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## White fibers anatomy through dissection - Klingler Method and its clinical correlation

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**Abstract.** White fiber anatomy is classified according to its function: association, commissural, and projection. The most studied are the superior longitudinal fascicle, inferior longitudinal fascicle, uncinate fascicle, and inferior frontal occipital fascicle, because of their anatomy and function. In this experimental investigative study in the laboratory, the Klingler technique was used for white matter fiber dissection of ten normal brains. During this period, we observed the anatomical and clinical correlation of the superior longitudinal fascicle, inferior longitudinal fascicle, uncinate fascicle, and inferior frontal occipital fascicle. This study allowed us to understand the important part of dissection in anatomy studies, even with the presence of more modern techniques such as tractography.

**Keywords:** superior longitudinal fascicle, white fibers, uncinate fascicle, inferior frontal occipital fascicle, inferior longitudinal fascicle.

### INTRODUCTION

The white matter is a bundle of myelinated nerve fibers called fascicles or tracts. White matter fibers are classified according to their functions: association, commissural, and projection. The association fibers are of two types: the small ones, also called “U fibers,” which connect adjacent gyri up to the lower portion of the sulcus, and the long ones, which connect brain lobes on the same side of the hemispheres, the most studied being the superior longitudinal fascicle (SLF), inferior longitudinal fascicle (ILF), uncinate fascicle (UF), inferior frontal occipital fascicle (IFOF) (Catani et al. 2002). The commissural fibers interconnect the two cerebral hemispheres: corpus callosum, anterior commissure, and hippocampal commissure. On the other hand,

projection fibers connect the cerebral cortex with the medulla and trunk, such as the corona radiata and internal capsule (Duffau 2011).

The SLF is divided into three parts. Its function is to connect the frontal lobe to the parietal and temporal ILF (Klingler and Gloor 1960, Janelle et al. 2022), with fibers connecting the temporal lobe to the occipital lobe (Janelle et al. 2022). UF, connects the frontal lobe to the temporal lobe, and IFOF, connects the frontal lobe to the occipital lobe (Klingler 1935).

One way to study white fibers is by dissecting brains, a method described by Josef Klingler in 1935 (Klingler 1935) that remains the most widely used method today. There are variations in the method, altered by the author himself in later works (Klingler and Gloor 1960), but it consists of three stages: fixation in formaldehyde, cooling, and thawing. A study by Dziedzic et al. (Dziedzic et al. 2021), who analyzed 37 articles regarding variations in Klingler's method, it was found that the time taken to fix formaldehyde varied from 8 h to 3 months, freezing from 8 h to 3 months, cooling temperature from -5 to 80°C, and formaldehyde solution for storage from 4-10% in concentration. However, even with divergences, satisfactory results can be obtained, with the most important being the freeze-thaw process, as demonstrated by Zemmoura et al. (Zemmoura et al. 2016), because it preserves the myelin sheath; consequently, the structure of the axon, destroying the cellular matrix and glial cells, makes it easier to expose and separate the fibers during dissection.

This study specifically focused on dissecting three key white matter fibers: the uncinate fascicle, superior longitudinal fascicle, and inner frontal occipital fascicle. By dissecting these fibers, this study aimed to provide a deeper understanding of their anatomy and function.

## MATERIALS AND METHODS

This was an experimental investigative study in the laboratory that meticulously utilized the Klingler technique to dissect white matter fibers (Guerrero et al. 2019). This technique, known for its precision, involves four distinct steps: fixation, freezing, unfreezing, and dissection (Klingler and Gloor 1960, Duffau 2011).

Ten normal adult brains were carefully fixed in 10% formalin solution for a minimum period of three months. Subsequently, the superficial veins and arachnoid membranes were meticulously removed. The brains were then frozen at temperatures between 0 °C and 5 °C for three weeks, a step that allows formalin to crystallize between the fibers, expanding and separating them for

further preservation and observation. Subsequently, the samples were frozen and preserved in formalin. Dissection was performed using wooden spatulas (Klingler and Gloor 1960, Duffau 2011).

## RESULTS

The dissection was made by completely removing the brain cortex (Figure 1), and in the lateral region of the encephalon, the U fibers were removed from the superior temporal gyrus, going up into the superior frontal gyrus, passing through the inferior frontal gyrus and medial frontal gyrus to reveal the partially horizontal and vertical superior longitudinal fasciculus. Subsequently, the U fibers were detached from the precentral, postcentral, superior parietal, angular, and supramarginal gyri to completely expose the horizontal superior longitudinal fasciculus.

The uncinate fasciculus was more internally localized than the superior longitudinal fasciculus. To locate it, removing the U fibers from the inferior and medial temporal gyrus, in addition to the short and long gyrus cortex of the insula, inside the Sylvian fissure is necessary. The inferior frontal occipital fasciculus is mainly located behind the frontal and occipital lobes and passes underneath the internal capsule.



