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ORIGINAL ARTICLE

New insights in the limbic modulation of visual inputs: The role of the inferior longitudinal fasciculus and the Li-Am bundle

Francesco Latini

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Abstract Recent anatomical and DTI data demonstrated new aspects in the subcortical occipito-temporal connections. Although a direct (inferior longitudinal fasciculus, ILF) pathway has been previously described, its fine description is still matter of debate. Moreover, a fast and direct subcortical connection between the limbic system and the occipital lobe has been previously recognized in many functional studies but it still remains poorly documented by anatomical images. We provided for the first time an extensive and detailed anatomical description of the ILF subcortical segmentation. We dissected four human hemispheres with modified Klingler's technique, from the basal to the lateral occipito-temporal surface in the two steps, tracking the ILF fibers until their cortical termination. Pictures of this direct temporo-occipital pathway are discussed in the light of recent literature regarding anatomy and functions of occipito-temporal areas. The dissection confirmed the classical originating branches of ILF and allowed a fine description of two main subcomponent of this bundle, both characterized by separate hierarchical distribution: a dorsal ILF and a ventral ILF. Moreover, a direct pathway between lingual cortex and amygdala, not previously demonstrated, is here described with anatomical images. Even if preliminary in results, this is the first fine description of ILF's subcomponents. The complex but clearly segregated organization of the fibers of this bundle (dILF and vILF) supports different level of functions mediated by visual recognition. Moreover, the newly described direct pathway from lingual to amygdala (Li-Am), seems involved in the limbic modulation of visual processing, so it may support physiological conditions the crucial role of this connection in human social cognition. In pathological conditions, on the other hand, this may be one of the hyperactivated pathways in temporo-occipital epileptic and nonepileptic syndromes.

Keywords ILF · White matter · Social cognition · Lingual · Amygdala · Li-Am · Temporo-occipital connections

F. Latini (✉)
Division of Neurosurgery, Department of Neuroscience and Rehabilitation, S. Anna University Hospital, Ferrara, Italy
e-mail: francesco.latinimd@gmail.com

Introduction

Since its initial description [27, 72], the inferior longitudinal fasciculus (ILF) has been the subject of several contrasting studies. While some authors consider the ILF to be the major occipito-temporal associative tract [24, 27, 40], others deny its existence [72, 73, 87]. The Klinger methods allowed the first 3D description of the ILF [56] even if the anatomical dissection of this associative bundle is not so simple to demonstrate because of its strict interconnection between the optic pathways in human and also in nonhuman brain. For instance, Tusa and Ungerleider [87] were unable to demonstrate long associative fibers interconnecting occipital and anterior temporal lobes distinct from those of the optic radiation using blunt dissection in human and monkey. While the anatomical evidence for an ILF was disputed, over the last century, several neuropsychological syndromes have been attributed to a disruption of specific fiber connections between visual and temporal cortex. These syndromes include: associative visual agnosia [48], prosopagnosia [6, 59], visual amnesia (a deficit of registering novel visual experiences in short-term memory with the preserved ability to register novel, nonvisual experiences [75]), and visual hypo-emotionality (a deficit of visually evoked emotions with preserved emotional responses to nonvisual stimuli [5, 82]) [36, 37, 39]. All these authors share the common idea that the transection or reduction of fractional anisotropy (FA) of the pathways between "visual" areas, "emotional" and "memory" areas result in a visually specific semantic [66] emotional or memory deficit. Advances

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in noninvasive functional imaging and the doctrine of functional specialization have led to a reinterpretation of some of these syndromes in terms of damage of specialized cortical modules (e.g., prosopagnosia with lesions of face-specialized cortex) [80]. However, some deficits seem still better explained by a disconnection than a loss of specialized cortex (e.g., visual amnesia and visual hypo-emotionality) [15, 70]. Recent DTI studies have confirmed the classical anatomical description of ILF (direct pathway) and also seemed to confirm the neurophysiological data regarding the latency of activation of visual neurons in occipital region and in medial temporal structures [47, 90]. Unfortunately, this method could not describe the fine cortical terminations of this bundle and could neither give a real segmentation of the pathways' subcomponents. As widely demonstrated, anatomical studies represent often the best option to understand or confirm connections between different cerebral areas, even if the complex architecture of ILF is really difficult to discover with classical Klingler's technique, because of the multiple interconnected boundaries present in a thin sub cortical layer. In our opinion, this is the first anatomical study focusing on the ILF segmentation. Particular attention is focused on the hierarchical distribution of the different fiber subgroups especially the ones in relationships with the limbic system. Their comprehension can be crucial to define the true cortical areas sub-served by this important and at the same time poorly understood bundle.

Methods

Four human cerebral hemispheres (two right and two left), obtained from fresh autopsy specimens, were fixed in 10 % formalin solution for at least 40 days. The pia mater, arachnoid membrane, and vascular structures were carefully removed. The specimens were then washed under running water for several hours, afterward, the specimens underwent freezing at −35 °C for 48 h and then thawed before performing the dissection. After every session, the specimens were covered with alcohol solution. Before the dissection started, a detailed study of the superficial anatomy of the sulci and gyri was reported. The specimens were dissected in a stepwise manner, from basal surface to the lateral surface, with a modified fiber dissection technique in respect to the one described by Klingler [52, 53, 56, 86]. The dissections were performed under the loops magnification (0.4–0.6–1–2.5–4). Microscopic dissectors were used in the initial steps of the dissection, to peel away the brain cortex preserving after the first step the most superficial subcortical fibers of the basal and lateral brain surface. Once the fibers of the ILF were identified, the remaining dissection was performed using curving metallic dissectors with various tip sizes. Several digital pictures were acquired during dissection.

