Chapter 4

Macroconnectomic networks of the human brain

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Introduction

Part of why we often cause deficits we don't understand is that we are working with outdated models of the brain and its organization, sometimes ones created by people dead for around 130 years. The idea that higher brain functions can be assigned to individual areas of cortex has long been debunked and we should stop teaching it. We should also stop teaching trainees that there are unimportant parts of the brain. Bad models lead to bad results.

The brain is extremely complex and one chapter is unlikely to provide all the answers, but this chapter is written to update surgical models based on the following principles:

(1) Brain functions arise from large-scale structures synchronizing their oscillatory activities in the proper context.
(2) Cortical organization can better be described in terms of large-scale collections of areas which coordinate their activities more often than they do with other areas. These are termed brain networks.
(3) Large-scale networks are usually connected physically by set of white matter bundles.
(4) Most higher cognitive functions result from within network activity or coordination of networks.

This discussion is organized around the major white matter bundles which we first describe and then describe the networks they describe. Because most networks can be easily described as a single tract or a small set of tracts, this seems like a logical grouping. This is also why diffusion tractography is such a useful tool in knowledgeable hands: if you know the tract location, you can usually predict where the function is.

New Techniques for Management of 'Inoperable' Gliomas. https://doi.org/10.1016/B978-0-12-813633-1.00004-9

The basic organization of the human white matter

While the white matter of the human cerebrum contains a massive number of connections, one simple grouping (Fig. 1) breaks them into three groups based on their basic orientation: the anterior-to-posterior lateral tracts, the rostral-to-caudal middle system, and the more complex medial system which includes the c-shaped corpus callosum weaving between several anterior-t-posterior tracts. Notably, a few tracts, including the FAT, are orthogonal to this schema, but mostly this works as a starting point. Fig. 2 summarizes the tracts contained within each system.

Middle system and the FAT

These are grouped together as they summarize much of the motor system (Fig. 3). The corticospinal tract is well known to most readers. The Frontal

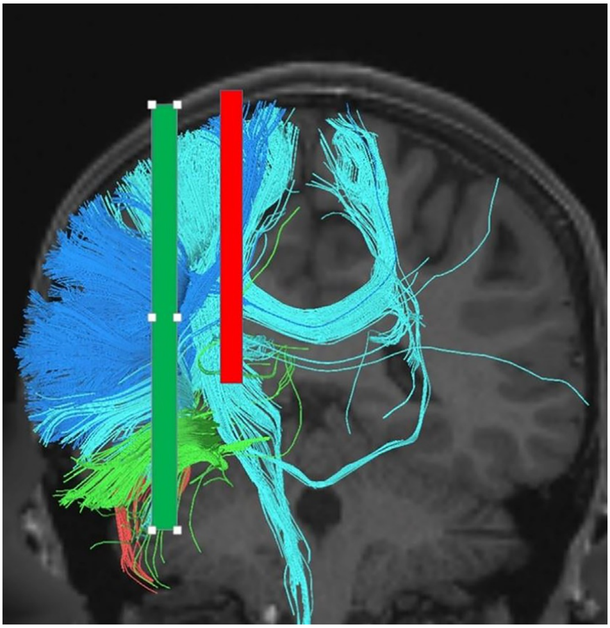

FIG. 1 A basic schematic overview of the white matter systems of the brain seen in coronal section. The *red lines* depict a set of arbitrary boundaries between the lateral, middle, and medial fiber systems. The lateral systems include the SLF, the IFOF, the ILF, the optic radiations, and the uncinate fasciculus. These fibers are principally running along the anterior-to-posterior axis. The medial system includes the cingulum, fornix, and corpus callosum and run either anterior to posterior or commissural (i.e., the corpus callosum). The middle system includes the corticospinal tract, the thalamic peduncles and their connections with the cortex, and the cortical communications with the basal ganglia, all of which make up the corona radiata. These fibers run along a rostral-caudal axis. There are tracts which cross these systems, namely the FAT, the middle longitudinal fasciculus (MdLF), the lateral thalamic peduncle, and the crossed semantic loop, however, most tracts obey this scheme.

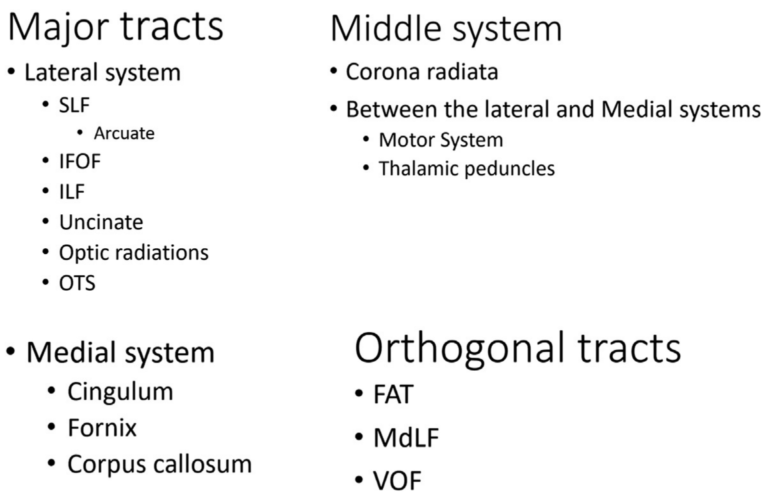

FIG. 2 A summary of the grouping of tracts contained within each of the groupings.

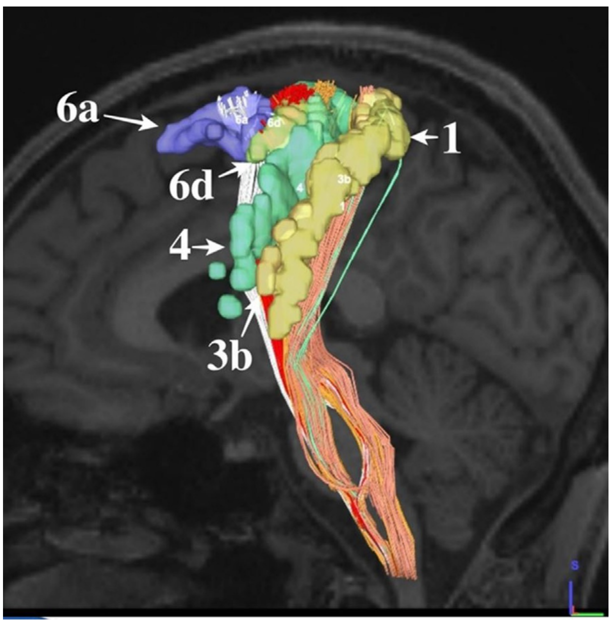

FIG. 3 Basic anatomy of the motor system.

