ORIGINAL COMMUNICATION

Anatomy and White Matter Connections of the Inferior Frontal Gyrus

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The inferior frontal gyrus (IFG) is involved in the evaluation of linguistic, interoceptive, and emotional information. A detailed understanding of its subcortical white matter anatomy could improve postoperative morbidity related to surgery in and around this gyrus. Through GQI-based fiber tracking validated by gross anatomical dissection as ground truth, we characterized the fiber tracts of the IFG based on relationships to other well-known neuroanatomic structures. Diffusion imaging from the Human Connectome Project for 10 healthy adult controls was used for fiber tracking analysis. We evaluated the IFG 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 demonstrate the location of major tracts. We identified four major connections of the IFG: a white matter bundle corresponding the frontal aslant tract connecting to the superior frontal gyrus; the superior longitudinal fasciculus connecting to the inferior parietal lobule, lateral occipital area, posterior temporal areas, and the temporal pole; the inferior fronto-occipital fasciculus connecting to the cuneus and lingual gyrus; and the uncinate fasciculus connecting to the temporal pole. A callosal fiber bundle connecting the inferior frontal gyri bilaterally was also identified. The IFG is an important region implicated in a variety of tasks including language processing, speech production, motor control, interoceptive awareness, and semantic processing. Postsurgical outcomes related to this region may be better understood in the context of the fiber-bundle anatomy highlighted in this study. Clin. Anat. 32:546–556, 2019. © 2019 Wiley Periodicals, Inc.

Key words: neurology; neurosurgery; humans; white matter; diffusion tensor imaging; connectome

INTRODUCTION

The inferior frontal gyrus (IFG) is known to be involved in several networks related to linguistic, interoceptive, and emotional function (Liakakis et al. 2011; Hagoort 2014). For example, the IFG is known to play roles in language production, fine motor control, and emotional awareness (Liakakis et al. 2011; Hagoort 2014). Lesion and human neuroimaging studies have demonstrated that the functional processes attributed

to the IFG may be disrupted as a result of neoplastic or neuropsychiatric disease (Alexander et al. 2001; Alexander et al. 2005; Jeong et al. 2009; Backasch et al. 2014). The IFG is also important in processes requiring the evaluation and report of semantic information (Hagoort 2014).

A significant feature of the left inferior frontal lobe is its long association as the center for language production, the so-called "Broca's Area" (Broca 1861), which when damaged can lead to expressive forms of aphasia (Broca 1861; Mohr et al. 1978; Kreisler et al. 2000). While speech and motor mapping is typical when operating near relevant eloquent regions of the cerebral cortex, an improved understanding of the subcortical white matter anatomy of the IFG could prove beneficial for the preservation of the white matter structures responsible for language production. For example, maintaining subcortical connectivity has been shown to decrease postoperative motor deficits in patients receiving DTI—based neuronavigation (Wu et al. 2007).

This study demonstrates the anatomic organization of the underlying white matter connections of the IFG. Through GQI-based fiber tracking validated by gross anatomical dissection as ground truth, we have characterized the white matter bundles of the IFG based on their anatomic connections and relationships to adjacent neuroanatomic structures.

METHODS

Defining Regions of Interest

The inferior frontal gyrus was divided into three distinct cortical regions: the pars orbitalis comprising the most anterior aspect of the gyrus, extending from the pars triangularis to the frontal pole, where the inferior, middle, and superior frontal gyri converge; the pars triangularis, representing the most sinusoidal part of the IFG with its apex pointing into the inferior frontal sulcus; and the pars opercularis comprising the posterior extent of the gyrus from the triangularis to the precentral sulcus. The orbitofrontal gyri resting in the anterior cranial fossa served as the medial boundary of the IFG. Based on these anatomical relationships, we defined three regions of interest (ROIs) for the purposes of performing deterministic tractograhy: an anterior ROI corresponding to the pars orbitalis, a middle ROI corresponding to the pars triangularis, and a posterior ROI corresponding to the pars opercularis. The inferior frontal sulcus, separating the IFG from the middle frontal gyrus, served as the superior boundary for all ROIs, while the Sylvian fissure served as the inferior boundary. The anatomy of these regions is delineated 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, 103,414, 105,115, 110,411, 111,312, 113,619, 115,320, 117,112, 118,730, 118,932). A multi-shell diffusion scheme was used, and the b-values were 990, 1985, and 1980 s/mm^2. Each b-value was sampled in 90 directions. The in-plane resolution was 1.25 mm. The diffusion data was 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 comparison between subjects (Evans et al. 1992). Tractography was performed in DSI Studio (Carnegie Mellon) using a region of interest 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 obvious spurious tracts that were not involved in the white matter pathway of interest. Tracts were identified in both hemispheres for all regions of the IFG.

The IFG was divided into three parts: an anterior part (pars orbitalis), a middle part (pars triangularis), and a posterior part (pars opercularis). Tractography was completed systematically along the length of the IFG 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 significant differences between cerebral hemispheres ($P \le 0.05$).

