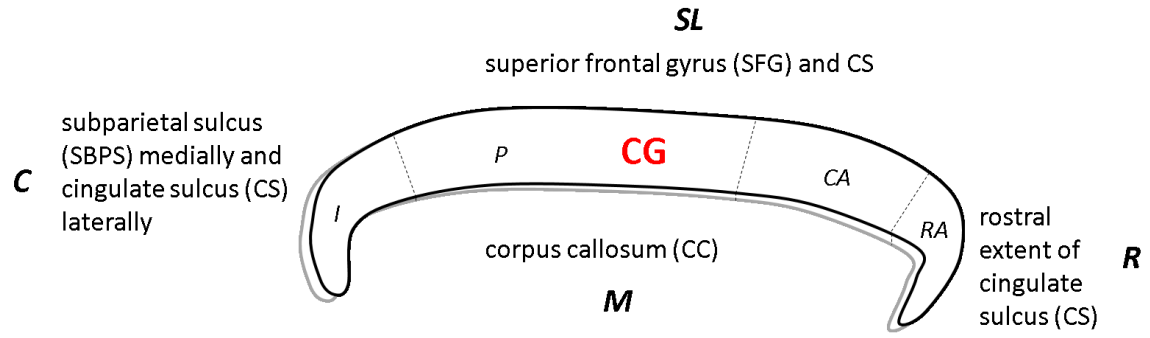

Figure 7. *The CG is situated on the medial surface, inferior to the medial portion of the SFG, and includes the rostral anterior (RA), caudal anterior (CA), posterior (P), and isthmus (I) divisions of the cingulate cortex. It is bound by the cingulate sulcus (CS), subparietal sulcus (SBPS), corpus callosum (CC) and the superior frontal gyrus (SFG). SL: superolateral, R: rostral, C: caudal, M: medial.*

The CG is situated on the medial surface of each hemisphere, inferior to the medial portion of the SFG. It is composed of the rostral anterior (RA), caudal anterior (CA), posterior (P), and isthmus (I) divisions of the cingulate cortex. Some parcellation protocols exclude the isthmus from the CG. It is difficult, however, to identify a landmark that clearly and consistently divides between the posterior and isthmus divisions. The isthmus, on the other hand, has a clear posterior border. For that reason, we include it as part of the CG in our protocol.

Figure 7 highlights all CG boundaries. The rostral boundary is the rostral extent of the CS (inferior to the superior frontal sulcus). The caudal boundary of the CG is the subparietal sulcus (SBPS, {122-123}) medially and the CS ({112-118}) laterally. The inferior boundary is the corpus callosum (CC) while the superolateral boundary is the SFG and CS.

Identify and draw the CG in sagittal view (roughly [310-323]) as follows:

1. Locate the CS and CG at the brain mid-sagittal line, or a few slices laterally from there using ([318-232]). The CG will be situated immediately superior to the corpus callosum and inferior to the SFG. Note the CS patterns and variations highlighted in ({112-118}). The CS may be a double sulcus, as in Figure 8, in which case the superior of the 2 curves marks the CG's superior border. Draw the CG's superior border in sagittal view, from the medial to the lateral direction until lateral boundaries (SFG and/or paracentral lobule) are reached. As mentioned in the 'notes to the user' section, limit the CS to the main segment, excluding any branching or connections.