Aslant Tract (FAT) (Fig. 4) was not really known until the diffusion tractography able to resolve crossing fibers showed that this large bundle was interdigitating into the superior longitudinal fasciculus (SLF). In short, the FAT connects the supplementary motor area to premotor areas including Broca's

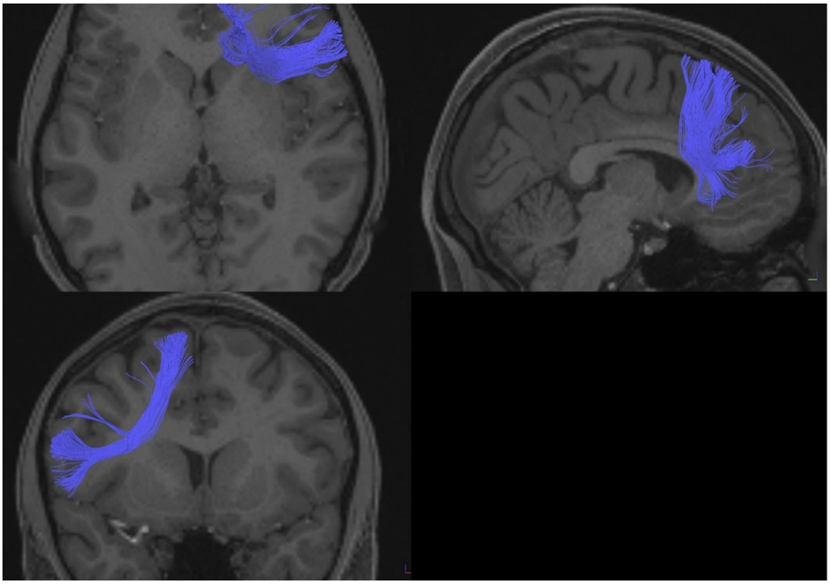

FIG. 4 Tractographic anatomy of the frontal aslant tract.

area, and links up parts of the salience network (described in more detail with the default mode network (DMN). The importance of preserving this orthogonal pathway is discussed in other chapters.

Cumulatively, the motor system is bouquet shaped and expands superiorly due to the number U-fiber and SLF connections between premotor, motor, sensory, and parietal cortices (Fig. 5). Also, as shown in Fig. 6, there are substantial contributions by SLF pathways to much of the premotor system, which has dorsal, ventral, and middle components.

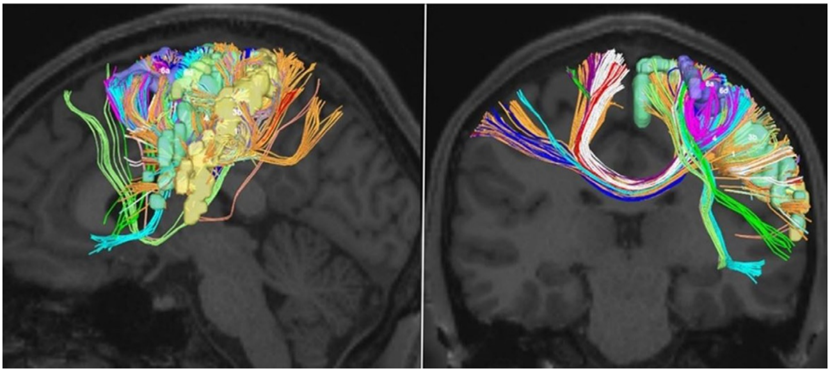

FIG. 5 Anatomy of the motor system minus the descending fibers.

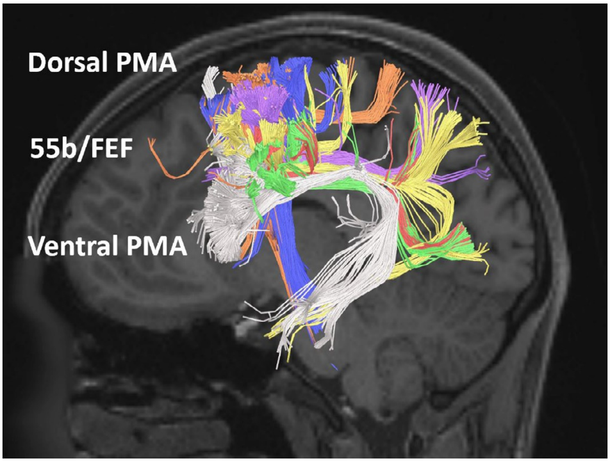

FIG. 6 Images demonstrating premotor system and its dense interconnections via U-fibers with the sensorimotor cortices and the parietal lobe, and its connections via the SLF/arcuate complex.

Lateral tracts

Superior longitudinal fasciculus

We start with the SLF as it is the dominant lateral tract, and it dominates our thinking about functional networks and glioma surgery. It is a massive tract, which covers a great deal of ground, and its preservation is integral to leaving the patient as a functional person. There are a large number of networks whose primary hubs require communication via the SLF, including the speech, neglect, praxis, and attention networks, and this means that there are few better ways to hurt someone than cutting through the core of the SLF complex.

The SLF has been described as being composed of four layers with the arcuate fasciculus being the lateral part of this tract, the arcuate fasciculus, and the SLF I, SLF II, and SLF III. In the description of functional networks, it is quite helpful to know these distinctions, as they help to reduce the mental complexity of this extensive tract to usable subunits. In surgery, these distances between systems are generally not observable or actionable, and thus distinctions are academic, and you should view the SLF as a single large tract.

It is easy to mistakenly view this as a c-shaped tract, as the bulk of it mirrors the c-shape of the hemisphere, however, by viewing it as a modified-Y shape (Fig. 7), you remind yourself of the parietal ramus, which is sizeable and essential for networks which engage the inferior parietal lobule, such as praxis. This ramus is the lateral margin of most medial parietal cuts, so it's critical to know it.

