Anatomy and White Matter Connections of the Superior Frontal Gyrus

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The superior frontal gyrus (SFG) is an important region implicated in a variety of tasks including motor movement, working memory, resting-state, and cognitive control. A detailed understanding of the subcortical white matter of the SFG could improve postoperative morbidity related to surgery around this gyrus. Through DSI-based fiber tractography validated by gross anatomical dissection, we characterized the fiber tracts of the SFG based on their relationships to other well-known neuroanatomic structures. Diffusion imaging from the Human Connectome Project from 10 healthy adult subjects was used for fiber tractography. We evaluated the SFG as a whole based on its connectivity with other regions. All tracts were mapped in both hemispheres, and a lateralization index was calculated based on resultant tract volumes. Ten cadaveric dissections were then performed using a modified Klingler technique to delineate the location of major tracts integrated within the SFG. We identified four major SFG connections: the frontal aslant tract connecting to the inferior frontal gyrus; the inferior fronto-occipital fasciculus connecting to the cuneus, lingual gyrus, and superior parietal lobule; the cingulum connecting to the precuneus and parahippocampal gyrus/uncus; and a callosal fiber bundle connecting the SFG bilaterally. The functional networks of the SFG involve a complex series of white matter tracts integrated within the gyrus, including the FAT, IFOF, cingulum, and callosal fibers. Postsurgical outcomes related to this region may be better understood in the context of the fiber-bundle anatomy highlighted in this study. Clin. Anat. 33:823-832, 2020. © 2019 Wiley Periodicals, Inc.

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INTRODUCTION

The superior frontal gyrus (SFG) has long been of interest to neuroscientists and neurosurgeons alike. Within Brodmann's original work, the SFG was divided into four distinct regions, including areas 6, 8, 9, and 32 (Petrides and Pandya, 1999, 2002). Since that time, newer cortical parcellation maps of the SFG have been proposed based on advanced neuroimaging techniques (Glasser et al., 2016). Analysis of the distinct regions comprising the SFG has been critical to better understand the functional role of this gyrus

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in human cognition and brain tumor surgery. As a result of these efforts, the SFG is now known to be involved in several functional networks related to motor activity (Nakamura et al., 1998; Martino et al., 2011), working memory (Owen et al., 1996; Courtney et al., 1998; Rowe et al., 2000), resting-state regulation, and cognitive control (Vincent et al., 2008; Niendam et al., 2012; Andrews-Hanna et al., 2014; Raichle, 2015). Lesion and human neuroimaging studies have also demonstrated that the functional processes attributed to the SFG can be disrupted as a result of neoplastic or neuropsychiatric disease (Luria and Tsvetkova, 1967; Robinson et al., 1998; Bannur and Rajshekhar, 2000; du Boisgueheneuc et al., 2006; Buckner et al., 2008).

A important feature of the SFG is its long association with the development of supplementary motor area (SMA) syndrome following tumor resection within the SMA (Bannur and Rajshekhar, 2000). The SMA occupies part of the posterior-most aspect of the SFG, and is characterized by hemiparesis and aphasia in the acute postoperative period (Bannur and Rajshekhar, 2000). A critical question, though, is how this syndrome develops. In order to begin answering this question, we must first understand how the SFG is linked to other aspects of the cortex, as an improved understanding of the white matter anatomy of the SFG could prove beneficial for the preservation of the white matter structures responsible for the functional networks associated with the gyrus. After all, maintaining subcortical connectivity has been shown to decrease postoperative motor deficits in patients undergoing DTI—based neuronavigation (Wu et al., 2007).

This study demonstrates the anatomic organization of the underlying white matter connections of the SFG. Through DSI-based fiber tracking validated by gross anatomical dissection as ground truth, we have characterized the white matter bundles of the SFG based on their anatomic connections and relationships to adjacent neuroanatomic structures. Our hope is that the subcortical white matter anatomy delineated within this study may help explain the subtle postsurgical neurologic deficits that can occur following tumor resection within and near the divisions of the SFG.

MATERIALS AND METHODS

Defining the Regions of Interest

For the purposes of performing fiber tractography, we divided the cortical surface of the SFG into two distinct components: (1) a supero-lateral surface comprising the medial apex of the SFG at the interhemispheric fissure extending toward the superior frontal sulcus infero-laterally and (2) a medial surface comprising the medial apex of the SFG at the interhemispheric fissure extending toward the cingulate sulcus infero-medially. These cortical surfaces were further divided into anterior, middle, and posterior thirds to better characterize



Fig. 1. (a) Antero-superior and (b) mid-sagittal views of a cadaveric brain specimen prior to dissection. Parts of the frontal, parietal, and occipital lobes are visualized and labeled. The superior frontal sulcus is demarcated by a series white blue dots in (a). The cingulate sulcus is demarcated by a series of black dots in (b). The lateral and medial surfaces of the superior frontal gyrus (SFG) are clearly seen. These surfaces were divided into thirds for the purposes of simplifying fiber tractography in DSI Studio (CC, corpus callosum; FP, frontal pole; LG, lingual gyrus; M, motor strop; MB, midbrain; MFG, middle frontal gyrus; PL, paracentral lobule; S, sensory strip; SFG, superior frontal gyrus; SPL, superior parietal lobule). [Color figure can be viewed at wileyonlinelibrary.com]

the origination and termination of tracts within the SFG. The frontal pole served as the anterior boundary for the SFG, while the precentral sulcus and paracentral lobule served as the posterior boundary for the SFG. The anatomy of these regions is shown in Figure 1.