Postmortem Dissections

To validate tractography results we sought to demonstrate the location of white matter tracts connecting to the IFG with gross anatomical dissections as ground truth (Catani et al. 2012; Burks et al. 2016; Burks et al. 2017a; Burks et al. 2017b). 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,
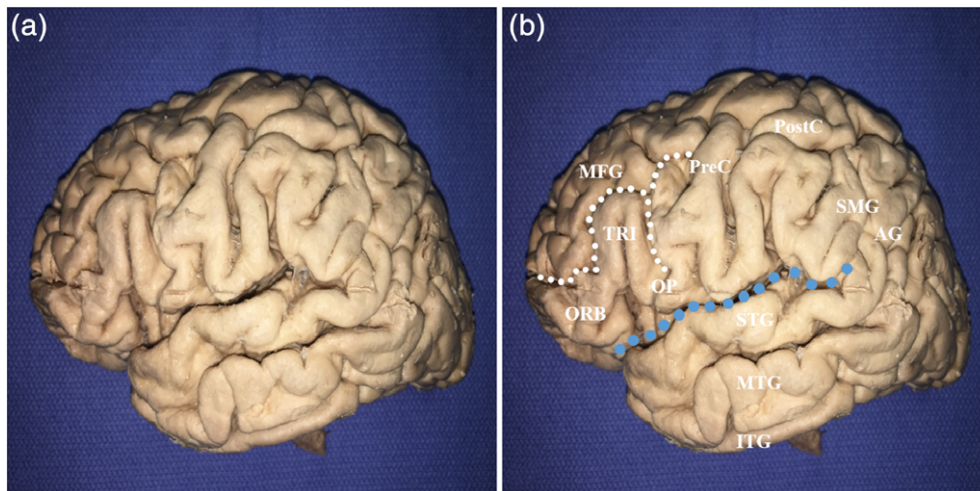
Fig. 1. (A, B) Lateral views are shown of a gross anatomic specimen prior to dissection. Parts of the frontal, parietal, and temporal lobes are visualized and labeled. The Sylvian fissure is demarcated by a series of blue dots, and the inferior frontal sulcus is demarcated be a series of white dots. The three regions of interest used in our analysis are labeled on the inferior frontal gyrus, including the OP (pars opercularis), TRI (pars triangularis), and ORB (pars orbitalis). MFG = middle frontal gyrus, PreC = pre-central gyrus, PostC = post-central gyrus, SMG = supramaginal gyrus, AG = angular gyrus, STG, MTG, and ITG = superior, middle and inferior temporal gyri. [Color figure can be viewed at wileyonlinelibrary.com]

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 white matter tracts were dissected in both hemispheres.

RESULTS

Long-Range Association Fibers

The IFG is connected to several long-range white matter tracts in the brain, including the frontal aslant tract, uncinate fasciculus, the superior longitudinal fasciculus and the inferior fronto-occipital fasciculus.

The frontal aslant tract and superior longitudinal fasciculus/arcuate fasciculus complex. The frontal aslant tract (FAT) runs in the lateral-medial direction as it arises from the posterior aspect of the IFG in the pars triangularis and pars opercularis. The tract curves gradually 90° before reaching the dorsal superior frontal gyrus, where it terminates in the region immediately anterior to the precentral gyrus (Fig. 2). The extent to which FAT fibers terminate anteriorly along the SFG was variable across subjects. However, no such fibers were found to terminate in the middle frontal gyrus or the frontal pole.

The fibers of the FAT course deep to the superior longitudinal fasciculus/arcuate fasciculus complex

(SLF/AF) which is directed orthogonally to the FAT in the anterior–posterior plane as it courses within the perisylvian white matter. Figure 2H demonstrates the relationship between the SLF/AF and the FAT in one cadaver brain. Careful removal of this white matter complex eventually reveals the fibers of the FAT.

The SLF/AF complex was identified coursing in the anterior–posterior plane, superficial to the FAT, with multiple terminations in the parietal, temporal, and occipital lobes (Fig. 3). SLF/AF fibers begin in the triangularis and opercularis, coursing in the rostro-caudal direction underneath the sensorimotor cortex. The first of set of fiber terminations occur in the inferior parietal lobule, after which SLF/AF fibers curve approximately 90° inferiorly to continue into the posterior most aspect of the superior temporal gyrus (corresponding to the AF) as well as parts of the lateral occipital lobe and middle temporal gyrus (corresponding to the SLF). Some SLF fibers were found to continue down the length of the temporal lobe to the temporal pole in the left cerebral hemisphere. In contrast, continuation of the SLF into the temporal pole in the right cerebral hemisphere was inconsistent across subjects.