The most obvious endpoints of the SLF complex are the supramarginal gyrus, the inferior parietal lobule, and the middle frontal and triangularis/orbitalis parts of the inferior frontal gyri (Fig. 8). The fact that this tract links the major language centers of the left hemisphere should be obvious to most

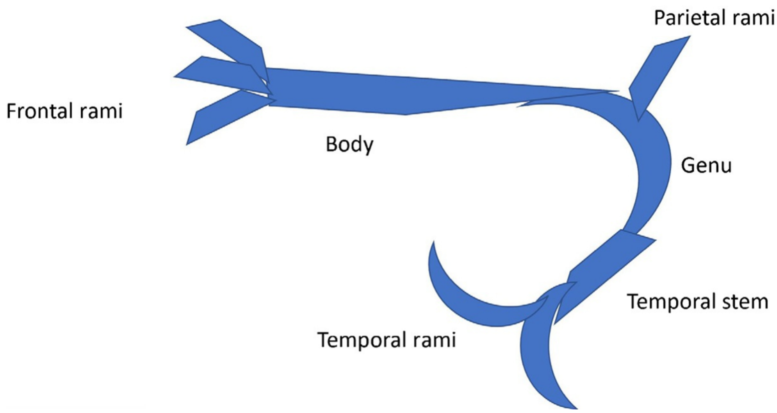

FIG. 7 Schematic representation of the basic organization of the SLF/arcuate system viewed as a single unit.

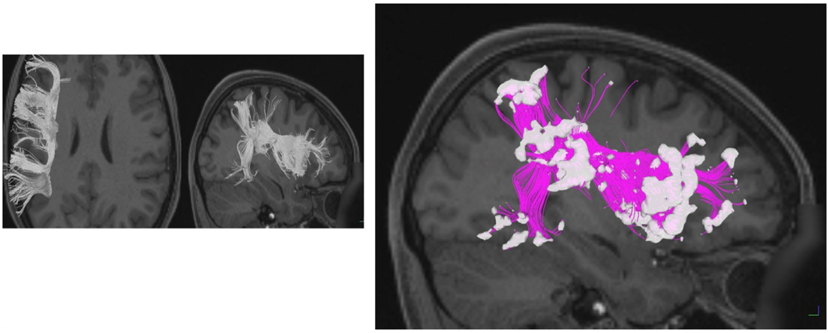

FIG. 8 Anatomy of the SLF, including tractographic images and a schematic demonstrating a simplified version of the anatomy of the SLF including its three primary rami. The image on the left demonstrates the anatomy of the tractin axial and sagittal projections. The image on the right indicates a *white balloon* on all of the termini of the tract, demonstrating its targets.

neurosurgeons, and this is how I view the left SLF, as a highway for phonemic and syntactic aspects of speech. It is critical to note that the SLF is fundamentally more complex than this, and it's carrying a great deal more information than this.

The SLF creates a virtual wall over the lateral hemisphere, and often makes the direct lateral approach to deep targets challenging or impossible.

Networks inside of the SLF system

Semantic language

A model of this left sided system shows many of the usual players, areas 44 and 45, the posterior MTG and superior temporal sulcus, and the arcuate connecting

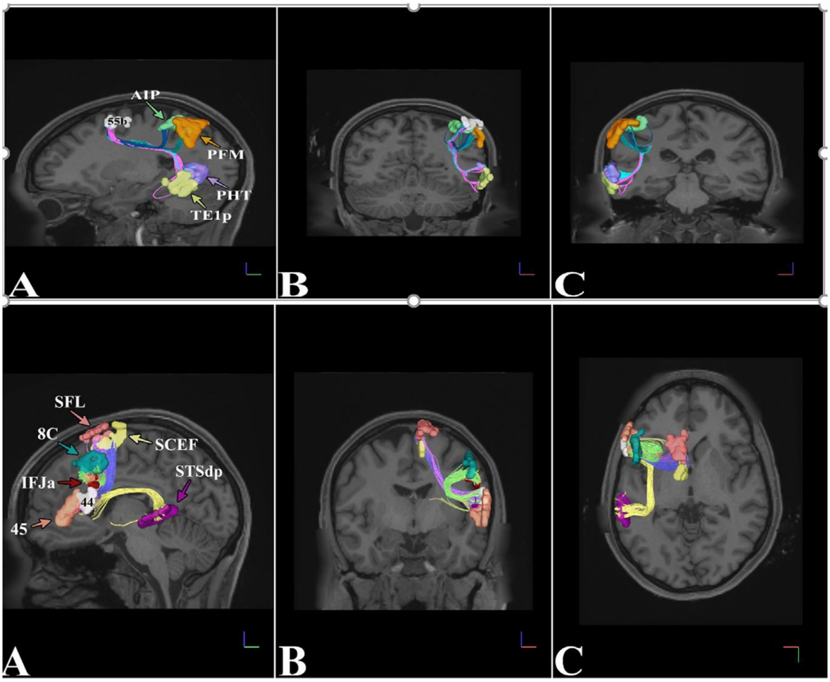

FIG. 9 Anatomic organization of the semantic language system. (A, B, C) demonstrate the two pathways in (A) sagittal, (B) coronal, and (C) axial planes.

them (Fig. 9). New to this model is area 55b, which is connected to the semantic language areas by SLF 2, as well as parietal contributions. SMA contributions to area 44 and neighboring areas like area 8C come from the FAT.

Auditory network

Connectomics has shown us that the auditory areas are highly complex with several subregions in the Heschl's gyrus and superior temporal gyrus (Fig. 10). These bilateral networks have their own connections via the arcuate to area 44, which is also part of this network as is 8C and the SMA.

Praxis network

Tool use is a left SLF network, interestingly though it also involves area 44 and other frontal regions involved in speech (Fig. 11). This highlights the fact that Broca's area is more complex than we have given it credit for.