Tractography

Publicly available imaging data from the Human Connectome Project was obtained for this study from the HCP database (http://humanconnectome.org, release Q3). Diffusion imaging with corresponding T1-weighted images from 10 healthy, unrelated subjects were analyzed during fiber tracking analysis (Subjects IDs: 100307, 103414, 105115, 110411, 111312, 113619, 115320, 117112, 118730, 118932). A multishell diffusion scheme was used, and the b-values were 990, 1985, and 1980 sec/mm². Each b-value was sampled in 90 directions. The in-plane resolution was 1.25 mm. The diffusion data were reconstructed using generalized q-sampling imaging with a diffusion sampling length ratio of 1.25 (Yeh et al., 2010).

All brains were registered to the Montreal Neurologic Institute (MNI) coordinate space (Evans et al., 1992), wherein imaging is warped to fit a standardized brain model for comparison between subjects (Evans et al., 1992). Tractography was performed in DSI Studio (Carnegie Mellon) using a region of interest (ROI) approach to initiate fiber tracking from a user-defined seed region (Martino et al., 2013). A two-ROI-approach was used to isolate tracts (Kamali et al., 2014).

Voxels within each ROI were automatically traced with a maximum angular threshold of 45°. When a voxel was approached with no tract direction or a direction change of greater than 45°, the tract was halted. Tractography was terminated after reaching a maximum length of 800 mm. In some instances, exclusion ROIs were placed to exclude spurious tracts that were not involved in the white matter pathway of interest. Tracts were identified in both hemispheres for all regions of the SFG as defined above.

The SFG was divided into six parts: antero-lateral and antero-medial regions, middle-lateral and middle-



Fig. 2. Depiction of the frontal aslant tract (FAT). (**a**, **b**) Tractographic representation of the FAT in the coronal plane. Tractography images are shown on T1-weighted magnetic resonance images with the lateral ventricles indicated by an asterisk (*). (**c**) Anatomy of the lateral frontal lobe prior to dissection of the FAT. (**d**, **e**) Gross anatomic dissection of the FAT extending from the postero-lateral superior frontal gyrus (SFG) to the pars opercularis and pars triangularis of the inferior frontal gyrus (IFG). Green streamlines are shown in (e) to indicate the pathway of the FAT fibers (CC, corpus callosum; IFG, inferior frontal gyrus; M, motor strop; MFG, middle frontal gyrus; S, sensory strip; SFG, superior frontal gyrus; TL, temporal lobe). [Color figure can be viewed at wileyonlinelibrary.com]

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medial regions, and postero-lateral and posteromedial regions. Tractography was completed systematically along the length of the SFG from anterior to posterior. All tractography was completed prior to cadaveric study. Lateralization indices (LI) were calculated based on resultant tract volumes from major identified tracts (De Schotten et al., 2011), and the unpaired *t* test was used to assess for any significant differences in tract volume between cerebral hemispheres ($P \le 0.05$).

PostMortem Dissections

To validate tractography results, we sought to demonstrate the location of white matter tracts originating from the IFG using gross anatomical dissection as ground truth.(Catani et al., 2012; Burks et al., 2016, 2017, 2018; Briggs et al., 2019) Postmortem dissections were performed using a modified Klingler technique (Koutsarnakis et al., 2015). Ten specimens were used for this study, obtained from our institution's Willed Body Program with approval of the state's anatomical board. The cadaveric brains were fixed in 10% formalin for at least 3 months after being removed from the cranium. Up until the time of dissection, the pia-arachnoid membrane was left attached.

After fixation with formalin, specimens were rinsed with water for 2 days, and then frozen at -10° C for 8 hr causing white matter disruption. After thawing, dissection of the "freeze-fractured" specimens began with removal of the meninges and identification of cortical anatomy, including gyri and sulci. Relevant cortical areas were identified first. Starting superficially, they were pealed back to reveal white-matter areas of interest. Care was taken to leave cortical areas corresponding to white matter tracts of interest intact in order to preserve anatomical relationships. Tracts were dissected with blunt instruments to avoid disrupting the natural tract anatomy. Photographs were taken at each stage of the dissection. All SFG tracts were dissected in both hemispheres.