**Figure 1.** Right hemisphere with remove cortex.

## DISCUSSION

*Superior longitudinal fasciculus (SLF)*

## Anatomy

The superior longitudinal fasciculus (SLF) - Figures 2-6 - is considered the largest associative fiber bundle system in the brain, which forms a wide arc around the upper edge of the insula and has the shape of a “C.” The SLF is part of the longitudinal associative fiber system that forms connections between the frontal, parietal, occipital, and temporal lobes around the Sylvian fissure of the ipsilateral hemisphere (Türe et al. 2000, Jellison et al. 2004, Fernández-Miranda et al. 2008, Dini et al. 2013, Janelle et al. 2022).

The SLF was identified as the most lateral fasciculus with an anteroposterior orientation in color-coded diffusion tensor imaging (DTI) maps. On T2-weighted sagittal images, the SLF can be recognized as a white substance surrounding the posterior margin of the insula (Fernández-Miranda et al. 2008). It can be roughly divided into (I) longer fibers that run medially within the fasciculus and connect the lateral frontal cortex with the dorsolateral parietal and temporal cortex and (II) shorter U-shaped fibers that run more laterally and connect the frontoparietal, parieto-occipital, and parietal-temporal cortex (Catani et al. 2002). It can also be divided into three segments (one long, one anterior, and one posterior segment), each connecting two regions of Broca’s, Wernicke’s, or Geschwind’s area (inferior parietal lobule) (Catani et al. 2002). The fibers originate in the prefrontal and premotor gyri (especially Broca’s area) and project posteriorly to Wernicke’s area (and the occipital lobe) before curving around the insula and putamen and running anteroinferiorly to the temporal pole. In addition, a few fibers originate in the insula of the Reil and project to the cortex of the other lobes (Catani et al. 2002).

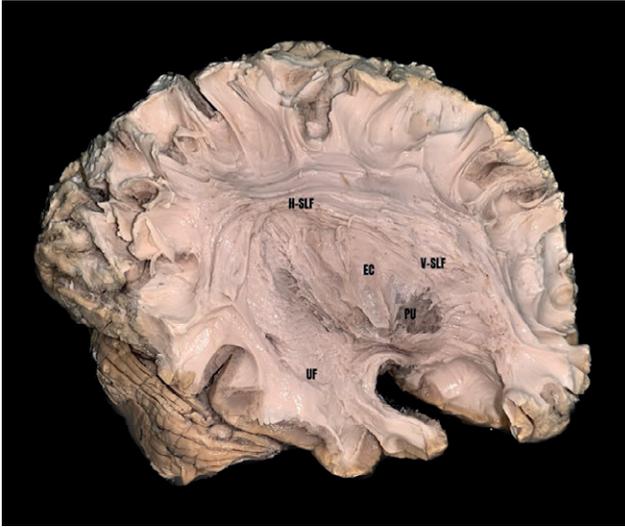
At the beginning of the 19th century, Reil and Autenrieth identified the SLF based on postmortem brain dissection. The first description describes them as a group of fibers located in the white matter of the temporal, parietal, and frontal lobes. This description was further refined by Burdach, followed by Dejerine in 1895, who introduced a perisylvian arcuate fiber tract connecting the posterior temporal lobe to the frontal lobe. They called this fiber bundle the arcuate fasciculus (AF) and used the term ‘superior longitudinal fasciculus’ as a synonym. A century later, Petrides and Pandya studied rhesus monkeys using an autoradiographic technique and divided the SLF into three segments. These authors distinguished SLF and AF as two distinct entities with

different orbits, thus blurring the classical description that prevailed at that time. The anterior segment of the AF appears to correspond to SLF III, and these two terms are used interchangeably. Thus, although these two bundles are distinct units, some of their subcomponents overlap, as if they share a subdivision: SLF III and the anterior segment of the AF (Janelle et al. 2022).