Neglect

Our studies confirm others work that neglect results from damage to the right SLF (Fig. 12). The network model is interesting and despite our initial thought

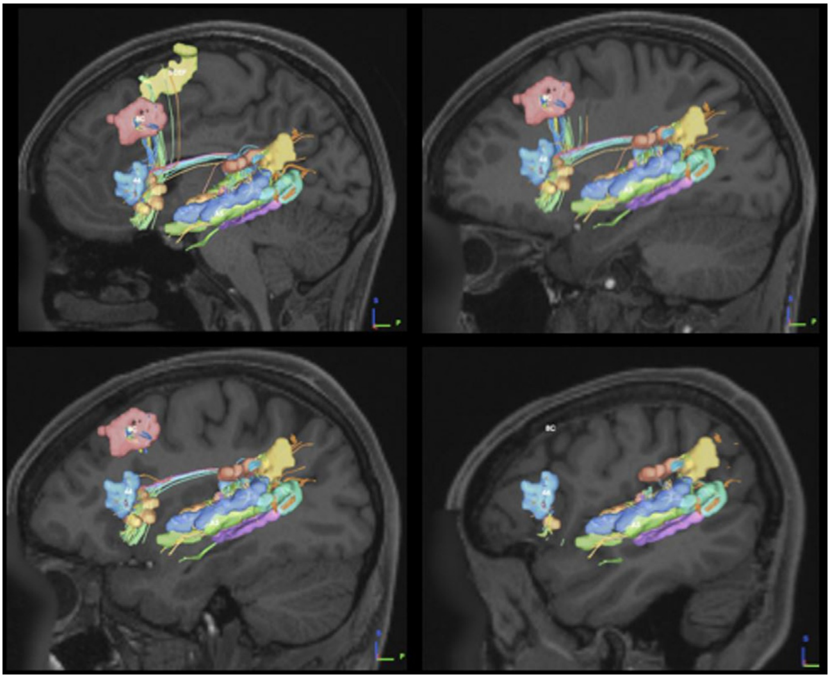

FIG. 10 Anatomic organization of the auditory network.

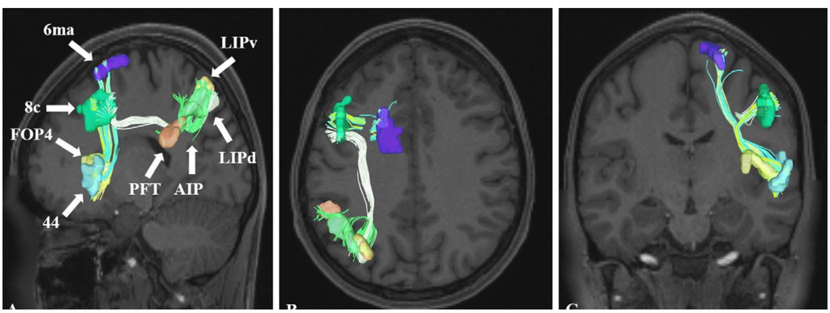

FIG. 11 Anatomic organization of the praxis network.

that this would result from the dorsal or ventral attention networks, the data support a more complex model linking parts of the olfactory, auditory, somatosensory, executive, and dorsal attention networks as well as an analog of the semantic network on the right at the superior temporal sulcus. Our best hypothesis is that the true network is not the cortical areas, but the wires which connect them in the SLF. This is consistent with what the binding problem neglect has thought to represent, namely creating a coherent view of the world from mixed sensory modalities.

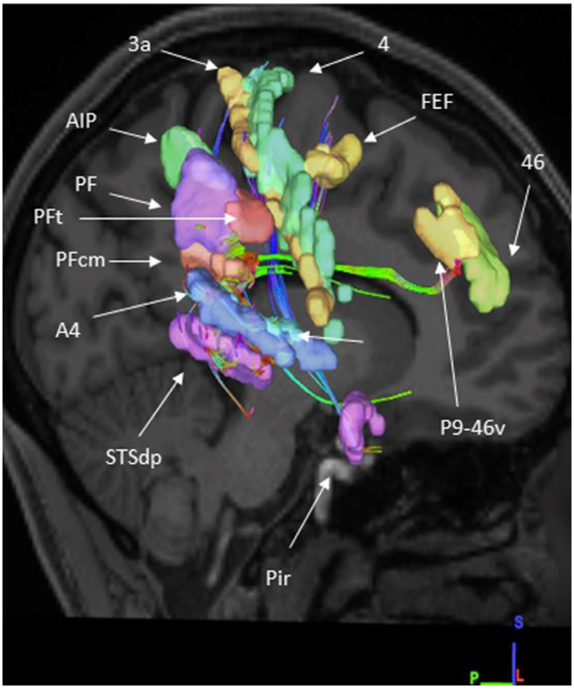

FIG. 12 Anatomic organization of the neglect network.

Dorsal attention network

This network (Fig. 13) is bilateral and is inside the SLF involving the frontal eye fields, the intraparietal sulcus, and the lateral visual areas. Interestingly, this network has shown up in many of our studies of higher cognitive abilities, such as math, and we currently think it is part of allocating cognitive resources to higher tasks.

Ventral attention network

This is a right sided network which also is an SLF network (Fig. 14).

Executive control network

This is one of the dominant networks of the human cerebrum and is involved in organizing goal-directed behaviors. It is discussed further with the control networks, such as DMN and salience networks, but as shown in Fig. 15, it is an SLF I-type network.

Inferior fronto-occipital fasciculus

The inferior fronto-occipital fasciculus (IFOF) is a large tract, however, it has a specific clinically important aspect for its anatomy (Fig. 16). It runs from

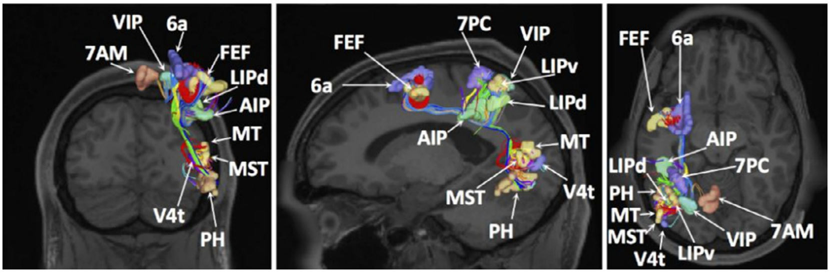

FIG. 13 Anatomic organization of the dorsal attention network.