Fig. 3. Depiction of the inferior fronto-occipital fasciculus (IFOF). Tractographic representation of the IFOF in the (**a**, **b**) sagittal and (**c**, **d**) axial planes. Tractography images are shown on T1-weighted magnetic resonance images. The IFOF fibers originate along the length of the superior frontal gyrus (SFG) before converging at the level of the insula and subsequently diverging in the deep white matter of the posterior temporal lobe to terminate in parts of the parietal and occipital lobes. (**e**, **f**) Gross anatomic dissection of the IFOF extending from the SFG to the cuneus (C) and lingual gyrus (LG). Orange streamlines are shown in (f) to indicate the pathway of the IFOF fibers. (**g**) Visualization of IFOF fibers terminating in the superior parietal lobule (SPL) following removal of the remaining opercular cortex (***) seen in (f). Orange streamlines are shown in (g) to indicate the pathway of the IFOF fibers (C, cuneus; LG, lingual gyrus; M, motor strop; MFG, middle frontal gyrus; S, sensory strip; SFG, superior frontal gyrus; SPL, superior parietal lobule; TP, temporal pole). [Color figure can be viewed at wileyonlinelibrary.com]

Long-Range Association Fibers

The SFG is connected to several long-range white matter tracts in the brain, including the frontal aslant tract (FAT), inferior fronto-occipital fasciculus (IFOF), cingulum, and a set of callosal fibers that interconnect the bilateral superior frontal gyri. The anatomy of these tracts as they originate from the SFG is described below.

The frontal aslant tract. The FAT connects the superior and inferior frontal gyri in both cerebral hemispheres. Fibers of the FAT arise within the supero-lateral

aspect of the SFG immediately anterior to the precentral gyrus where they begin to project inferiorly into the deep white matter of the posterior frontal lobe. These fibers then curve gradually in the infero-lateral direction (approximately 90°) to terminate in the pars opercularis and pars triangularis of the posterior inferior frontal gyrus (Fig. 2). The extent to which FAT fibers arise anteriorly along the SFG was variable across subjects. However, no FAT fibers were found to originate at the frontal pole. In addition, no FAT fibers were found to arise along the medial cortical surface of the SFG. Note that the fibers of the FAT course deep to the superior longitudinal fasciculus, which is directed orthogonally to the FAT in the anterior–posterior plane as it projects into the



Fig. 4. Depiction of the cingulum. (**a**–**c**) Tractographic representation of the cingulum in the (a, b) sagittal and (c) axial planes. Tractography images are shown on T1-weighted magnetic resonance images. (**d**, **e**) Gross anatomic dissection of the cingulum extending from the medial surface of the superior frontal gyrus (SFG) to the precuneus (PC). Some fibers of the cingulum can be seen projecting posteriorly around the splenium of the corpus callosum (CC) to terminate in the parahippocampal gyrus and uncus (U) within the medial temporal lobe (**f**). Note that the midbrain (MB) was cut in (f) to continue the cingulum fiber bundle dissection down into the medial temporal lobe. The cingulate sulcus is demarcated by a series of white dots in (d, e) Light blue streamlines are shown in (e, f) to indicate the pathway of the cingulum fibers (CC, corpus callosum; MB, midbrain; PC, precuneus; PL, paracentral lobule; SFG, superior frontal gyrus; T, thalamus; U, uncus). [Color figure can be viewed at wileyonlinelibrary.com]

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perisylvian white matter. Careful removal of the SLF fibers was critical to reveal the deep white matter fibers of the FAT.

The inferior Fronto-occipital fasciculus. Tractography corresponding to the IFOF is shown in Figure 3. Fibers corresponding to the IFOF were found to arise along the length of the supero-lateral SFG, where they converge infero-posteriorly within the subcortical white matter of the anterior insula in the extreme and external capsules. The fibers then run infero-lateral to the thalamus before beginning to diverge in the deep white matter of the temporal lobe. The diverging fibers of the IFOF continue to project posteriorly and superiorly, adjacent to the lateral ventricle, before terminating in parts of the parietal and occipital lobes. Specific terminations of the IFOF as it arises from the SFG include the medial-polar aspects of the cuneus and lingual gyrus as well as parts of the superior parietal lobule.