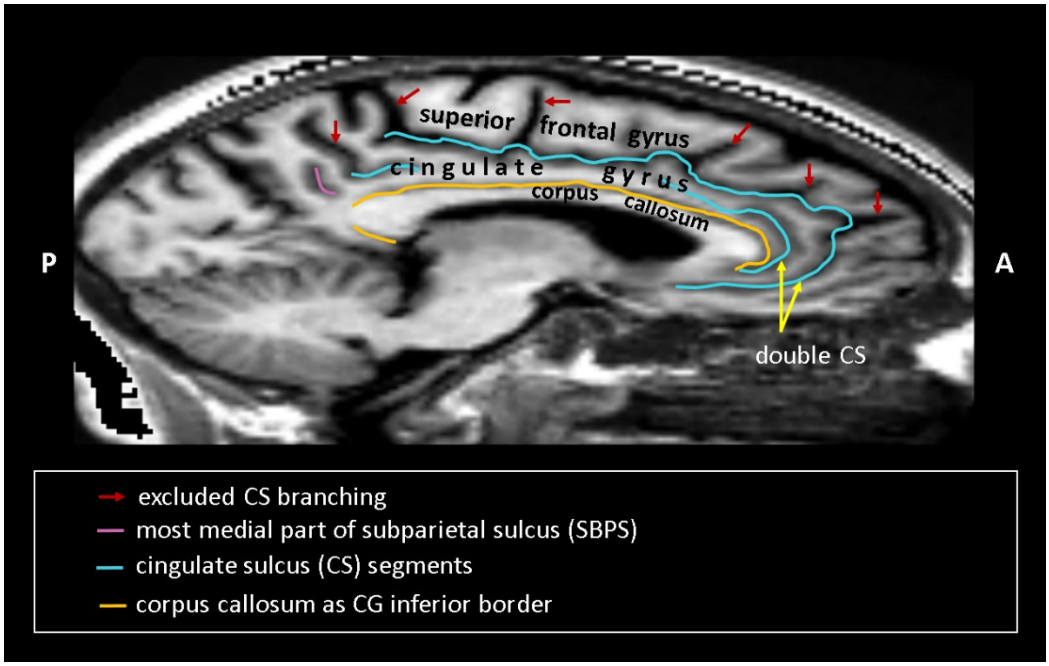

Figure 8. *The CG as seen at the mid-sagittal line, bound by the CS, SFG, corpus callosum and SBPS. This hemisphere has a double CS, in which case the CG is defined by the more superior one.*

2. Starting at the mid-sagittal line and going laterally, identify the SBPS. Mark only the medial-most of its branches in each slice ({122-123}) which will serve as the CG's caudal boundary medially (Figure 9). Continue segmenting in the lateral direction until the SBPS ends. As previously indicated, this sulcus isn't traditionally the boundary of choice in the popular protocols. It is however an easily identifiable landmark that will ensure consistent and repeatable CG segmentation.

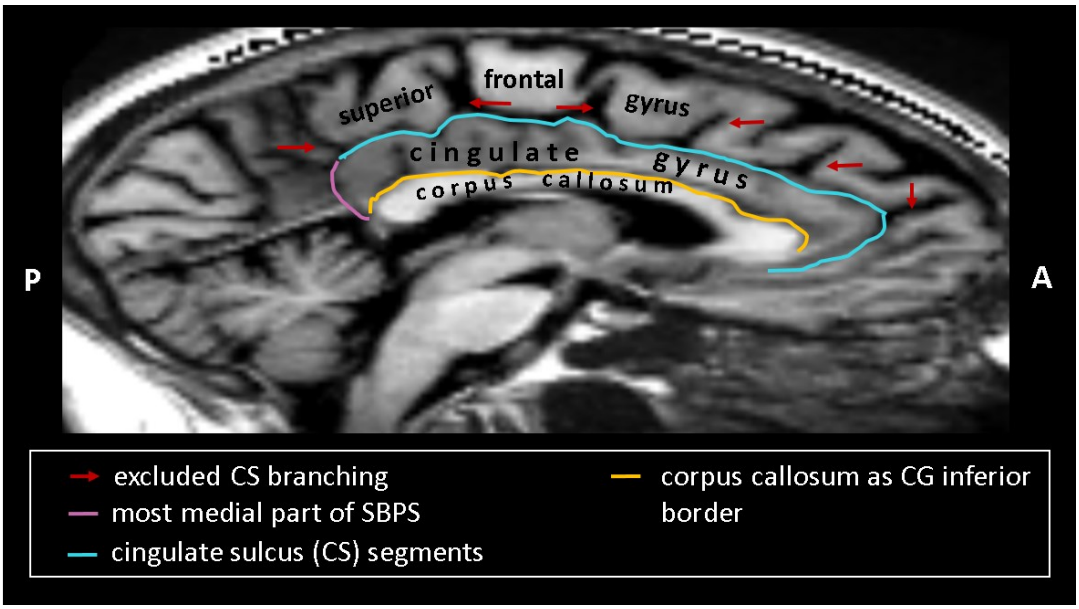

Figure 9. *The caudal border of the CG at the hemisphere's medial end is the medial portion of the SBPS. Superiorly it is bound by the CS and SFG, and medially by the corpus callosum.*

3. Once the SBPS has ended, continue to traverse the sagittal slices in the lateral direction, this time marking the posterior end of the CS as the CG's caudal boundary (Figure 10). Again, as in the first

step, limit the CS to the main segment, and use the superior-most curve in the event of a double sulcus. The CG ends laterally with the end of the CS's main segment.