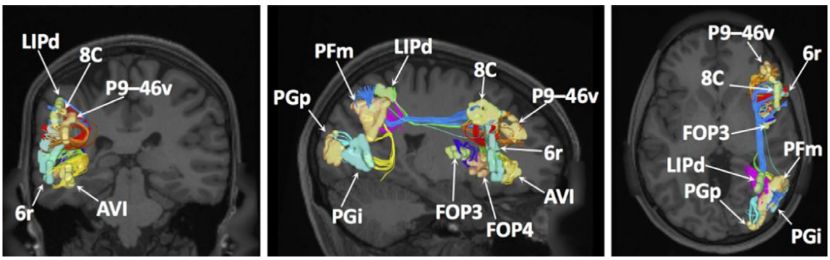

FIG. 14 Anatomic organization of the ventral attention network.

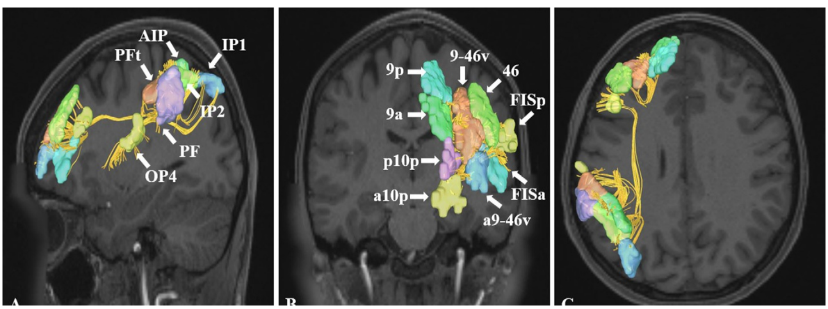

FIG. 15 Anatomic organization of the central executive network.

anterior to posterior connecting the inferior occipital and frontal lobes. While the tract fans out anteriorly in the frontal lobe and posteriorly in the occipital lobe, it is a tight bundle in the insula and limen insula. This means that if you are in IFOF fibers in the frontal or occipital regions you are working on fibers relevant to the area you have cut into, but in the insula you can destroy a lot of the tract all at once.

The occipital origins (Fig. 17) of this tract are principally in the lingula and cuneus and after hooking superiorly around the preoccipital notch before diverging from the inferior longitudinal fasciculus (ILF) and crossing at the TPO junction as a largely compact bundle. After bending anterosuperiorly at

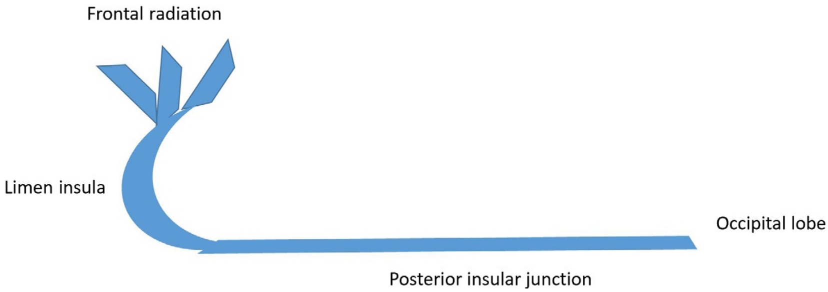

FIG. 16 Schematic representation showing the basic organization of IFOF.

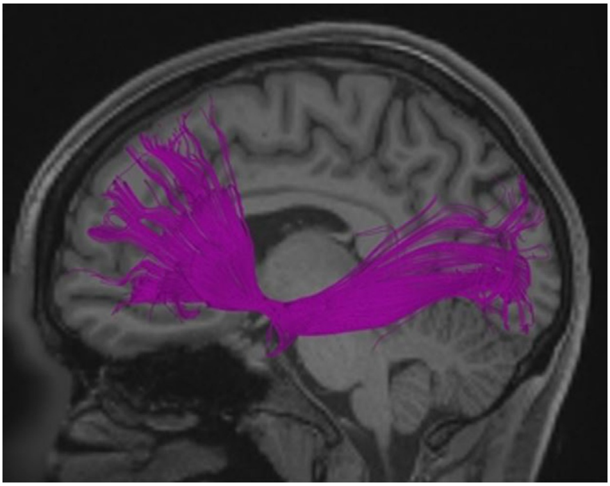

FIG. 17 Tractographic anatomy of the IFOF.

the limen insula, the fibers fan out. The bulk of these fibers head to the SFG where they interact with a large length of the gyrus. There are also communications with the IFG, and a lesser communication with the MFG.

Of note there is no SFOF that has been debunked, but the name stuck.

Inferior longitudinal fasciculus

The ILF is an anterior-to-posterior tract running from the occipital pole to the temporal pole running just deep into the fusiform gyrus on the inferior temporal/occipital surface (Fig. 18). This tract does not typically block a lateral approach to a deeper target in the way other lateral tracts do, however, it is a common path for the spread of gliomas.

It primarily connects the inferior temporal gyrus to the lingula, though some fibers extend superiorly into the temporal pole.

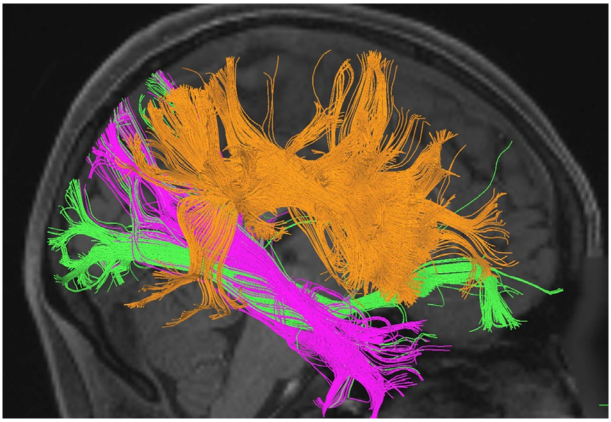

FIG. 18 Tractographic anatomy of the lateral system showing the SLF system in *orange*, the IFOF in *green* and the ILF in *pink*. Note that the ILF and IFOF begin together just above the preoccipital notch.