Cingulum. Cingulum fibers originate along the medial surface of the SFG with contributions from the anterior, middle, and posterior aspects of the gyrus. These fibers curve approximately 90° to continue their course posteriorly within the deep subcortical white matter of the cingulate gyrus. Most of these fibers project superiorly and medially to terminate



Fig. 5. Depiction of callosal fibers. $(\mathbf{a-c})$ Callosal fibers are seen originating and terminating within the superior frontal gyri bilaterally. Tractography images are shown on T1-weighted magnetic resonance images in the (a, b) axial and (c) coronal planes. $(\mathbf{d, e})$ Cadaveric dissection of the callosal fibers is shown in the coronal plane. Asterisks (*) are used to denote the position of the cingulate gyri bilaterally. Dark blue streamlines shown in (e) indicate the pathway of the callosal fibers (CC, corpus callosum; IFG, inferior frontal gyrus; MFG, middle frontal gyrus; SFG, superior frontal gyrus; T, temporal lobe). [Color figure can be viewed at wileyonlinelibrary.com]



Fig. 6. Representative example of a U-fiber. Intra-gyral U-shaped fibers were identified between adjacent parts of the superior frontal gyrus (SFG). An example of such a fiber is highlighted with a black box in (**a**) and magnified in (**b**). A black streamline is shown in (b) to indicate the pathway of the U-shaped fiber. In addition to the intra-gyral U-shaped fibers shown here, U-shaped fibers were also identified between the SFG and MFG. However, these are not shown in this figure (SFG, superior frontal gyrus). [Color figure can be viewed at wileyonlinelibrary.com]

within the precuneus. However, some fibers of the cingulum continue their course posteriorly before curving nearly 180° behind the splenium of the corpus callosum. From there, the fibers project into the deep subcortical white matter of the medial temporal lobe. These remaining fibers terminate within parts of the parahippocampal gyrus and uncus (Fig. 4). These results are consistent within the brain bilaterally.

Callosal Fibers. In addition to the three tracts described above, the left and right SFG are interconnected via a dense callosal fiber bundle. These callosal fibers project through the genu and body of the corpus callosum to connect the superior frontal gyri bilaterally (Fig. 5). More anterior callosal fibers project horizontally through the genu of the corpus callosum as they terminate within the frontal poles. More posterior callosal fibers, including those arising from the SMA, project vertically through the anterior body of the corpus callosum to connect homologous regions of the SFG bilaterally.

Short-Range Association Fibers

While the SFG is associated with four large white matter tracts, a plethora of U-shaped fibers were also

TABLE 1. Lateralization Indices for White MatterTracts of the Superior Frontal Gyrus

Tract	Volume/ Tract (left)	Volume/ Tract (right)	LI	<i>P</i> value
FAT	20.4	18.2	0.058	0.18
IFOF	42.7	42.1	0.006	0.41
Cingulum	22.9	24.3	-0.033	0.29

identified during fiber tracking analysis. To characterize all the U-shaped fibers identified during tractography is beyond the scope of this study. However, we have included a representative figure of some of the Ushaped fibers identified during gross anatomic dissection (Fig. 6). Intra-gyral fibers connecting different parts of the SFG were identified, as well as U-fibers connecting the SFG and MFG. Each U-shaped fiber exhibits a similar morphology with fibers arising within one part of the cortex before curving 180° underneath a sulcal structure to terminate in a part of the cortex adjacent to their origin.

Lateralization Indices

Table 1 lists the volumetric LI comparing the FAT, IFOF, and cingulum between left and right cerebral hemispheres during fiber tracking analysis. No differences in the LI were noted bilaterally for the tracts arising within the SFG.

DISCUSSION

In this study, we address the underlying subcortical anatomy of the SFG, a major part of the cortex involved in several white matter pathways. Functional preservation of cortical networks during cerebral surgery is in part dependent on preserving the white matter connections between the components of these networks (Duffau, 2012; Burks et al., 2016). Using DSI-based fiber tractography validated by gross anatomic dissection as ground truth, we have described the connections of the SFG within the context of the neuroanatomy visualized in 10 normal HCP subjects and 10 cerebral hemispheres, respectively. White matter projections from the SFG to parts of the temporal, parietal, and occipital lobes were observed across subjects and in cadaveric specimens with concordance between the two methodologies.

Relation between Gross Anatomic Dissection and Fiber Tractography

While gross anatomic dissection allowed for qualitative assessment of tract orientation, fiber tractography allowed us to quantify tract volumes to understand laterality. Morphology of the major tracts was consistent across subjects and within cerebral hemispheres, with long-range association fibers (including the FAT, IFOF, and cingulum) connecting the SFG to different parts of the parietal, occipital, and temporal lobes. Short association fibers were also identified connecting between adjacent parts of the SFG and to the MFG.

Functional Aspects of the Superior Frontal Gyrus

Motor function. The SFG has complex involvement in motor function. The medial SFG is composed, functionally, of the SMA and pre-SMA, as well as the supplementary eye field (SEF; Nachev et al., 2008). The pre-SMA is rostral to the SMA, and the SEF is located at the border between the SMA and pre-SMA (Nachev et al., 2008). The SMA holds a somatotopic organization of the body, with the lower extremities represented caudally and the upper extremities represented rostrally (Mitz and Wise, 1987; Fried et al., 1991; Luppino et al., 1991).