The inferior fronto-occipital fasciculus and uncinate fasciculus. Tractography corresponding to the inferior fronto-occipital fasciculus (IFOF) is shown in Figure 4. Fibers from the IFOF can be seen to leave the IFG from the pars orbitalis and pars opercularis before bending 90° to course in the extreme and external capsules that lie deep to the insular and opercular cortices. The fibers run infero-lateral to the thalamus
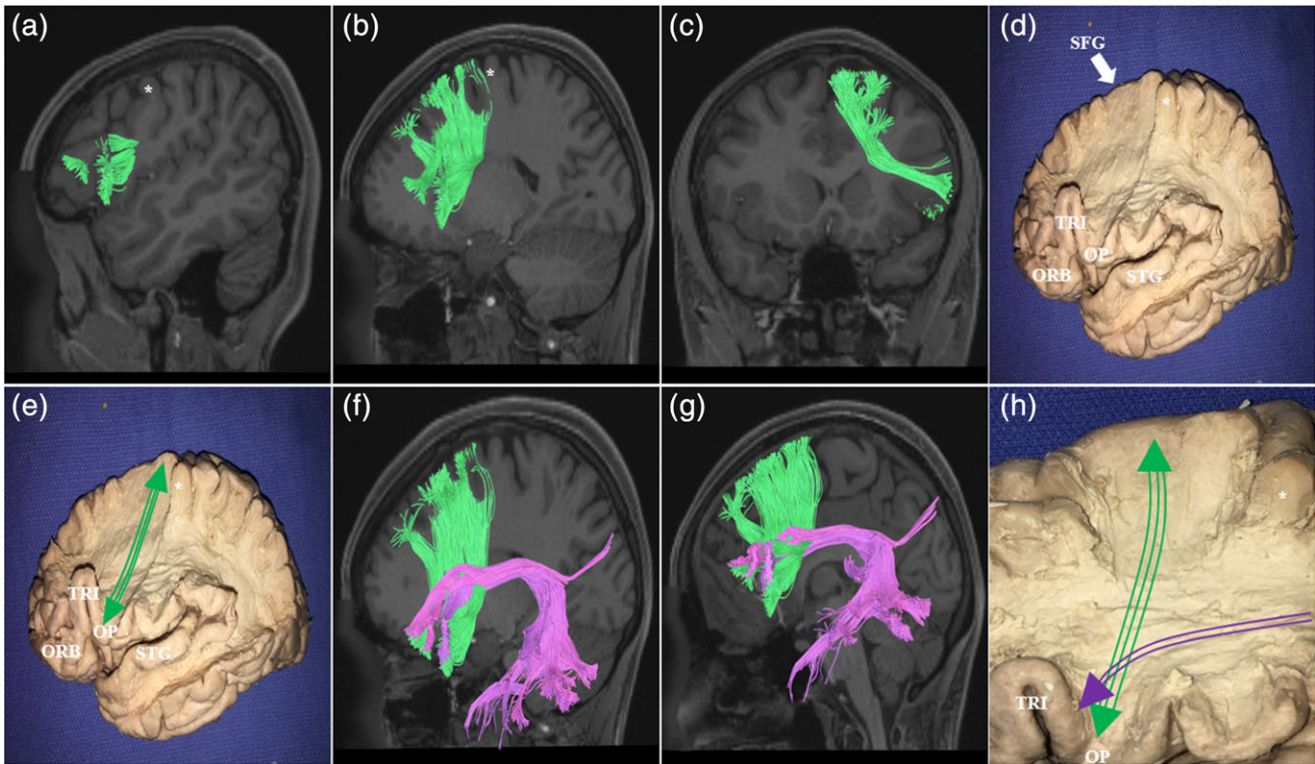
Fig. 2. Depictions of the frontal aslant tract (FAT). (A–C) Tractographic representation of the FAT in medial and lateral sagittal planes (A, B) as well as the coronal plane (C). Tractography images are shown on T1-weighted MRIs. (D, E) Gross anatomic dissection of the FAT extending from the opercularis and triangularis to the dorso-posterior superior frontal gyrus. Green arrows indicate the pathway of the white matter fibers (F, G) Representation of the FAT (green) and superior longitudinal fasciculus (SLF, purple) together on T1-weighted sagittal MRIs. The SLF is seen to run superficially over the FAT. (H) Gross anatomic dissection showing the relationship between FAT and SLF fibers arising from the IFG. ORB: orbitalis, TRI: triangularis, OP: opercularis, STG: superior temporal gyrus. *indicates the motor strip after dissection. [Color figure can be viewed at wileyonlinelibrary.com]

before emerging in the deep white matter of the temporal lobe. The IFOF then continues posteriorly, adjacent to the lateral ventricle, before terminating in different parts of the cuneus and lingual gyrus. Fibers from the inferior longitudinal fasciculus and IFOF appeared to run together during fiber tracking analysis and were difficult to separate during gross anatomical dissection. The relationship between these two fiber bundles is shown in Figure 4H. The ILF can be seen to course from the cuneus and lingual gyrus down the length of the temporal lobe, with terminations in the middle temporal gyrus and temporal pole. In contrast, IFOF fibers separate from the ILF within the posterior white matter of the temporal lobe to passes medially and anteriorly to the frontal lobe.

Like the IFOF, the uncinate fasciculus (UF) arises within the pars orbitalis and pars triangularis of the IFG. However, instead of coursing posteriorly to the occipital pole, the uncinate terminates in the temporal pole. After the uncinate arises from the anterior parts of the IFG, the tract bends 90° in the rostro-caudal plane to run deep to the insula within the extreme

and external capsule. The fibers of the uncinate then separate from the fibers of the IFOF, curving another 180° before terminating in the temporal pole (Fig. 5).

A callosal connection. In addition to the four tracts described above, a callosal fiber bundle was also identified arising from the IFG (Fig. 6). These fibers typically originate within the pars triangularis with a smaller proportion of fibers arising within the orbitalis. The fibers curve gently to pass through the supero-posterior part of the rostrum of the corpus callosum before terminating in the contralateral gyrus. These findings were consistent within both cerebral hemispheres across all 10 subject brains. Few, if any, callosal fibers were identified arising from the pars opercularis.