Uncinate fasciculus

Most of us are aware that this tract runs in the limen insula and connects the frontal and occipital lobes. Specifically, it connects the inferior frontal gyrus, pars triangularis to the anterior temporal lobe (Fig. 19).

It is laterally positioned relative to a similar bend in the IFOF, and this has caused the functions of these two tracts to become confused. Its most clinically relevant attribute is as a pathway of spread of gliomas from the temporal to the frontal lobes through the insula.

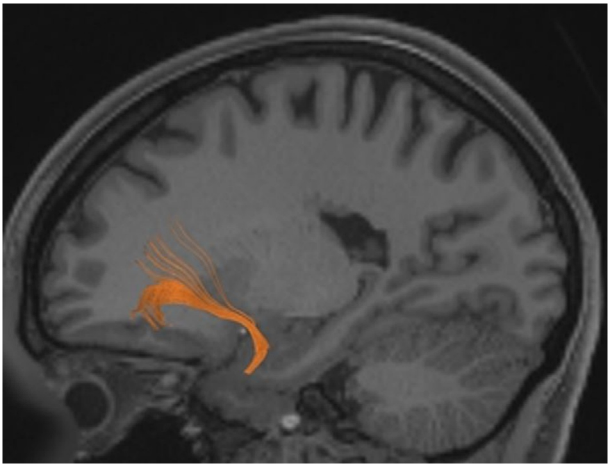

FIG. 19 Tractographic anatomy of the uncinate fasciculus.

IFOF/ILF/uncinate and the role of the temporal pole in language

There are ample data supporting the role of the left temporal pole in language. This has been termed semantic language, however, this is an unfortunate term, as the semantic areas (those which activate during tasks of semantic language) do not have substantial connections via the IFOF or ILF to the temporal pole. Various two-pathway models have been proposed about how these language problems occur. One model involves visual information flowing to area 45 via the IFOF. The problem we have found with this model is that none of the visual areas we have found connected to IFOF are high-level visual areas involved in object recognition, they are mostly connected to V1–4 and the dorsal visual stream (“where” pathway), neither of which seems to directly provide information needed to make visual matches by itself. Another involves the ILF carrying visual information to the temporal pole via ILF, which then communicates with area 45 via the uncinate. This is possible but the meaning of words is strongly localized to the back of the left temporal lobe in most people, and it’s hard to fit the ILF into that model. The most plausible model we are aware of (Fig. 20) involves a band of u-fibers in the middle temporal gyrus which directly links the semantic areas to the temporal pole. The functional connectivity map strongly suggests this is the connection and we and others have noted these fibers. This does not preclude a role for ILF or IFOF in the cognitive aspects of speech, as the visual system requires a large amount of top-down regulation to determine its processing scheme, and ILF and IFOF are well connected to do this. It is just hard for us to believe that by themselves they can help match visual images to words given their connection patterns.

This is obviously a critical question given the central importance of working in the temporal lobe in neurosurgery. Solving this mystery definitively is one of the greatest challenges of our generation.

The visual system

It is an understatement to say that the human visual system is highly complex, despite being localized to the occipital lobe. A substantial percentage of the white matter in the brain aims to link the visual system to the rest of the brain. Several tracts not previously described are discussed briefly with reference to the visual system.

Optic radiations

These are probably one of the better known white matter tracts to neurosurgeons so I will not belabor the point (Fig. 21). Probably the most surgically important aspect of this anatomy is that the optic radiations comprise the majority of the lateral wall of the atrium of the lateral ventricle, a fact which radically alters the ideal approach to the atrium and similarly positioned structures.

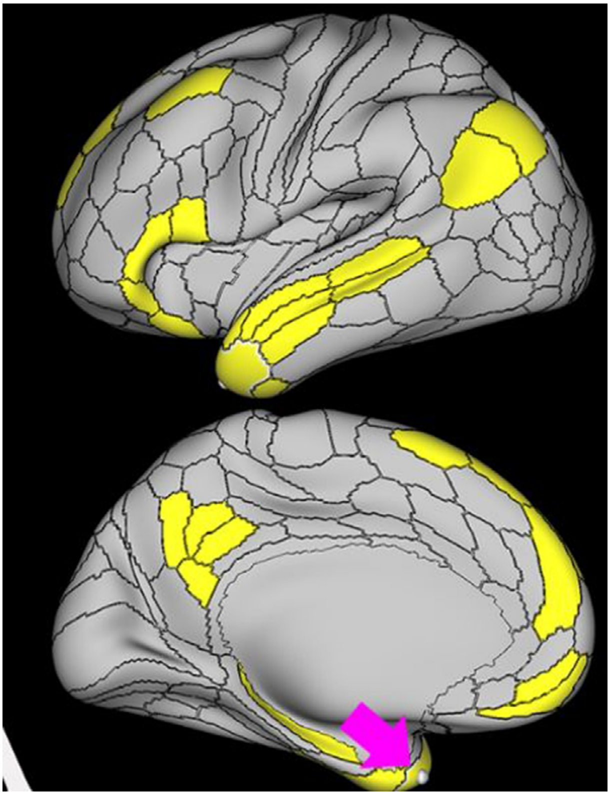

FIG. 20 Functional connectivity of area TGd which comprises the majority of the temporal pole. Note that the semantic areas in the superior temporal sulcus show connectivity to this area in a band which we have found is connected by a unique series of U-fibers running parallel to these areas. Also note that the default mode areas are also activated showing language and memory are DMN-related networks.

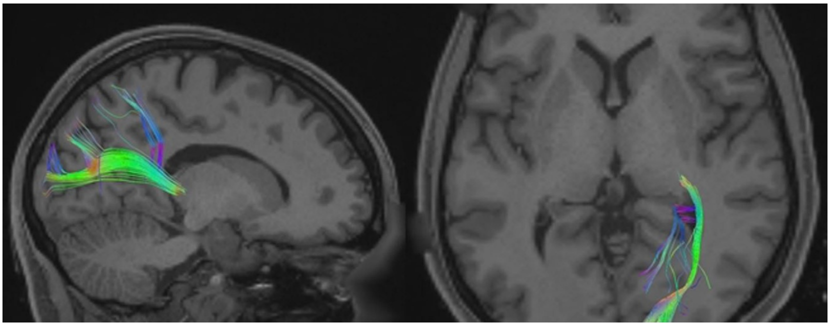

FIG. 21 Tractographic anatomy of the optic radiations.