The precise function of the SMA remains contested, but it has been in implicated in a variety of motor functions. In one electrophysiology study, stimulation of the SMA in epileptic patients elicited complex contralateral movements (Fried et al., 1991). In addition, early single-cell and electro-cortical recording studies in non-human primates have shown that SMA neuronal firing occurs prior to performing complex tasks (Brinkman and Porter, 1979; Tanji and Kurata, 1982). Other studies have shown that the SMA and pre-SMA fire during specific patterns of motor activity but not others. Some neurons will fire in advance of specific motor sequences (e.g., turn-pull-push a lever), but not others (e.g., turn-push-pull a lever; Tanji and Shima, 1994; Shima and Tanji, 2000). Other neurons will fire in advance of the third movement in a sequence irrespective of that specific sequence (Clower and Alexander, 1998). While the SMA and pre-SMA have many pro-motor functions, motor inhibitory activity has also been identified and is thought to prevent execution of unnecessary motor patterns in order to enhance motor control (Sumner et al., 2007). The posterior aspect of the SFG has also been implicated in synchronized movements of the hands bilaterally (Martino et al., 2011).

Stimulation of the SEF has been shown to induce saccadic eye movements; however, lesions in this area do not impede or disrupt function to the same degree as lesions within the frontal eye fields (Tehovnik et al., 2000). Stimulation of the SEF can also produce combined eye and head movements (Martinez-Trujillo et al., 2004).

In clinical translation, resection of tumors in the area of the SMA can result in the well-known SMA syndrome. The SMA syndrome is characterized by hemiparesis and occasional aphasia after resection a tumor abutting the SMA that typically resolve rapidly in the postoperative period (Bannur and Rajshekhar, 2000). However, the degree of symptom severity correlates with the extent of tumor resection (Zentner et al., 1996). Patients with lesions within the SMA may develop alien limb syndromes manifesting as non-volitional, stimulus driven grasping motions (Della Sala et al., 1991; Feinberg et al., 1992; Boccardi et al., 2002). Ultimately, the SFG has a variety of important functions related to motor activity, and lesions to the SFG, especially the SMA, can result in clinically significant motor deficits.

Memory and learning. The SFG has been implicated in working memory processes. Functional magnetic resonance imaging studies in humans have shown that an area along the postero-superior aspect of the superior frontal sulcus is involved in spatial working memory (Courtney et al., 1998). More specifically, activity in Brodmann Area 8 is associated with maintenance of spatial working memory items, as opposed to the selection of an item from one's working memory (Rowe et al., 2000). PET-based studies have also demonstrated that the SFG is involved in working memory tasks regardless of the memory domain involved (Owen et al., 1996). Lesion studies have shown that patients with left postero-lateral SFG lesions have impaired working memory performance, with the strongest deficits manifesting in complex spatial working memory tasks (du Boisgueheneuc et al., 2006).

The SFG also plays a role in motor learning. The pre-SMA, more than the SMA, is activated when individuals are in the process of learning new complex hand movements (Nakamura et al., 1998). Taken together, these studies demonstrate that the SFG is important in a variety of memory paradigms, perhaps most strongly in complex spatial memory tasks.

Self-reflection. Over the last several decades, advances in neuroimaging have allowed neuroscientists to identify the cortical regions of interest involved in the concepts of self-representation. One neuroanatomic study has shown that introspection is strongly associated with activity in the left SFG (Goldberg et al., 2006). Within this study, introspection was defined as an activity of self-reflection. Specifically, subjects were told to analyze their feelings after being exposed to different stimuli. Introspection lead to activation of the SFG with extension medially into the anterior cingulate gyrus (Goldberg et al., 2006).

Higher-order cognitive processing. In addition to motor and memory functions, the SFG has been implicated in multiple higher-order cognitive processes. The medial prefrontal cortex is one of the functional hubs of the default mode network (DMN; Andrews-Hanna et al., 2014). The DMN is a task-negative

distributed network that is silenced during goal-oriented cognitive activity (Raichle et al., 2001; Anticevic et al., 2012). The DMN is composed of the ventral medial prefrontal cortex, the dorsal medial prefrontal cortex, the posterior cingulate cortex, and the lateral parietal lobe (Raichle, 2015).

The DMN has shown to be active during selfreferential behavior (Gusnard et al., 2001). The medial prefrontal cortex has been directly implicated in this phenomenon (Gusnard et al., 2001). Increased pre-SMA activity within the SFG has also been detected during self-willed or internally motivated actions (Deiber et al., 1999; Jenkins et al., 2000; Nachev et al., 2005). In addition to self-referential behavior, the DMN is also involved in emotional processing and in the recollection of prior experiences (Raichle, 2015). Dysfunction and functional alterations of the DMN have been recorded in a number of neuropsychiatric diseases (Buckner et al., 2008).