Results

The dissection started from the occipito-temporal gyrus, just laterally to the collateral sulcus. The cortex of the fusiform gyrus was peeled away with extreme care, and then the cortex of the parahippocampal gyrus was then easily removed, revealing the radiation of the cingulum. The dissection continued peeling away the "U" fibers in the entire temporo-occipital surface. Then, we started removing the middle temporal gyrus (MTG) cortex, exposing the terminations of the C-shaped arcuate fasciculus (AF) in the middle and superior temporal gyrus (STG). The dissection of the inferior parietal lobule demonstrated the indirect component of superior longitudinal fasciculus (SLF). Thus, removing it, we exposed the complete C-shaped course of the AF. Underneath supramarginal gyrus (SMG), the fibers from AF turn forward and enter the frontal lobe, terminating in the inferior frontal gyrus (IFG) and middle frontal gyrus (MFG). This C-shape fasciculus turning around the insula, connects the temporal, occipital, parietal, and frontal lobes [63, 83, 86]. Moreover, in temporo-occipital basal regions, the AF terminations result partially overlapped with superficial fibers of ILF [34] (Fig. 1). Based on the anatomical landmarks previously identified by other authors [14, 24, 27, 63], the dissection proceeded recognizing the lateral portion of the inferior longitudinal fasciculus (ILF). The ILF is located deep in the temporal segment of the arcuate fasciculus, running inferiorly and laterally to the optic radiation (OR) and temporal horn of the lateral ventricle [14] (Fig. 1). Once the bundle has been identified and recognized as different from the sagittal stratum (SS), we have been able to track the fibers to the cortical terminations in occipital and temporal lobes. No long fibers were identified with an origin in the calcarine fissure. As classically described, we recognized all three branches of origin: a lateral occipital branch, a cuneal branch, and a lingual-fusiform branch.

ILF

Dorsolateral occipital termination appears to be the most superficial branch of ILF. The fibers arising from the anterior portion of the middle occipital gyrus just posterior to the human motion area (MT) [43] run laterally in the occipital white matter and we have been able to track this subcomponent of ILF trough the temporal WM until the TP (Figs 1, 2, 3). The cuneal branch represents the second dorsal component of ILF. Removing the lateral occipital component of ILF, we have been able to follow the fibers from the lateral portion of ILF until the cuneal cortex. All these fibers originate from medial cuneal cortex and at the level of the posterior horn of the lateral ventricle; they become a single bundle that become lateral and more superficial in respect to the SS (Figs. 3, 4, 5). ILF and IFOF, optic radiation and callosal (tapetal) fibers

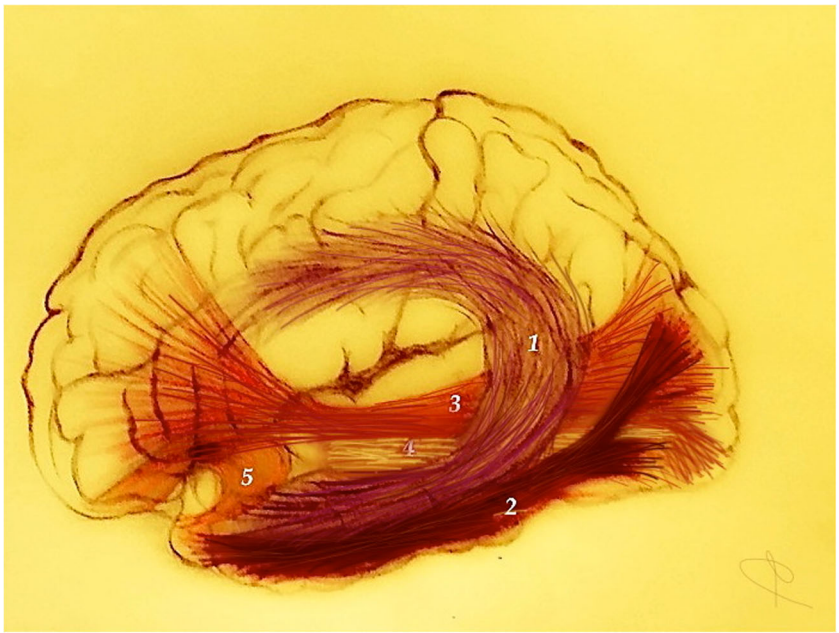

Fig. 1 Artistic illustration of the left hemisphere on lateral (sagittal) view with the main association bundles recreated. The ILF (dILF) originates from occipital extrastriate cortices (cuneal-dorsomedial/*DLOC*-dorso lateral), runs lateral to the IFOF terminations and OR and reach to the temporal pole. The temporal portion of ILF remains caudal in respect to the AF terminations, lateral and inferior in respect to the OR and ends at level of anterior portion of the middle and inferior temporal gyrus, just lateral to the UF temporal terminations. (*1*) arcuate fasciculus AF; (*2*) inferior longitudinal fasciculus ILF; (*3*) inferior fronto-occipital fasciculus *IFOF*; (*4*) optic radiation *OR*; (*5*) uncinate fasciculus *UF*

correspond respectively to the external, intermediate, and internal sagittal strata of Sachs [24, 27, 63]. ILF fibers run on the lateral surface of the brain until the temporal pole in T2–T3 subcortical regions, where the terminal fibers are lateral to the temporal terminations of uncinate fasciculus (UF) (Fig. 1). The SS external layer in the occipital pole (IFOF occipital termination) is identified to split the dorsal component (dILF) from the ventral component (vILF) (Figs. 1, 2, 3, 4, 5) [34, 58]. The ventral branch runs from the posterior part of the fusiform gyrus (FG) posterior and basal occipital region forward and slightly lateral, until the temporal pole following the course of the lateral ventricle (Figs 6 and 7). This ventral pathway represents the infero-lateral wall of the lateral ventricle for its entire course, and beyond the temporal horn it reaches to T3–T4 subcortical region, into the temporal pole (TP) (Figs. 6 and 7).