Short-Range Association Fibers

While the IFG is associated with four large white matter tracts, a plethora of U-shaped fibers were also identified during fiber tractography. To characterize all
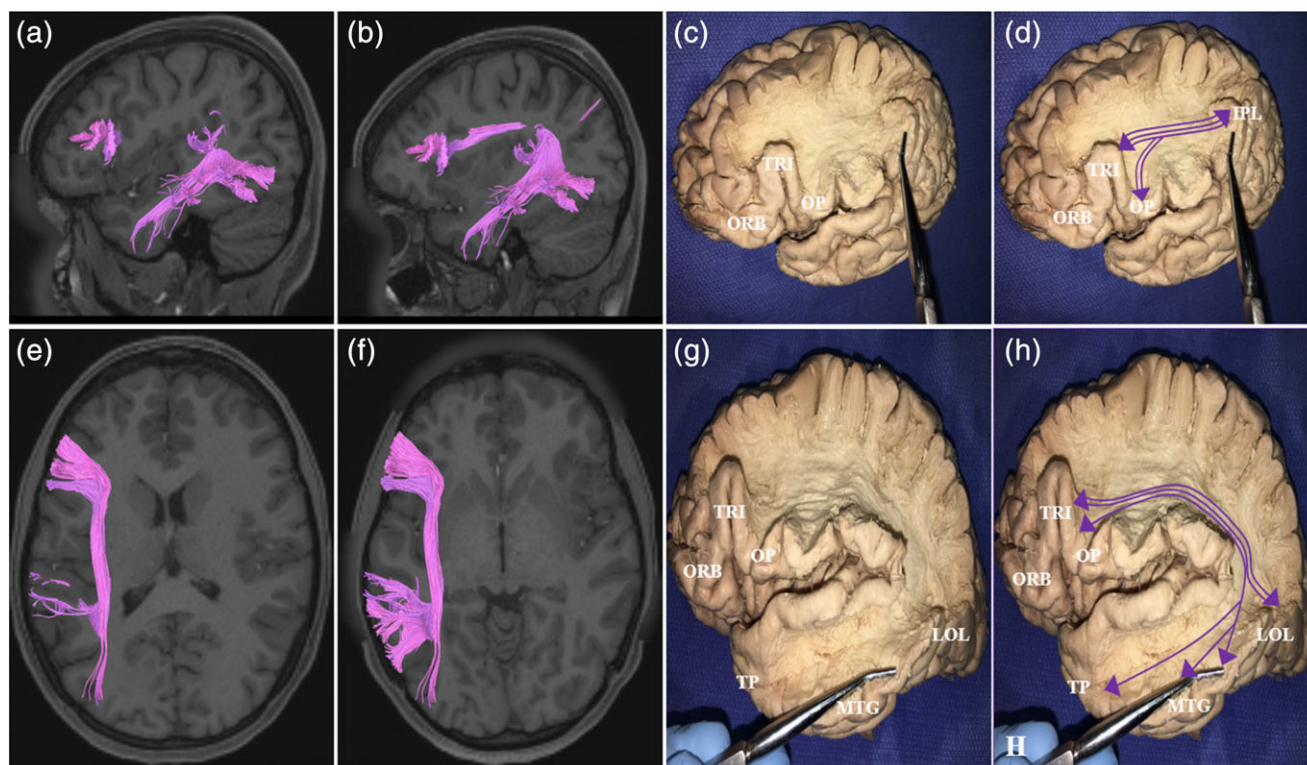
Fig. 3. (A, B) Tractographic representation of the superior longitudinal fasciculus (SLF) in the medial and lateral sagittal planes. Tractography images are shown on T1-weighted MRIs. (C, D) Gross anatomic dissection of the SLF extending from the opercularis and triangularis to the inferior parietal lobule (IPL). Purple arrows indicate the pathway of the white matter fibers. (E, F) Additional tractography of the SLF in the axial plane with fibers terminating in the occipital and temporal lobes. (G, H) Further along in the gross anatomic dissection of the SLF with fibers extending from the opercularis and triangularis to lateral occipital lobe (LOL), middle temporal gyrus (MTG), and temporal pole (TP). Purple arrows indicate the pathway of the white matter fibers. ORB = orbitalis, TRI = triangularis, OP = opercularis. [Color figure can be viewed at wileyonlinelibrary.com]

the U-shaped fibers identified during tractogrpahy is beyond the scope of this study. However, we have included a representative figure of some of the U-shaped fibers identified during gross anatomic dissection (Fig. 7). Intra-gyral fibers between the pars triangularis and pars orbitalis as well as pars triangularis and pars opercularis were identified. Fibers between the middle frontal gyrus and all three parts of the IFG were also identified, but are not shown in Figure 7. Each U-shaped fiber exhibits the same characteristic shape, arising within one part of the cortex before curving 180° to pass underneath a sulcal structure to terminate in a part of the cortex in close proximity to its origin.

Lateralization

Table 1 lists the lateralization indices comparing the FAT, SLF, IFOF, and uncinate fasciculi between left and right cerebral hemispheres during fiber tracking analysis. No differences in the lateralization indices were noted bilaterally for the tracts arising in the IFG.

DISCUSSION

In this study, we address the underlying subcortical anatomy of the IFG, a major part of the cortex involved in multiple 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). Using GQI-tractography validated by gross anatomic dissection as ground truth, we have described the connections of the IFG within the context of the neuroanatomy in 10 normal subjects and 10 cerebral hemispheres, respectively. White matter projections from the IFG to parts of the temporal, parietal, and occipital lobes were observed across subjects and cadaveric specimens with good concordance between methodologies.