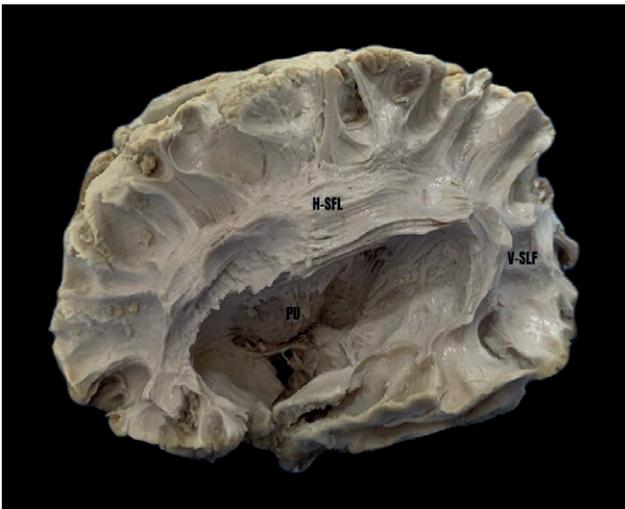
In a study by Schmahmann et al. (2007), the autoradiographic material (isotope) showed that the SLF I fiber bundle runs in the white matter of the superior parietal and frontal lobes. It lies dorsal to the CB and is distinct from it. It extends from the medial and dorsal parietal cortices to the dorsal part of the premotor and prefrontal cortices. SLF I connects the medial parietal areas PEc, PGM, 31, and the superior parietal lobe area PE with dorsal area 6, dorsal area 9, and the supplementary motor area (SMA) in the frontal lobe. Subcomponent II (SLF II) extends from the caudal inferior parietal lobe to the dorsal premotor and prefrontal cortices. It is located caudally in the white matter of the inferior parietal lobe and deep in the superior shoulder of the Sylvian fissure. Rostrally, it extends into the white matter below the premotor and prefrontal brain regions. SLF II connects area POa in the intraparietal sulcus (IPS) and areas PG and Opt of the inferior parietal lobe with areas BA 46, 9/46, 8Ad, and 6D of the frontal lobe. A subcomponent III fiber bundle (SLF III) was identified in the opercular white matter of the parietal and frontal lobes. It extends from the rostral inferior parietal lobe to the ventral part of the premotor and prefrontal cortices. The SLF III connects the area POa in the IPS and the areas PF, PFG, and PPop of the parietal lobe, as well as the ventral premotor area BA 6, 44, and the ventral prefrontal area 9/46v of the frontal lobe.



**Figure 2.** Horizontal superior longitudinal fasciculus. H-SLF: Horizontal Superior Longitudinal Fasciculus, EC: external capsule.



**Figure 3.** Superior longitudinal fasciculus and uncinete fasciculus. H-SLF: Horizontal Superior Longitudinal Fasciculus, V-SLF: Vertical Superior Longitudinal Fasciculus, EC: external capsule, PU: Putamen, UF: Uncinate Fasciculus.



**Figure 4.** Horizontal and Vertical superior longitudinal fasciculus. H-SLF: Horizontal Superior Longitudinal Fasciculus, V-SLF: Vertical Superior Longitudinal Fasciculus, PU: Putamen.

Anatomical variability can be observed at different levels in cortical morphology, cytoarchitecture, task-related activation, or dMRI connectivity patterns. Specifically, there are within-population differences in the SLF; the volume of the SLF may differ from individual to individual. The fractional anisotropy of the SLF also varies between individuals but is less than the volume (Janelle et al. 2022).



**Figure 5.** Horizontal superior longitudinal fasciculus. H-SLF: Horizontal Superior Longitudinal Fasciculus.



**Figure 6.** Horizontal and Vertical Superior longitudinal fasciculus. H-SLF: Horizontal Superior Longitudinal Fasciculus, V-SLF: Vertical Superior Longitudinal Fasciculus.

#### Dissecting description

Martino et al. (Martino et al. 2013) modified the classical method for dissecting fibers originally designed by Klinger. The aim was to preserve the cortex by removing only a minimum amount of tissue during dissection, thus enabling cortex-sparing dissection of the fibers. This approach identified two superficial segments of the SLF: the first, horizontally oriented, connects the inferior parietal lobe and the posterior part of the superior temporal gyrus to the frontal operculum. The sec-

ond component runs along the AF and connects the posterior part of the middle temporal gyrus to the posterior part of the inferior parietal lobe (the angular gyrus). A deeper fiber segment corresponding to classic AF has also been identified (Janelle et al. 2022).

The cortical gray matter and the adjacent superficial short fibers of the frontal, temporal, and parietal operculum; the middle frontal, superior, and middle temporal gyri; and the inferior parietal lobe must be removed to expose the SLF. The removal of the short fibers exposed the deeper long association fibers that descended from the gyri and traveled a variable distance to the distant gyri. The horizontal orientation of the long fibers at the depth of the inferior and middle frontal gyri, where they form a compact fasciculus of approximately 20 mm lateromedial diameter located 22–25 mm from the cortical surface, is evident (Fernández-Miranda et al. 2008). At the level of the temporoparietal junction area and approximately 20 to 25 mm from the cortical surface, a well-defined group of vertically oriented fibers running between the posterior part of the middle and superior temporal gyri and the region of the inferior parietal lobe can be seen (Fernández-Miranda et al. 2008). They form temporoparietal or vertical segments of the SLF. At a deeper level in the temporoparietal area, a group of fibers curving around the posterosuperior insular border and running between the posterior temporal and prefrontal regions can be seen. They form the frontotemporal or arcuate segments of the SLF (Fernández-Miranda et al. 2008).

### Clinical correlation

Each segment of the dominant superior longitudinal association system can be associated with a specific disorder: the frontoparietal segment with non-fluent aphasia, temporoparietal segment with intelligible aphasia, and frontotemporal or arcuate segments with conduction aphasia. Frequent combinations of white matter lesions can cause aphasic disorders (Fernández-Miranda et al. 2008).