The cognitive control network (CCN), also known as the fronto-parietal control system, is a superordinate network that comprises the dorsal regions of the lateral prefrontal cortex within the SFG, the anterior cingulate cortex, and the parietal cortex (Vincent et al., 2008). This network serves to facilitate executive function in a variety of domains (Niendam et al., 2012). In doing so, the CCN represents a bridge between the DMN and the dorsal attention network (Niendam et al., 2012).

Sensorimotor inputs into the dorsolateral prefrontal cortex of the SFG help to drive rule maintenance for motor actions as well as response selection and inhibition via the CCN (Asaad et al., 2000; Bellebaum and Daum, 2007). The dorsolateral prefrontal cortex also receives inputs from the anterior cingulate and parietal cortices that (1) allow for the detection of conflicting conditions indicating a need for better executive control and (2) allow for the parsing of stimulus salience in order to maximize the ability of the dorsolateral prefrontal cortex to shift attentional focus according to the demands of the task at hand (MacDonald et al., 2000; Miller and Cohen, 2001; Bunge et al., 2002, 2003; Egner and Hirsch, 2005; Kerns et al., 2005). The fact that different parts of the SFG are involved in the DMN and CCN pins it as a linkage point between these two networks.

Finally, the SFG has been implicated in the self-initiated, self-guided retrieval of semantic information (Binder and Desai, 2011). Indeed, ischemic damage to the SFG has been shown to result in a type of transcortical motor aphasia in certain patients (Luria and Tsvetkova, 1967; Robinson et al., 1998).

CONCLUSIONS

The SFG is involved in several functional processes including motor tasks, working memory, introspection, and high-order cognition. The cerebral networks related to these functions involve a complex series of white matter tracts including the FAT, IFOF, cingulum, and a dense set of callosal fibers, which integrate within and connect to the SFG. Improved understanding of the subcortical white matter anatomy delineated within this study may help explain the subtle postsurgical neurologic deficits that may occur following tumor resection within and near the divisions of this gyrus.

CONFLICT OF INTEREST

None.

REFERENCES

- Andrews-Hanna JR, Smallwood J, Spreng RN. 2014. The default network and self-generated thought: component processes, dynamic control, and clinical relevance. Ann N Y Acad Sci 1316:29–52.
- Anticevic A, Cole MW, Murray JD, Corlett PR, Wang XJ, Krystal JH. 2012. The role of default network deactivation in cognition and disease. Trends Cogn Sci 16:584–592.
- Asaad WF, Rainer G, Miller EK. 2000. Task-specific neural activity in the primate prefrontal cortex. J Neurophysiol 84:451–459.
- Bannur U, Rajshekhar V. 2000. Post operative supplementary motor area syndrome: clinical features and outcome. Br J Neurosurg 14: 204–210.
- Bellebaum C, Daum I. 2007. Cerebellar involvement in executive control. Cerebellum 6:184–192.
- Binder JR, Desai RH. 2011. The neurobiology of semantic memory. Trends Cogn Sci 15:527–536.
- Boccardi E, Della Sala S, Motto C, Spinnler H. 2002. Utilisation behaviour consequent to bilateral SMA softening. Cortex 38:289–308.
- Briggs RG, Chakraborty AR, Anderson CD, Abraham CJ, Palejwala AH, Conner AK, Pelargos PE, O'Donoghue DL, Glenn CA, Sughrue ME. 2019. Anatomy and white matter connections of the inferior frontal gyrus. Clin Anat 32:546–556.
- Brinkman C, Porter R. 1979. Supplementary motor area in the monkey: activity of neurons during performance of a learned motor task. J Neurophysiol 42:681–709.
- Buckner RL, Andrews-Hanna JR, Schacter DL. 2008. The brain's default network: anatomy, function, and relevance to disease. Ann N Y Acad Sci 1124:1–38.
- Bunge SA, Hazeltine E, Scanlon MD, Rosen AC, Gabrieli JD. 2002. Dissociable contributions of prefrontal and parietal cortices to response selection. Neuroimage 17:1562–1571.
- Bunge SA, Kahn I, Wallis JD, Miller EK, Wagner AD. 2003. Neural circuits subserving the retrieval and maintenance of abstract rules. J Neurophysiol 90:3419–3428.
- Burks JD, Boettcher LB, Conner AK, Glenn CA, Bonney PA, Baker CM, Briggs RG, Pittman NA, O'Donoghue DL, Wu DH. 2017. White matter connections of the inferior parietal lobule: A study of surgical anatomy. Brain Behav 7:1–12.
- Burks JD, Bonney PA, Conner AK, Glenn CA, Briggs RG, Battiste JD, McCoy T, O'Donoghue DL, Wu DH, Sughrue ME. 2016. A method for safely resecting anterior butterfly gliomas: the surgical anatomy of the default mode network and the relevance of its preservation. J Neurosurg 126:1795–1811.
- Burks JD, Conner AK, Bonney PA, Glenn CA, Baker CM, Boettcher LB, Briggs RG, O'Donoghue DL, Wu DH, Sughrue ME. 2018. Anatomy and white matter connections of the orbitofrontal gyrus. J Neurosurg 128:1865–1872.
- Catani M, Dell'Acqua F, Vergani F, Malik F, Hodge H, Roy P, Valabregue R, De Schotten MT. 2012. Short frontal lobe connections of the human brain. Cortex 48:273–291.
- Clower WT, Alexander GE. 1998. Movement sequence-related activity reflecting numerical order of components in supplementary and presupplementary motor areas. J Neurophysiol 80:1562–1566.
- Courtney SM, Petit L, Maisog JM, Ungerleider LG, Haxby JV. 1998. An area specialized for spatial working memory in human frontal cortex. Science 279:1347–1351.
- De Schotten MT, Dell'Acqua F, Forkel SJ, Simmons A, Vergani F, Murphy DG, Catani M. 2011. A lateralized brain network for visuospatial attention. Nat Neurosci 14:1245–1246.