Li-Am bundle

The dissection of medial structures in the occipital basal region surprisingly revealed a constant lingual branch of ILF, which arises from the mesial posterior lingual cortex. This bundle runs with the fusiform fibers for the average of its length, maintaining a medial and deeper position in respect to the other fibers. From the lingual cortex, these fibers describe an arch-shaped bundle that follows the other ventral pathway until the temporal horn, but this different fascicle leaves the other fibers to turn around the tip of the temporal horn reaching the medial temporal region. As we show in Figs. 6, 7, 8, this thin bundle seems to connect the medial posterior occipital region to the mesial temporal region. Indeed, this fascicle ends with a connection to the parahippocampal region, a few millimeters anteriorly to the head of hippocampus and more medial, into the amygdaloidal region (Li-Am) (Figs. 6, 7, 8).

Discussion

Anatomo-functional considerations on ILF

The aim of this study was, first of all, the analysis of the ILF cortical terminations in respect to the classical anatomical description and functional studies. Secondly, we focused attention on ILF subcomponent in order to achieve a better comprehension of this bundle trough the fine description of hierarchical distribution of ILF fibers. According to initial anatomical studies, we can confirm the existence of ILF as a direct bundle, connecting the temporal and occipital regions [27]. On the base of classical anatomical reports, the occipital branches of the ILF arise in extrastriate cortical regions on the dorsolateral occipital surface, dorsomedially from the cuneus and ventromedially from the posterior lingual gyrus and fusiform gyri. As classically described, our dissection confirms

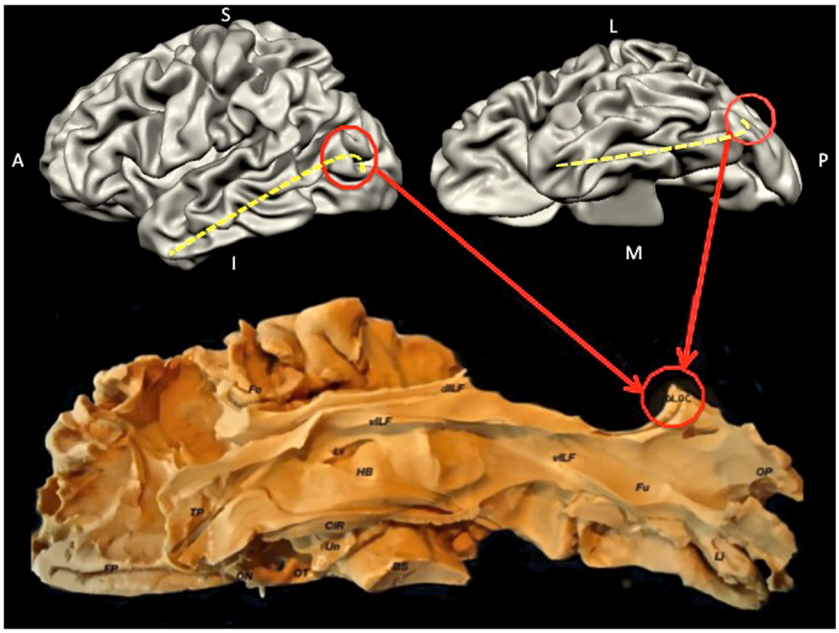

Fig. 2 Illustrations of left hemisphere with the red circle indicating the dorsolateral occipital cortex and the yellow dotted line that indicates the trajectory of the dorsal portion of ILF (*dILF*). The picture shows a latero-basal view of anatomical specimen. The lateral occipital branch appears to be the most superficial on lateral surface (lateral occipital cortex, DLOC, indicated by the *red circle*). The fibers from this branch run forward to the temporal pole creating the lateral portion of dILF. *A* anterior, *P* posterior, *M* medial, *L* lateral, *I* inferior, *S* superior, *BS* brain stem, *Li* lingual cortex, *Un* uncus, *ON* optic nerve, *OT* optic tract, *TP* temporal pole, *FP* frontal pole, *Fo* frontal operculum, *CiR* radiation of cingulum, *Lv* lateral ventricle, *HB* hippocampus body, *vILF* ventral component of inferior longitudinal fasciculus, *dILF* dorsal component of inferior longitudinal fasciculus, *Fu* fusiform branch, *OP* occipital pole