The frontoparietal segment of the SLF connects the prefrontal region with the inferior parietal lobule. The latter is a high-order association cortex that integrates inputs from different modalities and plays a vital role in spatial function in the nondominant hemisphere. The nondominant prefrontal region plays a vital role in regulating visual attention in different parts of the space. Thus, the non-dominant frontoparietal segment may serve as a conduit for visuospatial perception (Fernández-Miranda et al. 2008).

The temporoparietal segment of the SLF connects the inferior parietal lobule with the superior temporal

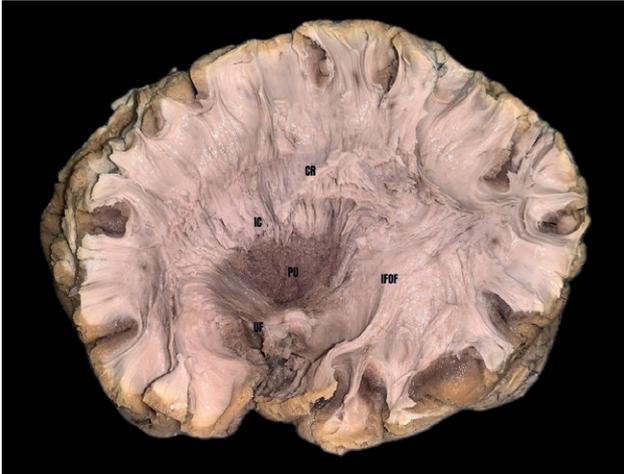
gyrus, which is associated with auditory information processing. Thus, the non-dominant temporoparietal (indirect pathways) and arcuate (frontotemporal and direct pathways) segments of the longitudinal superior fasciculus can process audio spatial and visuospatial information, respectively (Fernández-Miranda et al. 2008).

SLF III has similar connectivity to the AF and connects the inferior frontal gyrus to the ventral precentral gyrus. This suggests that it plays a role in speech in the left hemisphere, which was confirmed by Maldonado et al. through a brain electrical stimulation study. Wang et al. also reported a specific connectivity pattern for the suitable SLF III, which terminates at the proper pars triangularis. They found a solid leftward orientation of connections between the supramarginal gyrus, dorsal precentral gyrus, and caudal middle frontal gyrus. This fits with the role of the left SLF II in motor planning of speech and syntax processing. In a similar situation to SLF III, a suitable SLF II preferentially connects the angular gyrus and the superior parietal lobe with the caudal or rostral middle frontal gyrus. It is assumed that this system plays a role in regulating attention in spatial orientation. This is consistent with SLF II being responsible for faster and preferential visuospatial processing in the right hemisphere (Maldonado et al. 2012, Wang et al. 2016, Janelle et al. 2022).

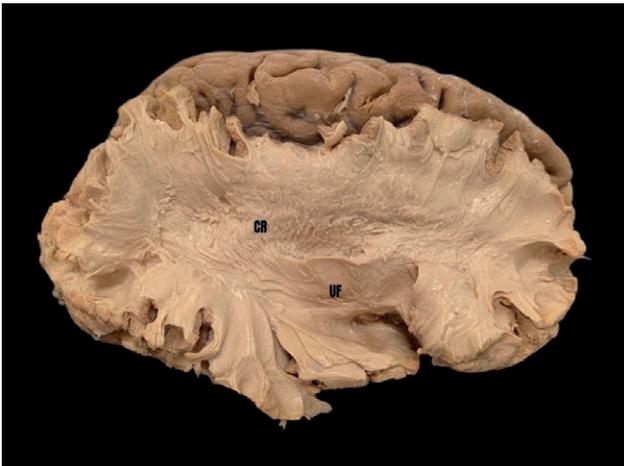
### *Uncinate Fasciculus (UF)*

#### Anatomy

The uncinate fasciculus (UF) - Figure 7-9 - is an essential long-range white matter association fiber tract that connects the anterior temporal lobe to the medial and lateral orbitofrontal cortices via a direct, bidirectional monosynaptic pathway (Türe et al. 2000, Catani et al. In 2002, Schmahmann, et al. 2007, Fernández-Miranda et al. 2008, Papagno et al. 2011, Von Der Heide et al. 2013). The UF is the most rostral fiber bundle in the temporal lobe (Schmahmann et al. 2007). It runs caudally through the white matter of the frontal lobe, bends sharply ventrally in the region of the limen insulae, and then spreads to reach the cortex of the anterior part of the superior and middle temporal gyri (Türe et al. 2000). UF has a pronounced hook shape that runs in an arc around the Sylvian fissure (Schmahmann et al. 2007, Von Der Heide et al. 2013). “Uncinate,” from the Latin *uncus*, means “hook-shaped.” It curves around the lateral sulcus and connects the inferior and orbital frontal gyri to the anterior temporal lobe (Dini et al. 2013).