- Deiber MP, Honda M, Ibañez V, Sadato N, Hallett M. 1999. Mesial motor areas in self-initiated versus externally triggered movements examined with fMRI: effect of movement type and rate. J Neurophysiol 81:3065–3077.
- Della Sala S, Marchetti C, Spinnler H. 1991. Right-sided anarchic (alien) hand: a longitudinal study. Neuropsychologia 29: 1113–1127.
- du Boisgueheneuc F, Levy R, Volle E, Seassau M, Duffau H, Kinkingnehun S, Samson Y, Zhang S, Dubois B. 2006. Functions of the left superior frontal gyrus in humans: a lesion study. Brain 129:3315–3328.
- Duffau H. 2012. The challenge to remove diffuse low-grade gliomas while preserving brain functions. Acta Neurochir 154:569–574.
- Egner T, Hirsch J. 2005. Cognitive control mechanisms resolve conflict through cortical amplification of task-relevant information. Nat Neurosci 8:1784–1790.
- Evans AC, Marrett S, Neelin P, Collins L, Worsley K, Dai W, Milot S, Meyer E, Bub D. 1992. Anatomical mapping of functional activation in stereotactic coordinate space. Neuroimage 1:43–53.
- Feinberg TE, Schindler RJ, Flanagan NG, Haber LD. 1992. Two alien hand syndromes. Neurology 42:19–24.
- Fried I, Katz A, McCarthy G, Sass KJ, Williamson P, Spencer SS, Spencer DD. 1991. Functional organization of human supplementary motor cortex studied by electrical stimulation. J Neurosci 11: 3656–3666.
- Glasser MF, Coalson TS, Robinson EC, Hacker CD, Harwell J, Yacoub E, Ugurbil K, Andersson J, Beckmann CF, Jenkinson M, Smith SM, Van Essen DC. 2016. A multi-modal parcellation of human cerebral cortex. Nature 536:171–178.
- Goldberg II, Harel M, Malach R. 2006. When the brain loses its self: Prefrontal inactivation during sensorimotor processing. Neuron 50:329–339.
- Gusnard DA, Akbudak E, Shulman GL, Raichle ME. 2001. Medial prefrontal cortex and self-referential mental activity: relation to a default mode of brain function. Proc Natl Acad Sci USA 98: 4259–4264.
- Jenkins IH, Jahanshahi M, Jueptner M, Passingham RE, Brooks DJ. 2000. Self-initiated versus externally triggered movements. II. The effect of movement predictability on regional cerebral blood flow. Brain 123(Pt 6):1216–1228.
- Kamali A, Sair HI, Radmanesh A, Hasan KM. 2014. Decoding the superior parietal lobule connections of the superior longitudinal fasciculus/ arcuate fasciculus in the human brain. Neuroscience 277:577–583.
- Kerns JG, Cohen JD, MacDonald AW, Johnson MK, Stenger VA, Aizenstein H, Carter CS. 2005. Decreased conflict- and errorrelated activity in the anterior cingulate cortex in subjects with schizophrenia. Am J Psychiatry 162:1833–1839.
- Koutsarnakis C, Liakos F, Kalyvas AV, Sakas DE, Stranjalis G. 2015. A laboratory manual for stepwise cerebral white matter fiber dissection. World Neurosurg 84:483–493.
- Luppino G, Matelli M, Camarda RM, Gallese V, Rizzolatti G. 1991. Multiple representations of body movements in mesial area 6 and the adjacent cingulate cortex: an intracortical microstimulation study in the macaque monkey. J Comp Neurol 311:463–482.
- Luria AR, Tsvetkova LS. 1967. Towards the mechanisms of "dynamic aphasia". Acta Neurol Psychiatr Belg 67:1045–1057.
- MacDonald AW, Cohen JD, Stenger VA, Carter CS. 2000. Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. Science 288:1835–1838.
- Martinez-Trujillo JC, Medendorp WP, Wang H, Crawford JD. 2004. Frames of reference for eye-head gaze commands in primate supplementary eye fields. Neuron 44:1057–1066.
- Martino J, Gabarros A, Deus J, Juncadella M, Acebes JJ, Torres A, Pujol J. 2011. Intrasurgical mapping of complex motor function in the superior frontal gyrus. Neuroscience 179:131–142.
- Martino J, Hamer PCDW, Berger MS, Lawton MT, Arnold CM, de Lucas EM, Duffau H. 2013. Analysis of the subcomponents and cortical terminations of the perisylvian superior longitudinal