It is also of relevance to note that the visual system probably works in large part by communicating with the pulvinar which are critical in serial visual processing. These fibers generally run in the same bundle as the optic radiations. There are numerous examples of this fact worth noting demonstrated in this chapter.

Middle longitudinal fasciculus

This is a misnamed tract as it is not a longitudinal tract (Fig. 22) in the way the SLF or ILF are. It would be better termed the occipital aslant tract (the OAT), as it runs from the medial to the lateral systems similar to the FAT.

It principally connects the upper cuneus to the superior temporal gyrus. The most logical explanation is that this is a mechanism of linking the dorsal visual pathway (which has later level processing cortices in these regions) with the semantic areas.

Vertical occipital fasciculus

While there has long been a goal to segregate the visual processing into the ventral ("what" pathway) and dorsal ("where" pathway) streams, the vertical occipital fasciculus (VOF) (Fig. 23) is a vertical pathway which directly connects these two areas.

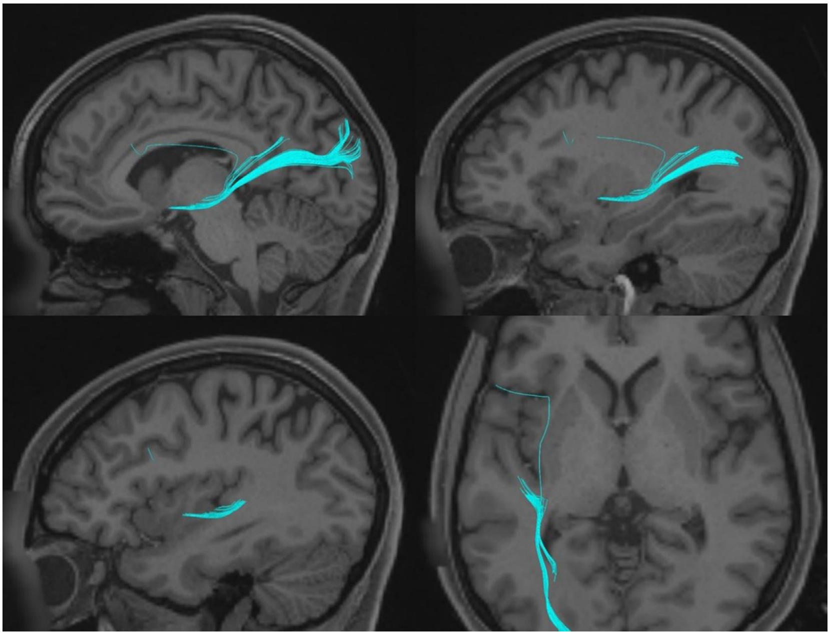

FIG. 22 Tractographic anatomy of the middle longitudinal fasciculus.

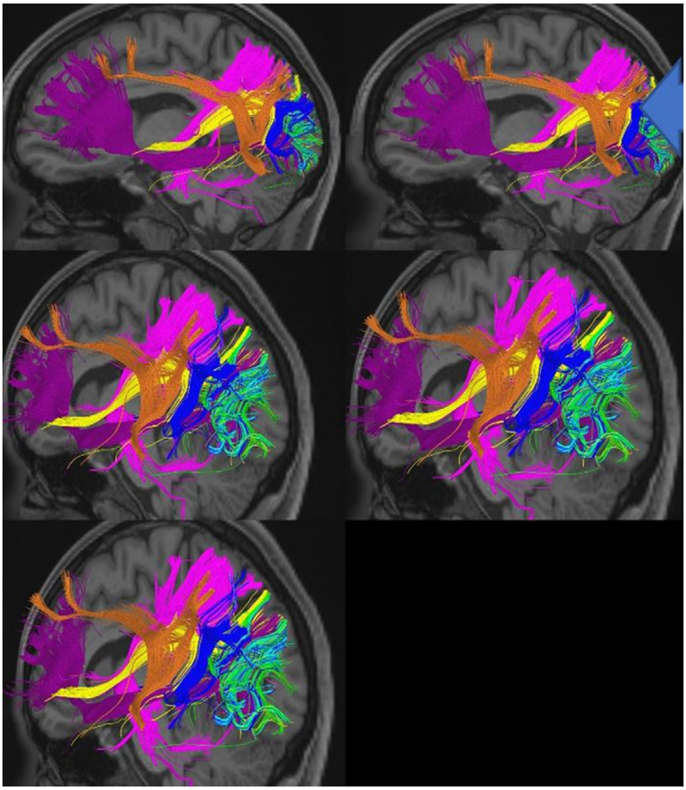

FIG. 23 Tractographic anatomy of the VOF in the greater context of the white matter of the entire visual system. Note that the VOF is the *orange* vertical pathway with an *arrow* highlighting it.

Occipitotemporal system

The occipitotemporal system (OTS) (Fig. 24) is the system of the lateral occipital lobe, and is composed of a dense collection of large and small U-fibers which connect the lateral occipital lobe. It is probably involved in reading.

Medial tracts

Cingulum

The cingulum is a c-shaped tract which runs in the center of the cingulate gyrus, the isthmus, and the parahippocampal gyrus (Fig. 25). Its primary branches are the superior frontal and subparietal gyri (probably part of the default mode network).

Corpus callosum

This well-known tract is really a collection of numerous c-shaped bihemispheric connections (Fig. 25). The basic parts (from anterior to posterior) are the rostrum, genu, body, and splenium. The majority of the callosal fibers connect

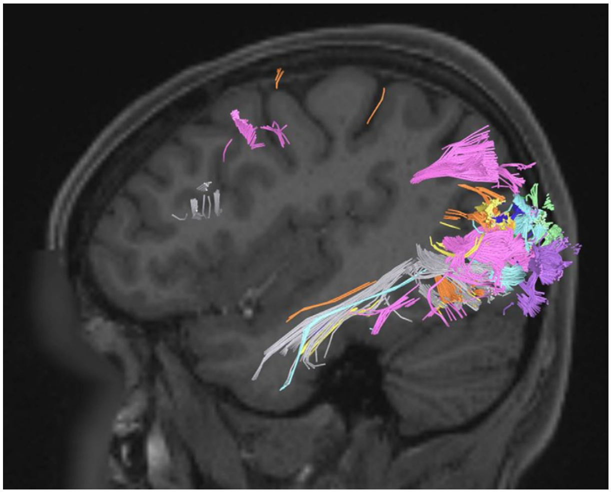

FIG. 24 Tractographic anatomy of the occipitotemporal system. Note that each area in this system has its tracts in a different color to highlight the nature of the system.