**Figure 7.** Uncinate Fasciculus and Inferior Fronto-occipital Fasciculus. UF: Uncinate Fasciculus and Inferior Fronto-occipital Fasciculus, IFOF: Inferior Fronto-occipital Fasciculus, CR: Corona Radiata, IC: Internal capsule, PU: Putamen.



**Figure 8.** Uncinate Fasciculus. UF: Uncinate Fasciculus and Inferior Fronto-occipital Fasciculus, CR: Corona Radiata.

The UF is often divided into three parts: dorsal/temporal segment, middle/insular segment, and ventral/frontal extension. The three main areas of the rostral temporal lobe are connected to the frontal lobe: the TS1 area of the rostral superior temporal region and the temporal pro-iso-cortex; the inferior temporal areas TEa, IPa, and TEI; and the ventromedial temporal areas TH, TL, and TF in the parahippocampal gyrus, entorhinal cortex, and amygdala (Schmahmann et al. 2007). The temporal segment originates from the uncus (Brodmann area [BA] 35), entorhinal and perirhinal cortex (BA 28, 34, and 36), and temporal pole/anterior temporal lobe (BA 20 and

38). BA 10, 11, 47/12, 13, 14, and 25 were connected to the orbital areas of the frontal lobe. The lateral prefrontal cortex originates or terminates in areas 10 and 47/12, and on the medial surface in areas 32 and the rostral area 24 (Schmahmann et al. 2007, Von Der Heide et al. 2013).

It is more prominent in the right hemisphere, indicating a more robust frontotemporal connectivity. The temporal fibers lie medial and anterior to the fibers of the inferior longitudinal fasciculus (Papagno et al. 2011). The anterior part of this tract is located inferior and medial to the fronto-occipital fasciculus. The UF borders the fronto-occipital fasciculus in its middle part before curving inferiorly and laterally towards the temporal pole and middle and superior temporal gyri (Dini et al. 2013). The UF then enters the outer capsule, and its fibers project medially to the insula and laterally to the lenticular nucleus (Dini et al. 2013).

In tractography, the dorsal and more lateral fibers run posteriorly from the frontal pole and unite with a more ventral and medial branch from the orbital cortex to form the uncinate. This runs a short distance below the frontal-occipital fasciculus before entering the temporal lobe as a single compact bundle in which the two divisions can still be distinguished. The uncinate fasciculus then forms an anteromedial hook end in the temporal pole, uncus, hippocampal gyrus, and amygdala (Catani et al. 2002).

The cell bodies of the UF are located in the temporal segment. From there, the UF runs upward across the lateral nucleus of the amygdala, through the limen insulae, and either near or through two smaller white matter tracts, the external capsule and the extreme capsule (Catani et al. 2002, Von Der Heide et al. 2013). In this region, the UF is inferior to the fasciculus frontalis occipitalis. Subsequently, it merges into the orbital regions of the frontal lobe (BA 11 and 47), where it has a horizontally oriented fan shape. The fan is divided into two branches: giant ventrolateral and smaller medial branches. The ventral branch ends in the lateral orbitofrontal cortex, whereas the medial branch ends in the frontal pole (BA 10). In adult humans, the UF has a width of 3–7 mm, height of 2–5 mm, and volume of ~140 mm<sup>3</sup> (Schmahmann et al. 2007, Von Der Heide et al. 2013).

#### Dissecting description

The UF was exposed on the cortical surface of the limen insulae. This thick, hook-shaped fasciculus forms the anterior part of the frontotemporal junction (also called the temporal stem) and, in its lateral part, connects the frontal-orbital region with the temporal pole to

form part of the ventral part of the extreme and external capsule. When the UF fibers were removed, several island-like grey matter masses interspersed with the fibers were exposed. These islands of gray matter form the ventral claustrum, which is connected in the superficial plane to the dorsal claustrum located above and behind the UF. The UF was dissected medially. In this case, the white fibers of the ventral part of the external capsule are exposed, connecting the frontonasal (gyrus rectus, subcallosal area) and temporomesial areas, as well as the gray matter of the ventral claustrum, which merges into the nucleus amygdaloid, located anteromedially of the UF (Wang et al. 2016).

### Clinical correlation

UF has been associated with various developmental and psychiatric disorders. Its location makes it susceptible to direct impact and shear injuries from head trauma. It is frequently associated with white matter damage and traumatic brain injuries. The anterotemporal lobe is typically associated with the limbic system and its functions are thought to be related to emotion and episodic memory (Von Der Heide et al. 2013).

The intertemporal lobe is involved in processing modality-specific information, such as auditory (rostral supratemporal gyrus), visual (rostral inferotemporal region), somatosensory and gustatory (rostral insular operant cortex), mnemonic (parahippocampal gyrus), and emotional (amygdala) information. The orbitofrontal area is involved in the regulation of behavior, emotions, decision-making, and self-regulation. The UF acts as a link between emotion and cognition (Fernández-Miranda et al. 2008, Von Der Heide et al. 2013).