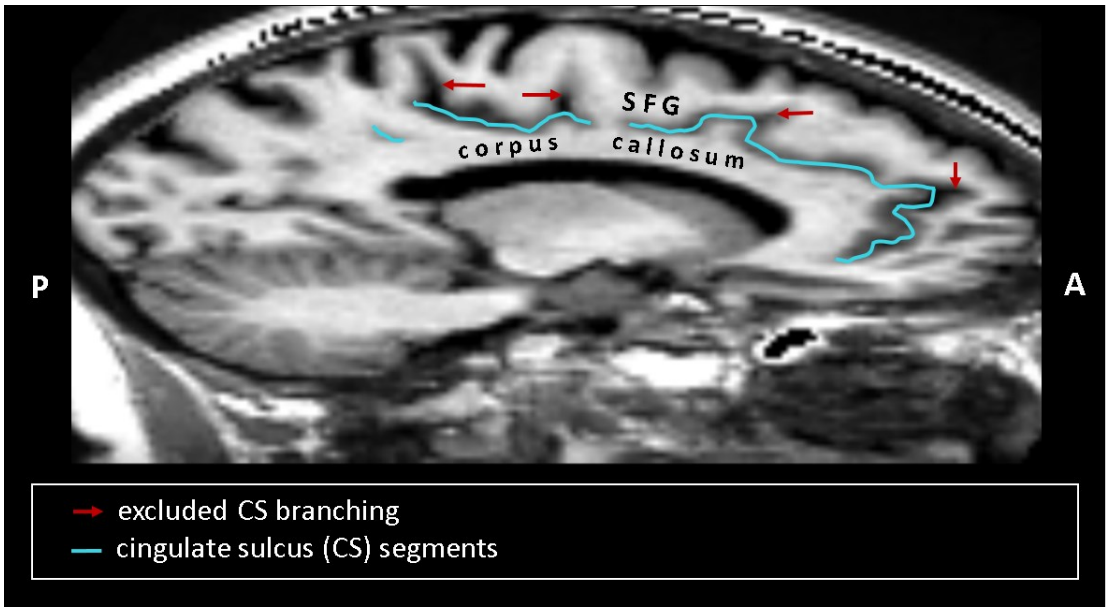

Figure 10. *In the lateral slices where the SBPS does not exist, the CS becomes the CG's caudal boundary.*

4. Identify the CC's superior surface, in all slices marked in the previous 3 steps. This surface sits immediately inferior to the CG making it its inferior border (Figures 8-9). Note that while traversing the volume laterally, the GM on the CG's inferior surface thins at one point and disappears leaving only WM (e.g., Figure 10). In such slices no inferior surface is to be drawn.
5. Now that all borders are marked, draw the CG continuously as the volume situated within them. This should be done in sagittal view, from medial-most to lateral-most slice.

Supramarginal Gyrus (SMG)

The SMG is situated in the parietal lobe and its boundaries are detailed in Figure 11. It is bound anteriorly by the inferior postcentral sulcus (IPS), also referred to as the ascending segment of the intraparietal sulcus ([6-7]). Posteriorly, it is initially (in the most lateral slices) bound by the lateral fissure's posterior end (pLF), and later by the anterior posterior segment of the superior temporal sulcus (apsSTS). The boundary becomes the sulcus intermedius primus (of Jensen), or SIP, more medially when the apsSTS ends. This gyrus is best identified and drawn in the sagittal view, where no cortical anatomy is superior to it. The SMG's inferior cut-off, or boundary, is unclear in popular protocols (Mikhael et al., 2017). To allow for consistent and repeatable segmentation, we have set it to (the imaginary horizontal line drawn in sagittal view at) the superior end of the lateral fissure's middle segment (mLF). In many sagittal slices the SMG's GM will not extend inferiorly to that point, however in the slices where it does, use this imaginary line as the cut-off. A rough guide to the SMG's location in Duvernoy reference atlas is on ([6-7, 10-13, 254-272]).