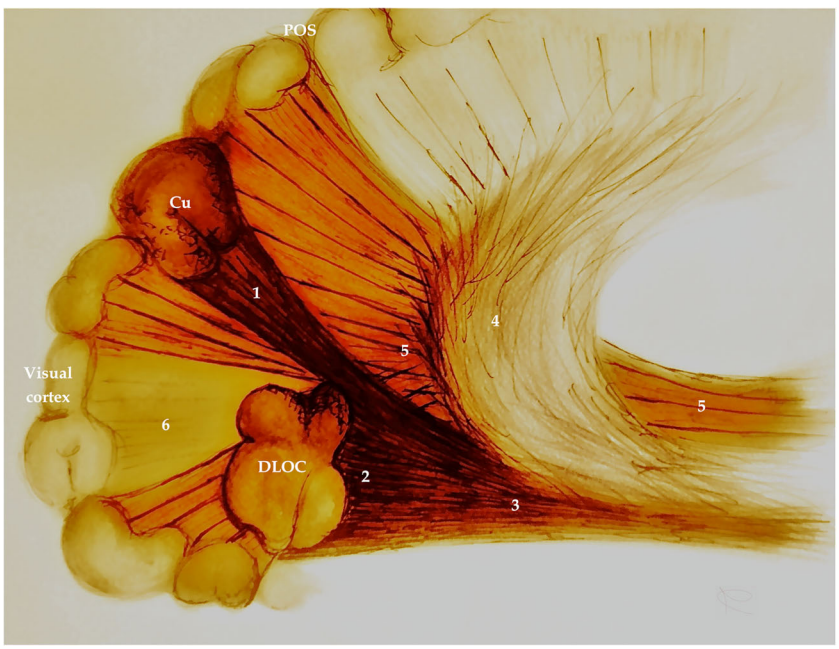

Fig. 3 Artistic illustration of detailed representation of the Dorsal ILF terminations. The dorsolateral occipital cortical termination (*2*) appears to be the most superficial branch of ILF. The fibers arising from anterior portion of middle occipital gyrus (*DLOC*) run laterally in the occipital white matter. The cuneal branch (*1*) represents the second dorsal component of ILF. All these fibers originate from medial cuneal cortex (*Cu*), just caudal in respect of the parieto-occipital sulcus (*POS*). At the level of the posterior horn of the lateral ventricle they become a single bundle (dILF, *3*) that turns laterally and more superficial in respect to the deeper fibers of IFOF within the sagittal stratum (*5*) and caudal in respect to the arcuate fasciculus (*4*). ILF and IFOF with optic radiation and callosal (tapetal) fibers correspond respectively to the external, intermediate, and internal sagittal strata of Sachs. In this picture, we can appreciate the different depth of the ILF (more superficial in the occipital portion) the IFOF (*5*) and more deep the OR (*6*) which reaches to the visual cortex medially in respect to the other bundles. The internal layer of SS is not represented

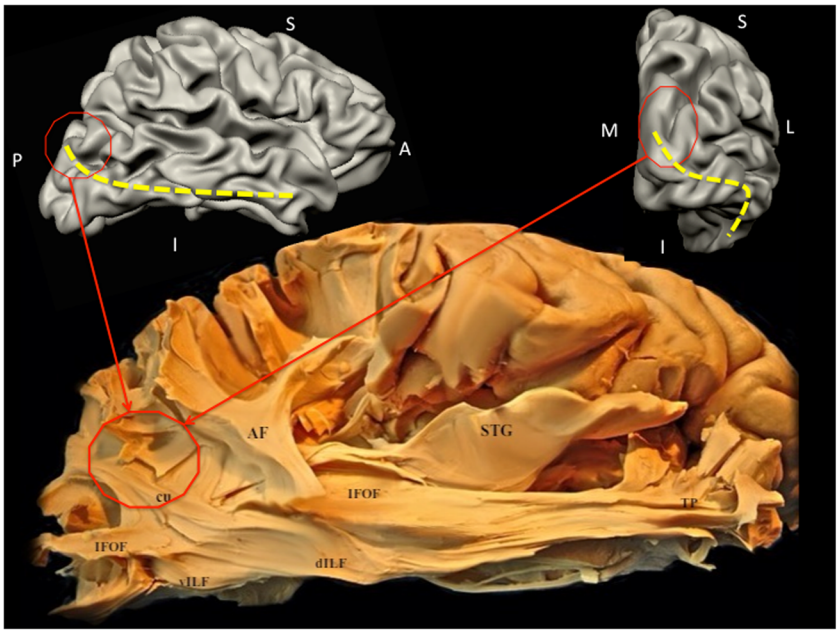

Fig. 4 Illustrations of right hemisphere with the *red areas* indicating the cuneal cortex in the occipital region. The *yellow dotted lines* indicate the trajectory of the dorsal portion of ILF (*dILF*) until the temporal pole. The picture shows the lateral view of an anatomical specimen after the removal of latero-occipital component of dILF. The cuneal branch represents the dorsomedial origin of ILF. These fibers are directed caudally and remain superficial in respect of the IFOF. At the level of posterior horn of the lateral ventricle they turn anteriorly and become parallel to the others fibers within the sagittal stratum (*IFOF*) until the temporal pole. The AF fibers (cut and retracted) is always cranial and more superficial in the temporal portion of these fibers. *A* anterior, *P* posterior, *I* inferior, *S* superior, *AF* arcuate fasciculus, *Cu* cuneal branch, *vILF* ventral component of inferior longitudinal fasciculus, *dILF* dorsal component of inferior longitudinal fasciculus, *STG* superior temporal gyrus; *IFOF* inferior occipito-frontal fasciculus

the three originating branches: a lateral occipital branch, a cuneal branch, and a lingual-fusiform branch.

From the functional point of view, it is currently thought that the posterior basal temporal areas are involved in visual recognition [16, 26, 33, 44, 45], with specific areas for faces (faces fusiform area (FFA), on the right hemisphere [50], tools (bilateral temporal regions [16]), houses (bilateral parahippocampal gyrus [33]), and words (visual word form area (VWFA), left hemisphere, dominant in language processing [22, 64]). We can suppose then, that both dILF and vILF represent a fast direct pathway which connects cortices activated by several visual inputs such as face, object, houses,