Several studies have reported altered functional activity in the frontal regions, along with increased activation in the limbic/paralimbic regions, in generalized anxiety disorder and social anxiety disorder. Some studies have reported that the neuronal regions connected by the UF (orbital frontal cortex and temporal pole) are relatively thinner or have a lower volume in psychopaths and individuals with antisocial personality disorder than in controls (Von Der Heide et al. 2013).

The literature discusses three functions of the UF: associative and episodic memory, linguistic, and social-emotional functions. Episodic memory-reversal learning; learning from feedback/rewards/punishments; forming associations that motivate behavior; value-based updating of stored representations. Language retrieval of proper names for individuals, possibly some aspects of semantic memory retrieval. Social-emotional processing: appraisal of stimuli, processing of social rewards, over-

riding the emotional meaning of concepts.

A literature review (Von Der Heide et al. 2013) found no evidence to support the claim that the UF plays a primary role in anxiety disorders or schizophrenia but found more substantial evidence for UF dysfunction in psychopathy and epilepsy.

The uncus is part of the olfactory cortex, the entorhinal cortex is closely associated with hippocampal episodic memory functions, the perirhinal cortex has a controversial function in object perception and high-level object memory, and the temporal pole and adjacent tissue form part of the anterior temporal lobe. Parts of the anterior temporal lobe (but not the temporal pole) are thought to play a role in certain types of semantic memory, and in the encoding and storage of social and emotional concepts (Von Der Heide et al. 2013).

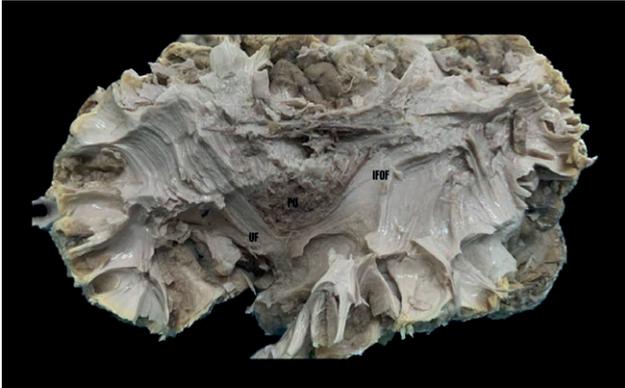
Interruption of the UF during anteromedial temporal lobectomy or transsylvian transinsular selective amygdalohippocampectomy for medial intractable temporal lobe epilepsy may be associated with the psychosocial clinical improvement observed after surgery, perhaps because the UF can no longer transmit pathological information from the temporal lobe to decision-relevant regions of the orbitofrontal cortex (Fernández-Miranda et al. 2008).

The UF plays a role in recalling personal names, as its removal results in a significant deficit, even when the temporal pole is spared. Furthermore, the results support the hypothesis that the retrieval of conceptual knowledge is separate from the retrieval of names (Papagno et al. 2011).

### *Inferior fronto-occipital fasciculus (IFOF)*

#### Anatomy

The Inferior Fronto-Occipital Fasciculus (IFOF) (Figures 7 and 9) represents one of the most extensive white matter tracts bridging the occipital lobe to the anterior regions, including the temporal and frontal lobes (Oishi et al. 2011). Understanding the inferior fronto-occipital fasciculus is essential to elucidate its cognitive and perceptual processing functions. Neuroscientific studies have used advanced brain imaging techniques such as magnetic resonance imaging and diffusion tractography to map the trajectory and connectivity of these nerve fibers. This knowledge is essential to better understand the role of the inferior fronto-occipital fasciculus in neurological and psychiatric conditions as well as to develop more effective diagnostic and treatment strategies for disorders that affect brain function (Surbeck et al. 2020).



**Figure 9.** Uncinate Fasciculus and Inferior Fronto-occipital Fasciculus. Uncinate Fasciculus and Inferior Fronto-occipital Fasciculus, IFOF: Inferior Fronto-occipital Fasciculus, PU: Putamen.

The IFOF spans across the occipital, parietal, and temporal cortices within the sagittal stratum, converges with the roof of the temporal horn, extends to the ventral aspect of the external/extreme capsule, proceeds beneath the insular lobe within the temporal stem, and ultimately terminates within the frontal lobe (Martino et al. 2013). Situated internally from the Uncinate Fasciculus (UF) (Wu et al., 2022), the IFOF exhibits a notable division into superficial and deep components at the ventral aspect of the external capsule. The IFOF superficial portion arches mediolaterally at the superior level, limiting the insular sulcus before culminating in the Inferior Frontal Gyrus (IFG) (Wu et al. 2022).