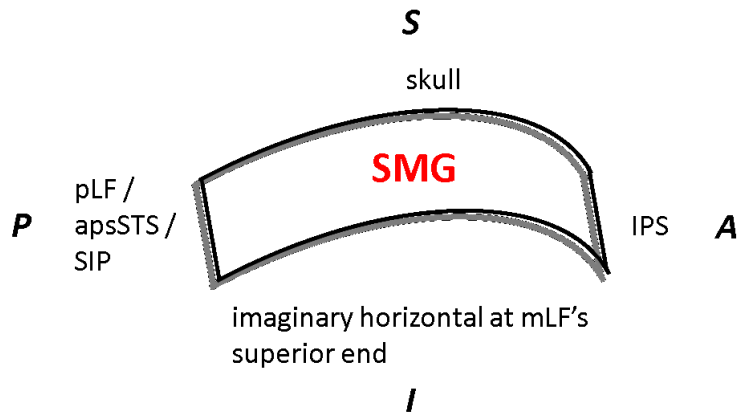

Figure 11. *The anterior (A), superior (S) and inferior (I) boundaries of the SMG do not change, while the posterior (P) boundary changes from pLF, to apsSTS then SIP as the volume is traversed medially in sagittal view.*

1. Starting with the most lateral slices in sagittal view, identify the first few where the lateral fissure's posterior end (pLF) extends superiorly all the way to the end of the cortical surface (towards the skull) cutting it into two ([254-257] and Figure 12a). In these slices, mark the pLF and IPS ({62-66}) which represent the SMG's posterior and anterior borders, respectively. Do not extend the inferior ends of these borders beyond the imaginary horizontal at the mLF's superior tip (i.e, SMG's inferior border).

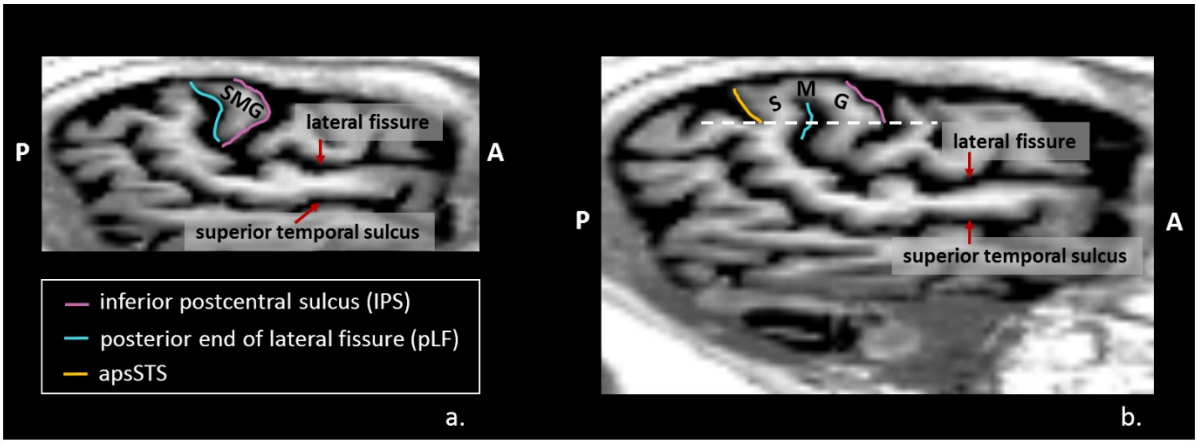

Figure 12. *Sagittal segmentation of the SMG borders. In the first few lateral slices, the SMG is posteriorly bound by the pLF which extends through the cortical surface towards the skull (a). In the following few slices, the SMG stretches over and straddles the pLF, and the apsSTS becomes the new posterior border (b). The SMG's inferior border is either the inferior tip of the apsSTS (yellow) or the mLF's superior end (dotted horizontal line); whichever comes first.*

2. Continuing medially, still in sagittal view, the SMG then straddles the pLF, and its posterior border becomes the apsSTS ([258-261] and Figure 12b). The IPS continues to be the SMG's anterior border. Identify and mark these 2 borders (apsSTS ({75-80}) and IPS) in these slices. Limit them inferiorly to either the inferior tip of the apsSTS or to the area superior to the imaginary horizontal at the mLF's superior end (i.e, SMG's inferior border); whichever comes first.