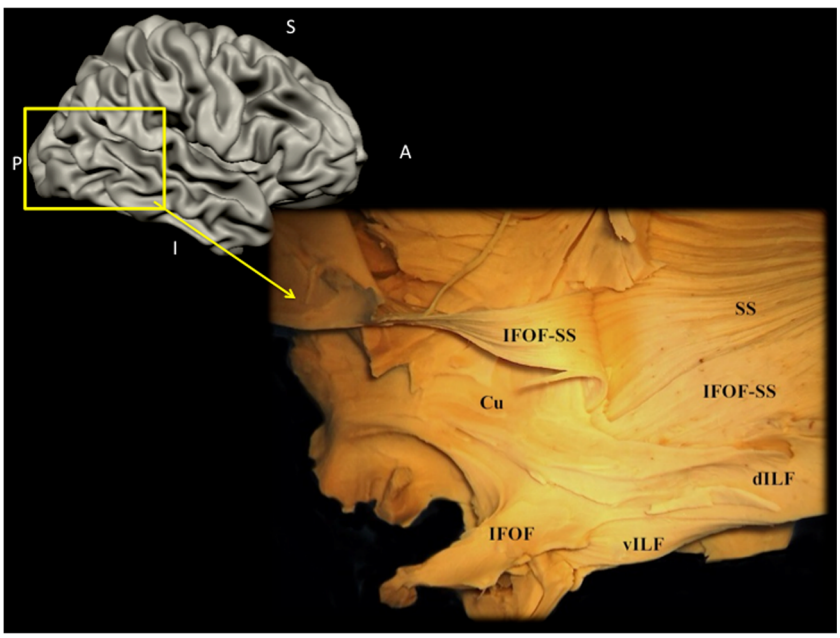

Fig. 5 Illustration of right hemisphere with the yellow rectangle indicating the anatomical region magnified in the picture. The picture shows with higher magnification the relationship between dILF and the other layers of SS. The AF fibers (more superficial) have been lifted under the metallic spatula. Parts of the SS have been opened and reflected posterior to show the deep component of SS. The inferior occipital terminations of IFOF (within the SS) seem to split the two components of ILF (dILF and vILF). *AF* arcuate fasciculus, *Cu* cuneal originating branch of dILF, *IFOF* inferior occipito-frontal fasciculus, *SS* sagittal stratum, *vILF* ventral component of inferior longitudinal fasciculus

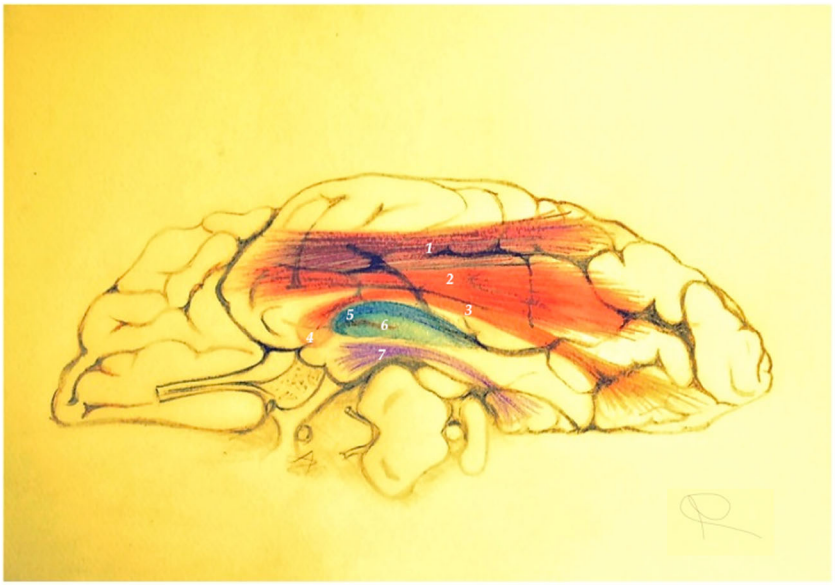

Fig. 6 Artistic illustration of a left hemisphere in a ventral (basal) view of the temporo-occipital region with the main white matter bundles recreated. The dILF (*1*) as previously described represents the most lateral component of this longitudinal pathway. The ventral component of ILF (vILF, *2*) originates from the fusiform subcortical white matter and runs forward as a single bundle along the infero-lateral wall of the lateral ventricle until the parahippocampal gyrus and the basal portion of temporal pole. The Li-Am bundle (*3*) is identified as originating from the lingual cortex, medially. The fibers within this thin bundle run with a arch-shaped trajectory following the infero-lateral wall of the lateral ventricle but always medial and deeper in respect to the vILF. So, in order to expose the Li-Am bundle part of the vILF needs to be removed or reflected. At the level of the tip of the temporal horn (*5*) the Li-Am bundle turns medially and it reach the amygdoidal region (*4*) just in front of the hippocampus (*6*). At the same depth, this region (*4*) shows a medial relationship with the radiation of cingulum (*7*)

animals (LO and V3–V7) [43], cortical regions involved in multimodal processing of stimuli (lateral infero-temporal multimodal area (LIMA) for language [21]) and anterior temporal pole, where the overlapped terminations between the ILF and the UF create a communication with (1) the semantic ventral stream (IFOF) for language analysis and (2) the dorsal visual stream (SLF-IFOF) involved in analysis of spatial position (the "where" and "how" pathway) of the visual cue [10, 41, 79]. Our hypothesis is supported by several data regarding the activation of LIMA served by this subcomponent of ILF, which appears as an optional component of both written and spoken word processing [9, 21]. Its multimodal activation pattern fits the general role of the left lateral temporal cortex in providing a convergence zone supporting the linkage of orthographic, phonemic, and semantic information [8, 12, 13, 17, 25, 29, 31, 38, 68, 71, 88, 92]. Indeed, posterior inferior lesions of the lateral temporal cortex yield word-finding difficulties, which may reflect impaired links between word forms and semantics [18, 20, 21, 30, 35, 62].