It is important to know that the IFOF can be classified into two parts: (I) a superficial dorsal component, which establishes connections between the pars triangularis and orbitalis with the superior parietal lobe and the posterior segments of the superior and middle occipital gyri, and (II) a deep ventral component, which establishes connections between the posterior segment of the inferior occipital gyrus and the posterior basal temporal region with three distinct areas within the middle frontal gyrus (MFG), dorsolateral prefrontal cortex (DLPFC), and orbitofrontal cortex (Oishi et al. 2011).

#### Dissecting description

The superficial and dorsal subcomponent fibers of the IFOF connect to different cortical regions of the parietal and occipital lobes. In the superior parietal lobe, the IFOF dorsal fibers, which course through the superior portion of the sagittal stratum along the superior aspect of the atrium lateral surface, determine their trajectory at the superior parietal lobe convexity

surface. In addition, the superior and middle occipital gyri fibers run through the middle portion of the sagittal stratum along the superior part of the occipital horn lateral surface, terminating in the posterior regions of the superior and middle occipital gyri (Martino et al. 2013).

Moreover, the deeper and ventral subcomponents of the IFOF are associated with the regions of the occipital and temporal lobes. The fibers directed towards the inferior occipital gyrus navigated through the inferior portion of the sagittal stratum and along the inferior aspect of the lateral surface of the occipital horn, concluding their trajectory in the posterior part of the inferior occipital gyrus. Meanwhile, fibers directed towards the posterior and basal temporal regions diverge from the main bundle to encircle the inferior border of the atrium and occipital horn, eventually terminating in the posterior part of the fusiform gyrus, temporo-occipital sulcus, and inferior temporal gyrus basal surface (Martino et al. 2013).

#### Clinical correlation

Studies utilizing electrostimulation of white matter pathways have revealed that the IFOF holds significant relevance in semantic processing, as it serves as a connecting channel between two areas associated with this function: the occipital associative extrastriate cortex and the temporal-basal region. In this context, intraoperative electrical stimulation (IES) of the IFOF induces semantic paraphasia, which means that the action can be executed. However, this did not correspond to the developer's intent (Duffau et al. 2008). Recent research has highlighted that the IFOF from the left hemisphere is related to semantic working memory (Horne et al. 2022) and that the right IFOF has been associated with emotion recognition (Philippi et al. 2009).

#### CONCLUSION

In this study, we applied the Klinger Method to dissect SLF, UF, and IFOF. By delineating their stream anatomically, we can understand the anatomy and function of the fasciculus more clearly. In MRI fiber tractography, there is considerable variability in segmentation protocols, fiber overlap, and techniques that affect the results, which the dissection would not deal with, as it enables the differentiation of one fiber from another and allows a better understanding of white fiber anatomy and function.