Relation between Gross Anatomic Dissection and Fiber Tractography

While gross anatomic dissection allowed for qualitative understanding of tract orientation, fiber tractography
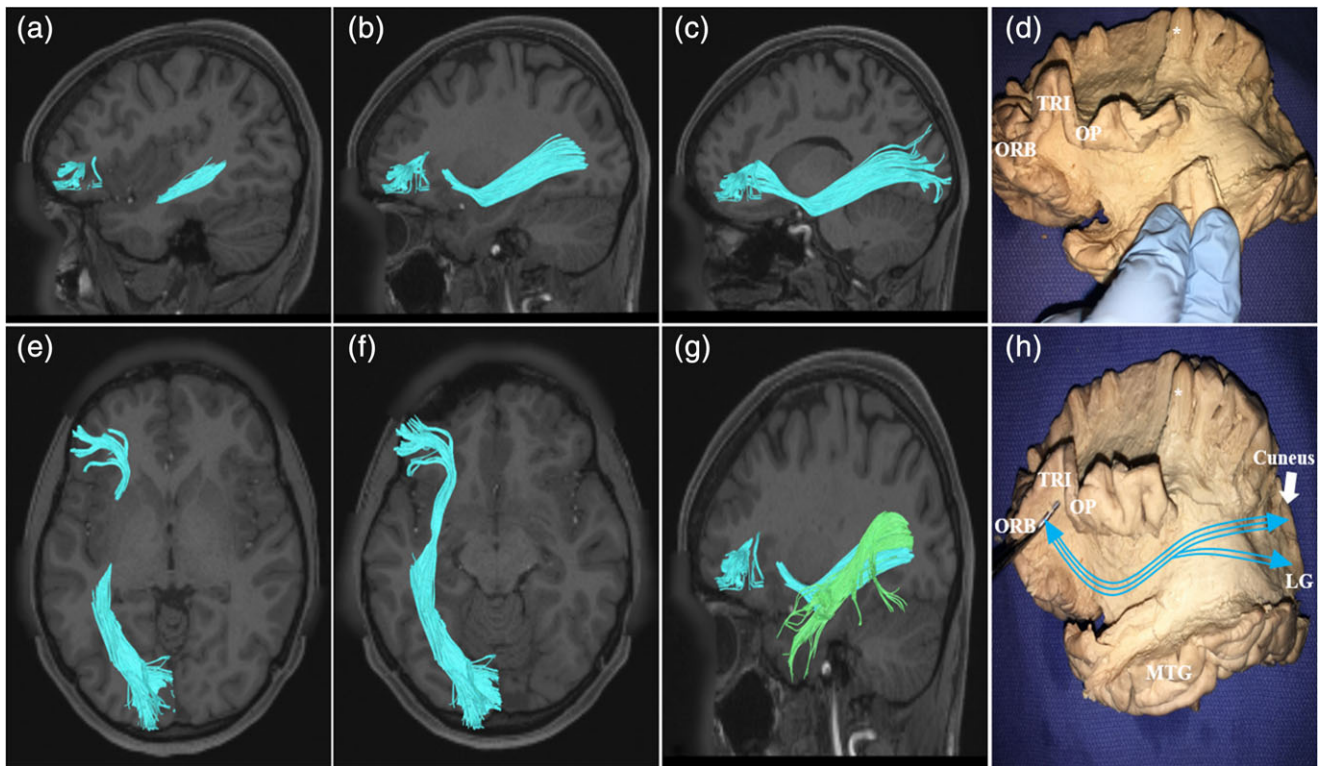
Fig. 4. (A–C). Tractographic representation of the inferior fronto-occipital fasciculus (IFOF) in the medial and lateral sagittal planes. Tractography images are shown on T1-weighted MRIs. (D, H) Gross anatomic dissection of the IFOF extending from the orbitalis and triangularis to the cuneus and lingual gyrus. Blue arrows indicate the pathway of the white matter fibers. The insula, superior temporal gyrus and inferior parietal lobule have been removed to visualize the entire tract. (E, F) Additional tractography of the IFOF in the axial plane with fibers terminating in the occipital lobe. (G) Representation of the tractographic relationship between IFOF (blue) and the inferior longitudinal fasciculus (green). Posteriorly, the green and blue fibers run together before IFOF separates to pass medially, deep to the insula and terminate in the inferior frontal gyrus. ORB = orbitalis, TRI = triangularis, OP = opercularis. MTG = middle temporal gyrus, LG = lingual gyrus. [Color figure can be viewed at wileyonlinelibrary.com]

allowed us to quantify tract volumes to understand laterality. Morphology of the major tracts was consistent across subjects and cerebral hemispheres, with long association fibers (including the FAT, SLF, IFOF, and uncinate) connecting the IFG to different parts of the parietal, occipital, and temporal lobes. Short association fibers were also identified connecting between adjacent parts of the IFG and middle frontal gyrus (MFG).

Functional Aspects of the Inferior Frontal Gyrus

Functions of the pars opercularis (BA 44). The pars opercularis, also known as Brodmann area 44 (BA 44), and the pars triangularis, known as Brodmann area 45 (BA 45), classically compose Broca's region in the IFG of the left cerebral hemisphere (Friederici 2009). Broca's area has long been associated with tasks involving the deconstruction of linguistic syntax and its analysis, as well as the construction of lexical meaning from semantic memory stores in other regions of the brain (Liakakis et al. 2011; Hagoort 2014). The contributions of the pars opercularis to language function have been demonstrated with newer technologies, including a recent study using repetitive transcranial magnetic stimulation (TMS) (Kuhnke et al. 2017). TMS applied to the left posterior IFG disrupted language processing of sentences with complex syntax (Kuhnke et al. 2017).