Li-Am Bundle

For the first time, we identified a separate lingual component of ILF, which maintains medial position in respect to the other fibers for the entire length of the vILF. This Li-Am pathway describes an arch-shaped bundle that follow the other ventral pathway until the temporal horn, where it leaves the other fibers to turn around the tip of the temporal horn reaching the medial temporal region just anterior to the hippocampus, within the amygdaloidal region (Figs. 6, 7, 8). Even if not yet validated on a large number of specimens, this bundle may represent the key of the visual limbic pathway that subserves emotional, learning, and memory functions that are modality-specific to vision [18]. Several DTI studies reported correlations between reduced FA in some portions of the ILF and impairments of higher visuo-perceptual functions [76] including object and picture naming [57, 81], dyslexia [28, 74, 84], and alexia [32]. Moreover, according to Catani et al. [14] the role of this ventral bundle is even more complex. Indeed, once that emotional valence of a visual stimulus has been identified, the signals will be fed-back directly to early visual areas, enhancing the visual processing of emotionally significant stimuli. The emotional context in which a stimulus is encountered can markedly affect the memory trace of that stimulus. Indeed our visual system gradually modifies the way it processes sensory stimulation according to prior experience [60, 77, 79, 93]. Hung et al. demonstrated how the early amygdala activation indicates a fast and an automatic response, independent of the location of the fearful stimuli in the visual field [46]. So we may identify in lingual-amygdaloidal bundle the pathway subserving fast limbic response to visual stimuli figured in many other studies. The functions of these brain regions are essential for interpersonal communication [85]. The amygdala serves as a protective "brake" in social

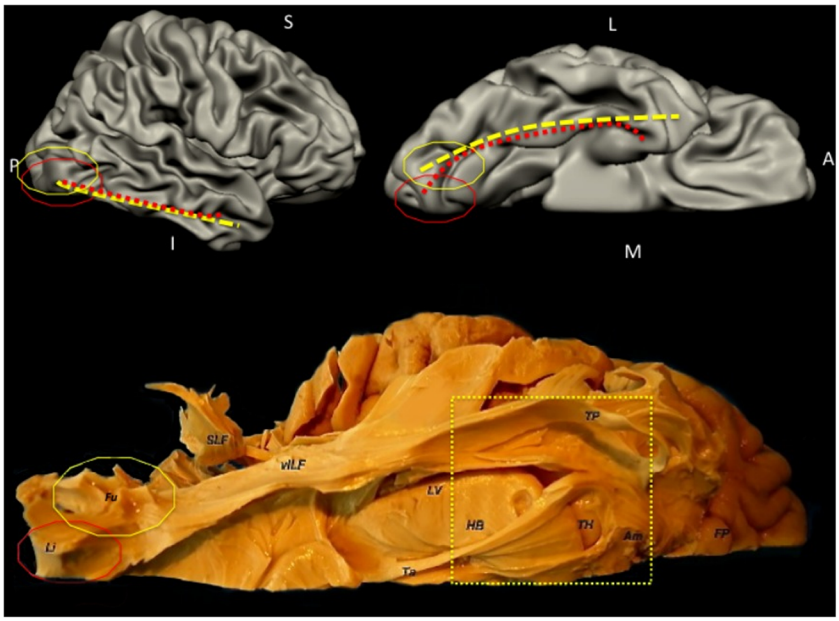

Fig. 7 Illustrations of right hemisphere with the *red areas* indicating the lingual cortex and the *yellow area* indicating the fusiform region in the occipital basal region. The *yellow dotted line* describes the trajectory of the ventral portion of ILF (*vILF*) from the posterior part of fusiform gyrus until the basal cortex of temporal pole. The *red dotted line* indicates the trajectory of the lingual-amygdaloidal bundle (Li-Am). The picture shows a basal view of ventral originating branches of ILF. The first branch arises from the posterior occipito-temporal gyrus-fusiform region (*Fu*, *yellow area*), inferiorly and medially to the dorsolateral component of ILF, and sagittal stratum previously described. This ventral branch runs from posterior and basal occipital region forward, until the temporal pole. This ventral pathway represents the infero-lateral wall of lateral ventricle for its entire course, and beyond the temporal horn it reaches to T3–T4 subcortical region (vILF-T4), into the temporal pole (*TP*). The lingual branch of ILF (Li), originates from the mesial and posterior lingual cortex (*Red areas*). This bundle runs with the fusiform fibers for the average of its length, maintaining a medial position in respect to the other fibers. From the lingual cortex these fibers (Li-Am) describe an arch shaped bundle that follow the other ventral pathway until the temporal horn, but surprisingly this fascicle leaves the other fibers to turn around the tip of the temporal horn reaching the medial temporal region. *SLF* superior longitudinal fasciculus, *Li* lingual subcortical region, *Fu* fusiform branch, *LV* lateral ventricle, opened, *HB* hippocampus body; *TH* Temporal Horn, opened, *Am* amygdala, *Ta* tapetal fibers, *TP* temporal pole; *FP* frontal pole, *Li-Am* lingual-amygdaloidal bundle