## REFERENCES

- Catani M, Howard RJ, Pajevic S, Jones DK (2002) Virtual in Vivo Interactive Dissection of White Matter Fasciculi in the Human Brain. *NeuroImage* 17: 77–94. <https://doi.org/10.1006/nimg.2002.1136>
- Dini L, Vedolin L, Bertholdo D, Grando R, Mazzola A, Dini S, Isolan G, Da Costa J, Campero A (2013) Reproducibility of quantitative fiber tracking measurements in diffusion tensor imaging of frontal lobe tracts: A protocol based on the fiber dissection technique. *Surgical Neurology International* 4: 51. <https://doi.org/10.4103/2152-7806.110508>
- Duffau H (Ed.) (2011) *Brain mapping: from neural basis of cognition to surgical applications*. Springer, Wien ; New York, 392 pp.
- Duffau H, Gatignol P, Mandonnet E, Capelle L, Taillandier L (2008) Intraoperative subcortical stimulation mapping of language pathways in a consecutive series of 115 patients with Grade II glioma in the left dominant hemisphere. *Journal of Neurosurgery* 109: 461–471. <https://doi.org/10.3171/JNS/2008/109/9/0461>
- Dziedzic TA, Balasa A, Jeżewski MP, Michałowski Ł, Marchel A (2021) White matter dissection with the Klingler technique: a literature review. *Brain Structure and Function* 226: 13–47. <https://doi.org/10.1007/s00429-020-02157-9>
- Fernández-Miranda JC, Rhoton AL, Álvarez-Linera J, Kakizawa Y, Choi C, De Oliveira EP (2008) Three-dimensional microsurgical and tractographic anatomy of the white matter of the human brain. *Neurosurgery* 62: SHC989–SHC1028. <https://doi.org/10.1227/01.NEU.0000297076.98175.67>
- Guerrero M, del Sol M, Ottone NE, Guerrero M, del Sol M, Ottone NE (2019) Preparación de Hemisferios Cerebrales para Disección de Tractos. *International Journal of Morphology* 37: 533–540. <https://doi.org/10.4067/S0717-95022019000200533>
- Horne A, Ding J, Schnur T, Martin R (2022) White Matter Correlates of Domain-Specific Working Memory. *Brain Sciences* 13: 19. <https://doi.org/10.3390/brainsci13010019>
- Janelle F, Iorio-Morin C, D'amour S, Fortin D (2022) Superior Longitudinal Fasciculus: A Review of the Anatomical Descriptions With Functional Correlates. *Frontiers in Neurology* 13: 794618. <https://doi.org/10.3389/fneur.2022.794618>
- Jellison BJ, Field AS, Medow J, Lazar M, Salamat MS, Alexander AL (2004) Diffusion Tensor Imaging of Cerebral White Matter: A Pictorial Review of Physics, Fiber Tract Anatomy, and Tumor Imaging Patterns. *AJNR: American Journal of Neuroradiology* 25: 356–369.
- Klingler J (1935) Erleichterung der makroskopischen Präparation des Gehirns durch den Gefrierprozess. Orell Füssli. Available from: <https://books.google.com.br/books?id=U3PUSAAACAAJ>.
- Klingler J, Gloor P (1960) The connections of the amygdala and of the anterior temporal cortex in the human brain. *Journal of Comparative Neurology* 115: 333–369. <https://doi.org/10.1002/cne.901150305>
- Maldonado IL, Mandonnet E, Duffau H (2012) Dorsal Fronto-Parietal Connections of the Human Brain: A Fiber Dissection Study of Their Composition and Anatomical Relationships. *The Anatomical Record* 295: 187–195. <https://doi.org/10.1002/ar.21533>
- Martino J, De Witt Hamer PC, 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 Structure and Function* 218: 105–121. <https://doi.org/10.1007/s00429-012-0386-5>
- Oishi K, Mori S, Donohue PK, Ernst T, Anderson L, Buchthal S, Faria A, Jiang H, Li X, Miller MI, Van Zijl PCM, Chang L (2011) Multi-contrast human neonatal brain atlas: Application to normal neonate development analysis. *NeuroImage* 56: 8–20. <https://doi.org/10.1016/j.neuroimage.2011.01.051>
- Papagno C, Miracapillo C, Casarotti A, Romero Lauro LJ, Castellano A, Falini A, Casaceli G, Fava E, Bello L (2011) What is the role of the uncinate fasciculus? Surgical removal and proper name retrieval. *Brain* 134: 405–414. <https://doi.org/10.1093/brain/awq283>
- Philippi CL, Mehta S, Grabowski T, Adolphs R, Rudrauf D (2009) Damage to Association Fiber Tracts Impairs Recognition of the Facial Expression of Emotion. *The Journal of Neuroscience* 29: 15089–15099. <https://doi.org/10.1523/JNEUROSCI.0796-09.2009>
- Schmahmann JD, Pandya DN, Wang R, Dai G, D'Arceuil HE, De Crespigny AJ, Wedeen VJ (2007) Association fibre pathways of the brain: parallel observations from diffusion spectrum imaging and autoradiography. *Brain* 130: 630–653. <https://doi.org/10.1093/brain/awl359>
- Surbeck W, Hänggi J, Scholtes F, Viher PV, Schmidt A, Stegmayer K, Studerus E, Lang UE, Riecher-Rössler A, Strik W, Seifritz E, Borgwardt S, Quednow BB, Walther S (2020) Anatomical integrity within the inferior fronto-occipital fasciculus and semantic processing deficits in schizophrenia spectrum disorders. *Schizophrenia Research* 218: 267–275. <https://doi.org/10.1016/j.schres.2019.12.025>

- Türe U, Yaşargil MG, Friedman AH, Al-Mefty O (2000) Fiber Dissection Technique: Lateral Aspect of the Brain. *Neurosurgery* 47: 417–427. <https://doi.org/10.1097/00006123-200008000-00028>
- Von Der Heide RJ, Skipper LM, Klobusicky E, Olson IR (2013) Dissecting the uncinate fasciculus: disorders, controversies and a hypothesis. *Brain* 136: 1692–1707. <https://doi.org/10.1093/brain/awt094>
- Wang X, Pathak S, Stefaneanu L, Yeh F-C, Li S, Fernandez-Miranda JC (2016) Subcomponents and connectivity of the superior longitudinal fasciculus in the human brain. *Brain Structure and Function* 221: 2075–2092. <https://doi.org/10.1007/s00429-015-1028-5>
- Wu Y, Liu J, Yu G, Jv R, Wang Y, Zang P (2022) Association fiber tracts related to Broca's area: A comparative study based on diffusion spectrum imaging and fiber dissection. *Frontiers in Neuroscience* 16: 978912. <https://doi.org/10.3389/fnins.2022.978912>
- Zemmoura I, Blanchard E, Raynal P-I, Rousselot-Denis C, Destrieux C, Velut S (2016) How Klingler's dissection permits exploration of brain structural connectivity? An electron microscopy study of human white matter. *Brain Structure and Function* 221: 2477–2486. <https://doi.org/10.1007/s00429-015-1050-7>