The pars opercularis is also recruited during phonological processing and production (Hagoort 2014). White matter connections corresponding to the FAT are thought to help coordinate the motor actions necessary for speech production (Martino et al. 2012; Budisavljevic et al. 2017; Szmuda et al. 2017). Several studies have described a white matter pathway connecting the dorsal posterior SFG in the region of
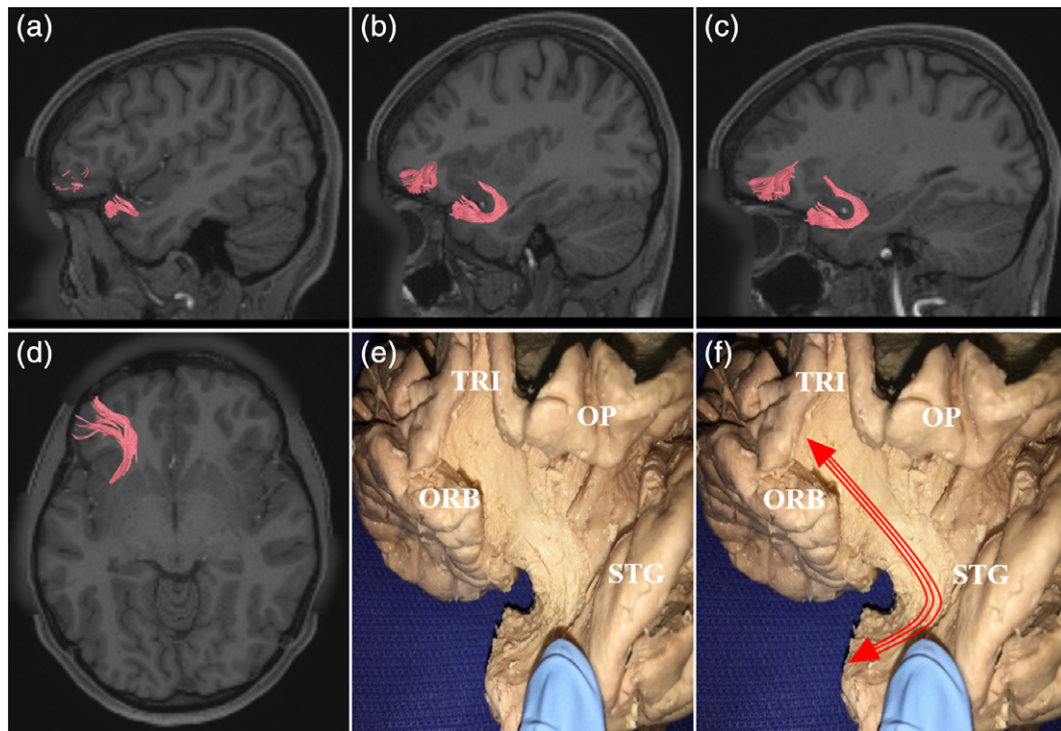
Fig. 5. (A–D) Tractographic representation of the uncinated fasciculus in medial and lateral sagittal planes (A–C) as well as the axial plane (D). Tractography images are shown on T1-weighted MRIs. (E, F) Gross anatomic dissection of the uncinate extending from the orbitalis and triangularis to the polar region of the temporal lobe. Red arrows indicate the pathway of the white matter fibers. ORB = orbitalis, TRI = triangularis, OP = opercularis, STG = superior temporal gyrus. *indicates the motor strip after dissection. [Color figure can be viewed at wileyonlinelibrary.com]

the supplementary motor area to Broca's area in the IFG (Lawes et al. 2008; Oishi et al. 2008). Our description of the FAT in this study is consistent with these results. However, others have reported that the FAT is strongly left-lateralized between cerebral hemispheres (Dick et al. 2014; Martino and De Lucas 2014). In this study, we did not find a statistically significant difference in the lateralization index between right and left cerebral hemispheres for the FAT arising from the IFG.

The pars opercularis also plays a role in motor inhibition processing (Rae et al. 2015). Specifically, the superior pars opercularis of the right hemisphere has been demonstrated to be involved in inhibiting motor responses (Rae et al. 2015). The IFG indirectly mediates response inhibition by increasing the excitatory activity of the pre-supplementary motor area as it directly influences the subthalamic nucleus to regulate and inhibit motor cortex output (Rae et al. 2015). At least one study has implicated the FAT in motor inhibition processing of bilateral hand movements (Budisavljevic et al. 2017), implicating this white matter bundle in transmitting motor inhibitory information from the IFG to the supplementary motor area.

Finally, the pars opercularis has been shown to be involved in a variety of tasks requiring working memory, such as associative learning, recall of topographic routes, and verbal memory (Liakakis et al. 2011), processes that can be disrupted under disease states. For example, pathologic activation patterns of the right pars opercularis have been implicated in the impaired agency attributions found in schizophrenia, reflecting a role for BA 44 in the disentanglement of information regarding neural representations of self and others (Backasch et al. 2014). Additionally, patients with behavioral-variant frontotemporal dementia have demonstrated deficits in categorizing the type of emotion displayed by the gait patterns of 3D-generated avatars (Jastorff et al. 2016). These deficits were attributed to disrupted communication between the left IFG and the contralateral anterior insula, amygdala, and anterior temporal lobe (Jastorff et al. 2016). The series of structural connections disrupting communication between these areas is not yet fully understood. However, research into the dynamic causal processes of the cerebral cortex may elucidate these connections in the future.