situations [1]. Lesions of the amygdala cause a lack of fear and lead to a kind of "socially uninhibited" pattern of behavior, which can be seen in people without fear who cannot avoid persons bearing them potential harm. Furthermore, amygdala lesions also have deleterious consequences on primate social behavior [1]. In support of this view, recent imaging studies have found neuromodulatory effects of the amygdala on extrastriate visual cortex [61, 69], and psychophysical studies have identified an equivalent modulatory effect of emotional content on visual perceptual processing [2]. Thus, it has been hypothesized [4] that improved occipito-temporal connectivity may contribute to developmental and individual differences in social cognition. Choi et al. [19] suggest that an imbalance between the integrity of the left and right ILF may predispose individuals to interpret relatively neutral stimuli in a more negative way, which may increase their vulnerability to psychopathology. Recent data seem to encourage the idea of a symmetric development of ILF in a nonpathologic condition. Considering the imitated number of specimens, we did not recognize quantitative or morphologic interhemispheric variability nor in dorsal or in ventral subcomponents. Hence, we believe that this symmetry could justify the residual functioning in the visual input processing after ILF damages due to primitive lesions or, for example, temporal lobectomy. The loss of symmetry on the other hand could lead the network to express positive symptoms due to the hyperactivation of the subserved cortical areas and seizures. The actual seizure focus, in these cases, might be obscured by rapid propagation of the ictal epileptic activity from one brain region to another. This has been described in patients with occipital lobe seizures spreading to the temporal lobe [67]. Occipital lobe epilepsy (OLE) represents less than 10 % of extratemporal epilepsies and as few as 2 % of resective epilepsy procedures [7, 55]. Sir William Richard Gowers first described OLE in 1879 as "epileptoid attacks with visual auras" in a patient with a parieto-occipital tumor [42]. Although there are typical clinical features of occipital lobe attacks such as visual hallucinations, ictal blindness, and oculomotor symptoms, patients with OLE may also have features of temporal or fronto-parietal epilepsy [89]. The specific localization of OLE is difficult due to the deep location of the occipital lobe relative to scalp EEG and the potential for rapid propagation of seizures through functional white matter tracts [3, 54]. This has led some authors to speculate

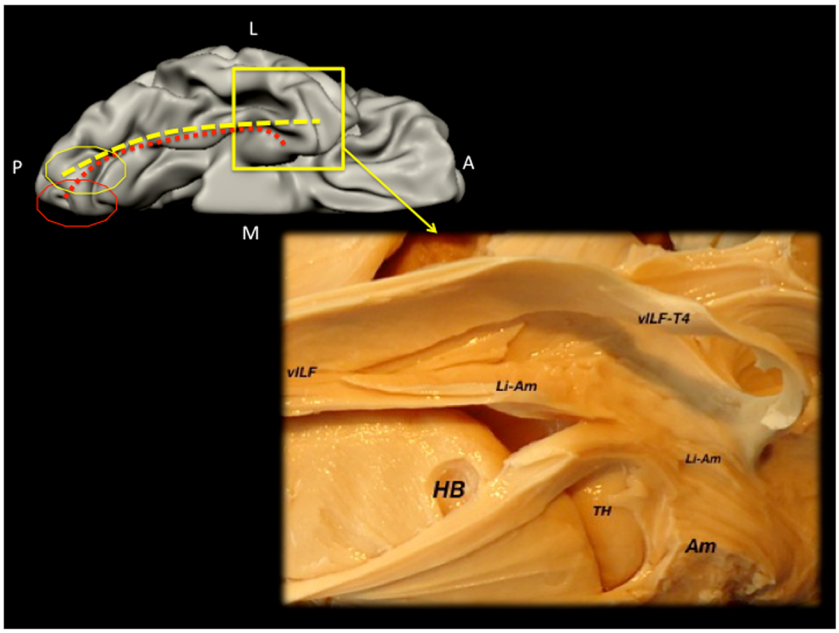

Fig. 8 Illustration of the basal surface of the right hemisphere, with the two components of the vILF. The *yellow dotted line* describes the fusiform component, originating from the posterior fusiform area (*yellow circle*) running inferiorly and lateral to the ventricle. The *red dotted line* describe the Li-Am bundle originating from the lingual cortex (*red circle*), which runs in a arch shaped trajectory until the mesial temporal lobe . The picture shows the area described by the *yellow rectangle* in Fig. 7. Particular of this is the thin bundle (Li-Am) which connects the medial posterior occipital region to the mesial temporal region. Indeed, this fascicle ends with a connection to the parahippocampal region, few millimeters anterior to the head of hippocampus and more medial, close to amygdale nucleus. *HB* hippocampus body, *TH* temporal horn, opened; *Am* amygdala, *Li-Am*, lingual-amygdaloidal bundle, *vILF* ventral component of inferior longitudinal fasciculus, *vILF-T4* anterior termination of vILF at the level of parahippocampal gyrus (T4)

that some forms of nonlocalizable epilepsy may have their onset within the occipital lobes [49]. In OLE, the most common findings on scalp EEG are spikes and sharp waves in temporal and temporo-occipital regions [89]. In 50 % of patients with OLE, temporal lobe automatisms have been seen [78], probably related to rapid propagation from the occipital lobe to anterior temporal regions [89]. Hence, the clinical evidences of variable epileptic propagation have been demonstrated with basic researches involving evoked potential excitability studies in humans and anatomic studies with tracer injections and single-unit recordings with histological studies in animals. These reports confirmed the involvement of the amygdala and the hippocampus in the epileptogenic network [11, 51, 91]; it is reasonable to think, therefore, that this pathway of propagation involves the inferior longitudinal fasciculus [23, 65]. We can suppose that the Li-Am bundle which represents a direct connection from V4 (BA 19) to the hippocampus and amygdala, could be one of the most frequent hyperactivated ways of the epileptic onset propagation in OLE. The recognition of the different pathways direct involved in OLE onset and its propagation could be crucial to define a most effective strategy to prevent new seizures (i.e., in order to avoid specific stimuli) to determine outcome and to choose eventually the best therapeutic option, modulating bundles activity or interrupting in according to the new anatomical landmarks. More anatomical and functional studies are needed in order to better understand this new/old anatomical pathway.