fasciculus: a fiber dissection and DTI tractography study. Brain Struct Funct 218:105–121.

- Miller EK, Cohen JD. 2001. An integrative theory of prefrontal cortex function. Annu Rev Neurosci 24:167–202.
- Mitz AR, Wise SP. 1987. The somatotopic organization of the supplementary motor area: intracortical microstimulation mapping. J Neurosci 7:1010–1021.
- Nachev P, Kennard C, Husain M. 2008. Functional role of the supplementary and pre-supplementary motor areas. Nat Rev Neurosci 9:856–869.
- Nachev P, Rees G, Parton A, Kennard C, Husain M. 2005. Volition and conflict in human medial frontal cortex. Curr Biol 15:122–128.
- Nakamura K, Sakai K, Hikosaka O. 1998. Neuronal activity in medial frontal cortex during learning of sequential procedures. J Neurophysiol 80:2671–2687.
- Niendam TA, Laird AR, Ray KL, Dean YM, Glahn DC, Carter CS. 2012. Meta-analytic evidence for a superordinate cognitive control network subserving diverse executive functions. Cogn Affect Behav Neurosci 12:241–268.
- Owen AM, Evans AC, Petrides M. 1996. Evidence for a two-stage model of spatial working memory processing within the lateral frontal cortex: a positron emission tomography study. Cereb Cortex 6:31–38.
- Petrides M, Pandya DN. 1999. Dorsolateral prefrontal cortex: Comparative cytoarchitectonic analysis in the human and the macaque brain and corticocortical connection patterns. Eur J Neurosci 11:1011–1036.
- Petrides M, Pandya DN. 2002. Comparative cytoarchitectonic analysis of the human and the macaque ventrolateral prefrontal cortex and corticocortical connection patterns in the monkey. Eur J Neurosci 16:291–310.
- Raichle ME. 2015. The brain's default mode network. Annu Rev Neurosci 38:433–447.
- Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA, Shulman GL. 2001. A default mode of brain function. Proc Natl Acad Sci USA 98:676–682.
- Robinson G, Blair J, Cipolotti L. 1998. Dynamic aphasia: an inability to select between competing verbal responses? Brain 121(Pt 1): 77–89.
- Rowe JB, Toni I, Josephs O, Frackowiak RS, Passingham RE. 2000. The prefrontal cortex: response selection or maintenance within working memory? Science 288:1656–1660.
- Shima K, Tanji J. 2000. Neuronal activity in the supplementary and presupplementary motor areas for temporal organization of multiple movements. J Neurophysiol 84:2148–2160.
- Sumner P, Nachev P, Morris P, Peters AM, Jackson SR, Kennard C, Husain M. 2007. Human medial frontal cortex mediates unconscious inhibition of voluntary action. Neuron 54:697–711.
- Tanji J, Kurata K. 1982. Comparison of movement-related activity in two cortical motor areas of primates. J Neurophysiol 48:633–653.
- Tanji J, Shima K. 1994. Role for supplementary motor area cells in planning several movements ahead. Nature 371:413–416.
- Tehovnik EJ, Sommer MA, Chou IH, Slocum WM, Schiller PH. 2000. Eye fields in the frontal lobes of primates. Brain Res Brain Res Rev 32:413–448.
- Vincent JL, Kahn I, Snyder AZ, Raichle ME, Buckner RL. 2008. Evidence for a frontoparietal control system revealed by intrinsic functional connectivity. J Neurophysiol 100:3328–3342.
- Wu J-S, Zhou L-F, Tang W-J, Mao Y, Hu J, Song Y-Y, Hong X-N, Du G-H. 2007. Clinical evaluation and follow-up outcome of diffusion tensor imaging-based functional neuronavigation: a prospective, controlled study in patients with gliomas involving pyramidal tracts. Neurosurgery 61:935–949.
- Yeh F-C, Wedeen VJ, Tseng W-YI. 2010. Generalized Q-sampling imaging. IEEE Trans Med Imag 29:1626–1635.
- Zentner J, Hufnagel A, Pechstein U, Wolf HK, Schramm J. 1996. Functional results after resective procedures involving the supplementary motor area. J Neurosurg 85:542–549.