3. Continuing medially after the apsSTS has ended, identify and mark the SIP ([266-272]) as the SMG's new posterior border and IPS as its anterior border (Figure 13a). The SMG ends at the inferior ends of these borders or at the imaginary horizontal drawn at the mLF's superior end- whichever comes first. Continue to outline the IPS and SIP in sagittal view until the SIP's medial tip is reached which may be easier to identify in axial view (Figure 13b). Once again, the SMG cut-off point in sagittal view is the horizontal at the mLF's superior end.

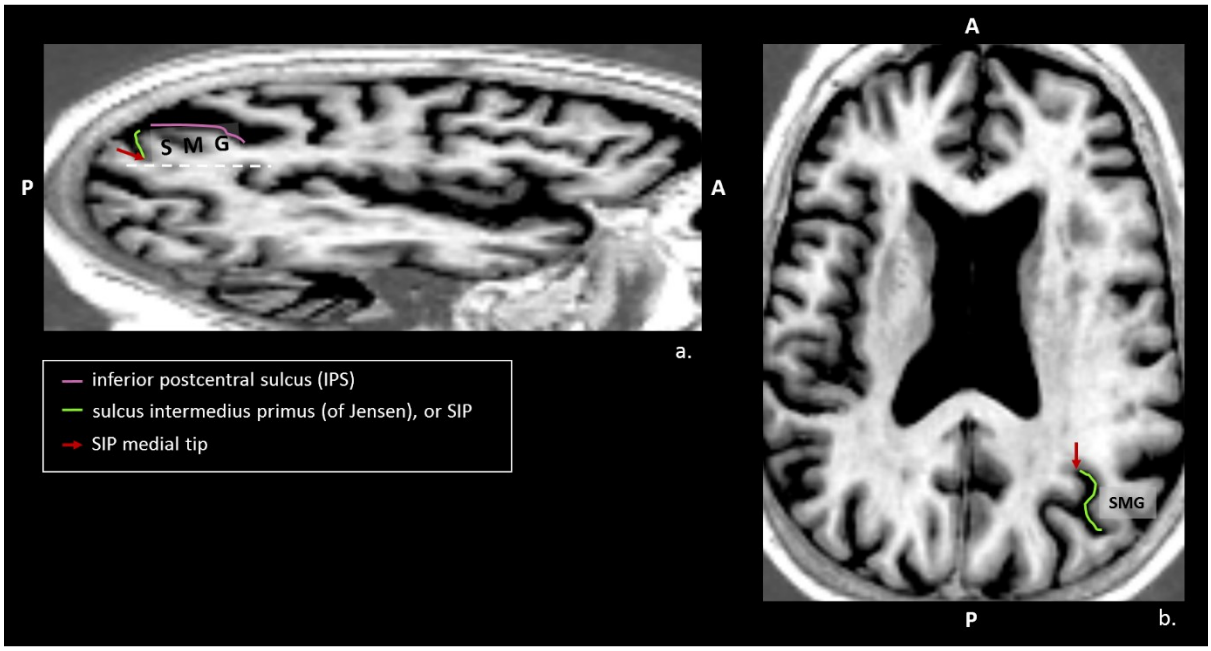

Figure 13. *Continuing medially in sagittal view after the apsSTS has ended, mark the SIP as the SMG's posterior border (a), with guidance from the axial view for its medial tip (b). As in the more lateral slices, the IPS is the SMG's anterior border. Ensure that the cut-off point in sagittal view is the horizontal at the mLF's superior end should the 2 borders extend beyond it.*

4. Go back through all marked slices, and draw the SMG as the region situated within the borders marked in the previous steps. All drawing should be done in the sagittal view, from lateral to medial direction.

References

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