Functions of the pars triangularis (BA 45). As noted above, the pars triangularis (BA 45) comprises part of Broca's area along with the pars opercularis (BA 44). Whereas the opercularis mediates the processing of syntactic information, the pars triangularis is
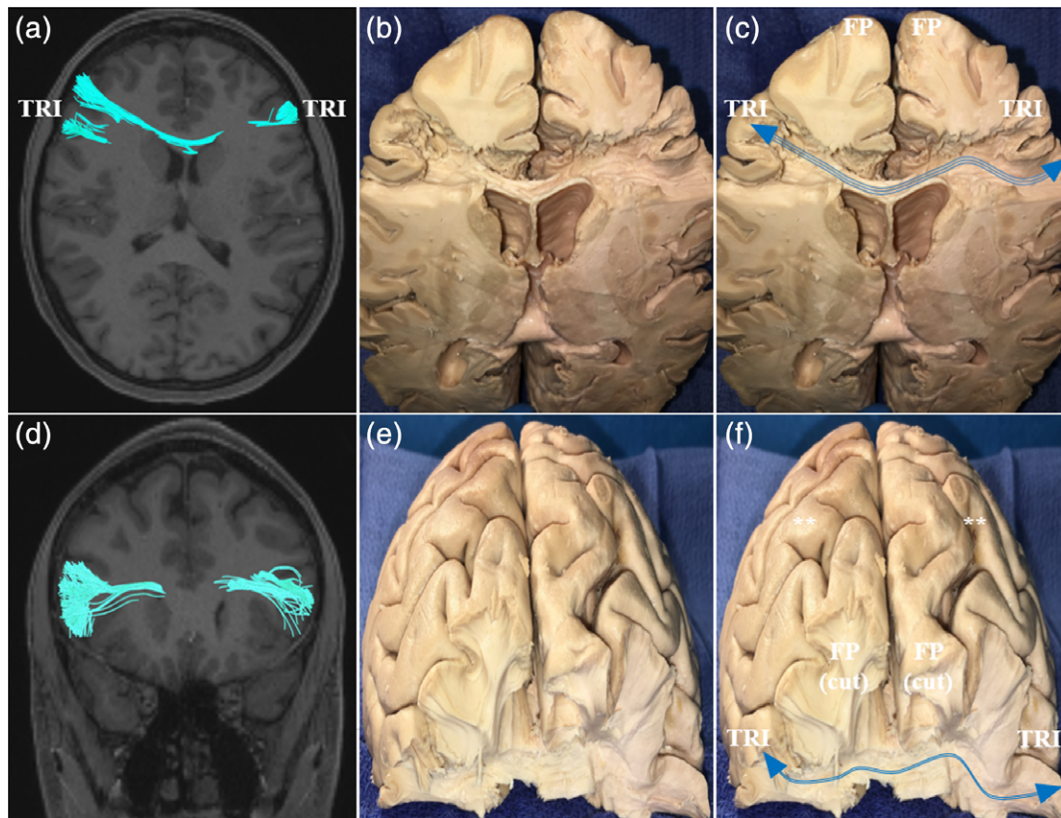
Fig. 6. (A) Callosal contralateral fibers (light blue) originating and terminating within the inferior frontal gyri bilaterally. Fibers are shown on an axial T1-weighted MRI. (B, C) Cadaveric dissection of the callosal fibers (blue arrows) in the axial plane. (D) Callosal contralateral fibers (light blue) are shown again originating and terminating within the inferior frontal gyri bilaterally on a coronal T1-weighted MRI. (E, F) Cadaveric dissection of the callosal fibers (blue arrows) in the coronal plane. The frontal poles (FP) have been removed to show the horizontal orientation of the fibers. TRI = triangularis, FP = frontal pole. *indicates the motor strip. [Color figure can be viewed at wileyonlinelibrary.com]

heavily involved in semantic, phonologic, and syntactic processing in the left hemisphere (Jeong et al. 2009; Liakakis et al. 2011; Zhu et al. 2012; Hagoort 2014). The left triangularis has also been implicated in such tasks as the generation of rhymes, synonyms, inner speech, lexical decision-making, and the retrieval and unification of semantic information (Liakakis et al. 2011; Zhu et al. 2012; Hagoort 2014). However, such semantic functionality does not appear to be limited to the left hemisphere (Miotto et al. 2014; Tabei 2015). For example, in one study researchers found that after patients underwent resection for low-grade gliomas in areas known to support semantic memory, patients eventually recruited homologous regions in the contralateral hemisphere to support the semantic processes disrupted during tumor removal (Miotto et al. 2014). A second study has demonstrated that the right pars triangularis as well as the left pars orbitalis are recruited in perceptual emotion tasks, in which participants are required to determine the specific emotion that songs

are intended to evoke (Tabei 2015), further supporting a role for bilateral semantic task activation in the IFG.

Disruption of the functional connections between the pars triangularis of the left IFG and other cortical areas is associated with several neuropsychiatric disorders including schizophrenia (Jeong et al. 2009) and generalized anxiety (Cha et al. 2016). In schizophrenia, both functional and anatomic connectivity deficits have been reported in functional magnetic resonance imaging and diffusion tensor imaging studies involving the left pars triangularis, left middle temporal gyrus, left superior temporal sulcus, and the white matter tracts connecting these areas, including the superior longitudinal fasciculus/arcuate fasciculus complex, the inferior fronto-occipital fasciculus and the inferior longitudinal fasciculus (Jeong et al. 2009). These features have been hypothesized to underlie the abnormal semantic processing found in schizophrenia (Jeong et al. 2009). Persistent organic psychosis has also been reported following damage to
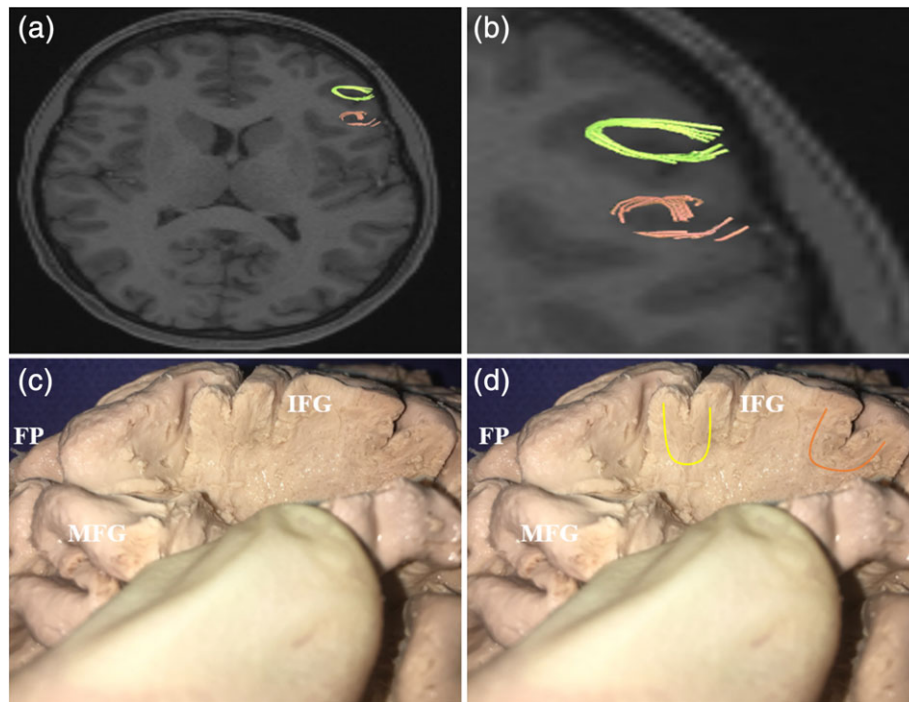
Fig. 7. Representative figure of U-fiber tractography and dissections. Intra-gyral U-shaped fibers were identified between the triangularis and opercularis (brown) and the triangularis and the orbitalis (yellow). U-shaped fibers were also identified between the inferior and middle frontal gyri (IFG, MFG), but are not shown here. FP = frontal pole. [Color figure can be viewed at wileyonlinelibrary.com]