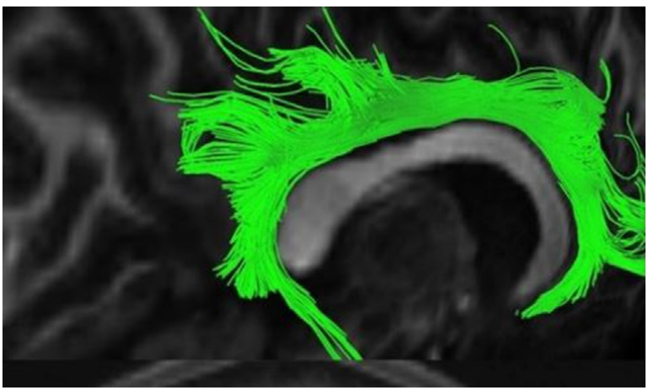

FIG. 25 Tractographic anatomy of the cingulum.

homologous contralateral brain regions. For example, large connections exist between homologous parts of the superior frontal gyrus, the superior parietal lobule, the medial occipital lobe, etc. There are homologous connections between more lateral cortices (e.g., middle frontal and inferior frontal gyri), and there are some connections between nonhomologous brain regions (as with what I term here the crossed FAT tract below which the middle frontal and inferior frontal gyri connect with the contralateral superior frontal gyrus) (Fig. 26).

Equally important is the relationship between the corpus callosal fibers and the cingulate gyrus and cingulum. The corpus callosum wraps inferiorly, then laterally, then superiorly around the cingulate gyrus and cingulum toward its target (Fig. 27). Because the cingulum and corpus callosum run roughly

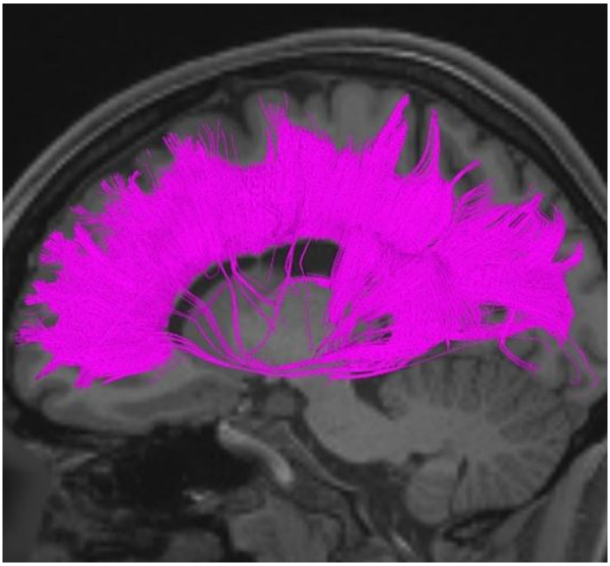

FIG. 26 Tractographic anatomy of the corpus callosum.

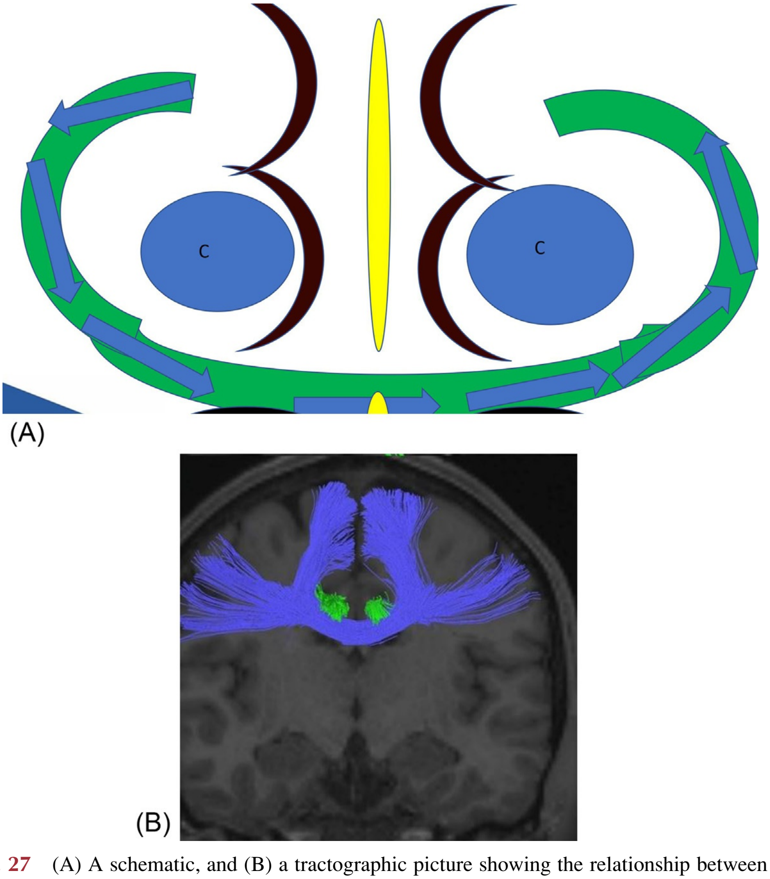

FIG. 27 (A) A schematic, and (B) a tractographic picture showing the relationship between the cingulum and corpus callosum.

perpendicular to each other, they do not cross, there is only occasional cross talk between their relevant gyri (there are also different types of cortex), and they can be dissected free from each other without too much difficulty in cadaveric fiber dissections. This relationship is critical for understanding how to safely remove butterfly gliomas.

The initiation axis

This collection of networks involves the default mode network, the executive control network, and the salience network. This network relationship is described in more detail in the chapter about butterfly gliomas and will not be repeated in this chapter.