Methodological considerations

Previous anatomical studies focused on the temporo-occipital connections have been performed with classical Klingler's technique for the specimens' preparation and dissection. If we consider the particular morphology of the basal region which, actually, because of gravity due to the standing position, results pressed down to the tentorium and middle cranial fossa from its own-weight, we hypothesized that subcortical organization of WM should have been slightly different in respect to another "not compressed" cortical regions. For this reason, we decided to start the dissection from the basal temporo-occipital region. The cortex and the superficial white matter layers were more carefully dissected on the basal surface than in other regions in order to preserve the hierarchical distribution of the longitudinal fibers. Moreover, we experimented this technique (described above) for specimen preparation that seems very useful in preserving the very thin layers, especially during the first step of dissection. The use of a microdissector since the first stage of dissection allowed us to be very careful in preserving the multiple subcortical layers and interestingly allowed us to clearly identify at each step the ILF fibers, also defining the trajectory of the very thin Li-Am

bundle which would have been damaged or neglected with standard dissection technique.

Limitations

The numbers of specimens represents the first and most important limitation. However, despite the restricted number of hemispheres dissected no anatomical variability was reported. The second limitation regards the preparation technique, because there are no sufficient data in literature about this modification from the standard Klingler's technique. Further studies are then required in order to validate this technique as trustable. Third, the white matter dissection studies in the past, explored preferentially the anatomy of the main bundles. The ILF incredibly received poor attention, so a more extensive fine description of the originating branches and fibers segregation are needed in order to confirm this peculiar subcortical anatomy.

Conclusion

According to our preliminary results, this is the first fine description of ILF's subcomponents. The complex but clearly segregated organization of the fibers of this bundle (dILF and vILF) is here for the first time described in details. These anatomical features seem to be constant and may support different levels of functions, mediated by visual recognition and modulated by the ILF relationships with the other main associative bundles. Moreover, this is the first anatomical description of a direct pathway from the lingual cortex to amygdala (Li-Am), which might be involved in the limbic modulation of visual processing. In physiological conditions, indeed, the interaction between ILF and Li-Am bundle may represent the anatomo-functional substrate of social cognition, which may originate from cortical activation in occipito-temporal cortices due to perception of visual inputs during childhood. The visual cues, for instance, would be filtered (i.e., categories, shapes, colors) and modulated in specialized cortical areas by limbic response, which can enhance (short subcortical fibers) or decrease attention on finer details. The expertise and emotional value of an object, a face, or a situation would continuously modulate our visual analysis. This neural circuit may create the human being's skill of reading, in more extensive sense, a word, a face expression or in generally each possible circumstance, creating and retrieving semantic and emotional memories. In pathological conditions, on the other hand, the Li-Am may be one of the hyperactivated pathways responsible for the fast temporal propagation of the epileptic focus elicited, for example, by visual stimuli in the occipital regions, with obvious possible therapeutic implications. Further anatomical and functional studies will be necessary to clarify the role of this newly described network.

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Comments

Guilherme Carvalhal Ribas, São Paulo, Brazil

The fiber dissection technique was already employed by early anatomists as Thomas Willis (1621–1675), Nicholas Steno (1638–1686), Raymond Vieussens (1641–1715), Charles Bell (1774–1842), Johan Christian Reil (1759–1813), Achille Foville (1799–1878), Bartholomeo Panizza (1785–1867), Louis Pierre Gratiolet (1815–1865), and Theodor H Meynert (1833–1892) among others[2,5] in order to understand the complex white matter architectural organization and to better describe its tracts, fasciculi, and commissural fibers, but it was only with the contribution of Joseph Klinger (1888–1963) that this technique became more feasible and widely used[4,5]. Klinger described in 1935 the freezing technique of previously formalin-fixed brains, which generates the development of formalin ice crystals between the fibers which facilitates their dissection that is done by their progressive peeling[3].

More recently, the advent of tractography, which is a 3D MRI modeling technique based on collected data obtained by diffusion tensor imaging (DTI) that evaluates brain water diffusion in a tensor, which is the major axis parallel to the direction of fibers—different bundles of fiber tracts make the water diffuse asymmetrically in a tensor, which is directly related with the number of fibers and is known as anisotropy—is generating a significant amount of imaging data which subsequently requires to be validated, and the Klinger technique or its variations still are the most practical way of doing it.

In this direction, Dr. Latini, taking into consideration also previous DTI findings, studied the inferior longitudinal fasciculus and its related subcomponents. Although based on the dissections of only four hemispheres of two brain specimens, this interesting article brings some more light into the understanding of the complex inferior longitudinal fascicle, and, above all, has the merit of describing a new bundle, the lingual-amygdaloidal bundle.

Nevertheless, for a proper appraisal of the author's study, it is important to consider that both fiber dissection and DTI techniques have similar limitations regarding the identification of small bundles, particularly in

regions where fibers intermingle. Even when the fiber dissection technique is done under magnification, it is very difficult to dissect and peel the multiple layers of fibers that are intermingled with fibers that run in other directions, and also to securely identify the fibers that belong to different fasciculi which are superimposed and running along the same direction. On the other hand, the DTI technique, although extremely helpful, uses a computer-based image analysis to do a nondirect measure of the fiber's structure and integrity, which implies some degree of subjectiveness since this technique is in part dependent on a number of factors under the control of the experimenter, such as the angular and anisotropy thresholds and the choice of the tractography algorithm itself, as stated by Catani et al.[(1)].

Considering these methodological issues and the small number of dissected specimens, the results of this elegant study, and their discussed inferential functional roles, should now motivate further research of this important subject in order to corroborate its findings and considerations.

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