the right IFG and its underlying white matter tracts, including the superior longitudinal fasciculus, secondary to hemispheric stroke (Devine et al. 2014).

In generalized anxiety disorder (GAD), the left IFG has been implicated as playing a regulatory role in threat evaluation (Cha et al. 2016). For example, it has been shown that the left IFG is involved in the evaluation of ambiguous stimuli with subsequent activation of the left ventromedial prefrontal cortex as to the nature of the stimulus, i.e. whether the stimulus is benign or threatening (Cha et al. 2016). Threat evaluation processing then continues within the amygdala (Cha et al. 2016). Putatively, the uncinate fasciculus has been proposed as the structural connection mediating this processing between the IFG, ventromedial prefrontal cortex and amygdala in the left cerebral hemisphere (Cha et al. 2016).

Finally, the pars triangularis in the right cerebral hemisphere has been implicated in sensorimotor

integration related to fine motor control (Papadelis et al. 2016), such as in tasks related to inhibition of movement, lifting objects with changing weight, go/no-go tasks, and movement imitation (Liakakis et al. 2011). For example, the right caudal IFG has been reported to interface external motor information of the hand and arm with an internal representation of their movements, while the right rostral IFG shows activity during visuomotor tasks requiring continuous error-monitoring (Papadelis et al. 2016). Such integration of visual and motor information is thought to be mediated by the inferior fronto-occipital fasciculus, allowing the delivery of information to and from areas of the frontal cortex and extrastriate visual areas (Papadelis et al. 2016).

Function of the pars orbitalis (BA 47). As with the pars triangularis and the pars opercularis, the pars orbitalis (BA 47) has been implicated in a variety of functions. The most inferior portion of the left pars orbitalis plays a role in behaviors related to emotion and empathy (Liakakis et al. 2011). For example, increased functional activity in this region has been demonstrated when individuals laugh or observe others laughing (Liakakis et al. 2011). The left orbitalis also shows increased functional activity when individuals experience subjective feelings of guilt (Liakakis et al. 2011). In one experiment conducted to study the neuroanatomic substrates of interpersonal interaction, the right

TABLE 1. Lateralization Indices for Inferior Frontal Gyrus White Matter Tracts

Tract	Volume/ Tract (left)	Volume/ Tract (right)	LI	P-value
FAT	20.4	24.0	−0.079	0.41
IFOF	24.3	27.0	−0.044	0.54
SLF	19.2	20.2	−0.013	0.85
Uncinate	28.4	34.0	−0.135	0.61

orbitalis was found to become active when an agent was required to cooperate with a helper to achieve a task. This region also showed increased activity during competitive blocking tasks requiring individuals to prevent agents from achieving their intended goal (Liu et al. 2015).

In disease, the left pars orbitalis exhibits reduced functional connectivity with regions of the default mode network in patients with bipolar disorder, possibly leading to some of the characteristic attributes described in the disease, such as the unwanted intrusion of emotional rumination (Roberts et al. 2017). Deficits from damage to the right orbitalis have also been seen in cases of anosognosia for hemiplegia following stroke (Kortte et al. 2015), highlighting the role of this region in identifying and understanding one's own motor behavior.

The right pars orbitalis is also involved in the construction of subjective confidence through the evaluation of prior expectations (Sherman et al. 2016). The right IFG is involved in a network consisting of the orbitofrontal cortex, which is responsible for inputs related to expectations and attention, and the intracalcarine sulcus, which is responsible for sensory input processing (Sherman et al. 2016). The right pars orbitalis is involved in calculating the discrepancy between an individual's prior expectations and his or her perceptual reality, to generate a confidence measure that is applied to an individual's cognitive choices (Sherman et al. 2016). The IFOF likely mediates part of this processing, as it connects parts of the cuneus and lingual gyrus around the calcarine sulcus to the IFG.

CONCLUSIONS

The inferior frontal gyrus is an important region implicated in a variety of tasks including language comprehension, speech production, semantic processing, fine motor control, interoceptive awareness, and emotion. The corresponding cerebral networks related to these functions involve a complex series of white matter tracts, including the superior longitudinal fasciculus/arcuate fasciculus complex, frontal aslant tract, uncinate fasciculus, and the inferior fronto-occipital fasciculus which integrate within and connect to the inferior frontal gyrus. 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 the inferior frontal gyrus.

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