European Journal of Radiology 82 (2013) 151–157

Contents lists available at SciVerse ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Middle longitudinal fasciculus delineation within language pathways: A diffusion tensor imaging study in human

Nicolas Menjot de Champfleur[a,b,*], Igor Lima Maldonado[a,b,e], Sylvie Moritz-Gasser[a,c], Paolo Machi[a], Emmanuelle Le Bars[a,b], Alain Bonafé[a,b], Hugues Duffau[a,d]

[a] Department of Neuroradiology, University Hospital Center, Gui de Chauliac Hospital, Montpellier, France
[b] Team "Plasticity of Central Nervous System, Stem Cells and Glial Tumors," Institut National de la Santé et de la Recherche Médicale Unité 1051, Institut of Neurosciences of Montpellier, Saint Eloi Hospital, Montpellier, France
[c] Department of Neurology, University Hospital Center, Gui de Chauliac Hospital, Montpellier, France
[d] Department of Neurosurgery, University Hospital Center, Gui de Chauliac Hospital, Montpellier, France
[e] Divisão de Neurologia e Epidemiologia (CPPHO), Complexo Hospital Universitário Professor Edgard Santos, Universidade Federal da Bahia, Salvador-Bahia, Brazil

ARTICLE INFO

Article history:
Received 2 May 2012
Received in revised form 17 May 2012
Accepted 19 May 2012

Keywords:
Diffusion tensor imaging
Tractography
Language Pathways

ABSTRACT

Introduction: The existence in the human brain of the middle longitudinal fasciculus (MdLF), initially described in the macaque monkey, is supported by diffusion tensor imaging studies. In the present work, we aim (1) to confirm that this fascicle is found constantly in control subjects with the use of DTI techniques and (2) to delineate the MdLF from the other fiber bundles that constitute the language pathways.
Materials and methods: Tractography was realized in four right-handed healthy volunteers for the arcuate fascicle, uncinate fascicle, inferior fronto-occipital fascicle, inferior longitudinal fascicle and the middle longitudinal fascicle. The fiber tracts were characterized for their size, mean fractional anisotropy (FA), for their length, number of streamlines, and lateralization indices were calculated.
Results: The MdLF is found constantly and it is clearly delineated from the other fascicles that constitute the language pathways, especially the ventral pathway. It runs within the superior temporal gyrus white matter from the temporal pole, then it extends caudally in the upper part of the sagittal stratum and the posterior part of the corona radiata, to reach the inferior parietal lobule (angular gyrus). We found a leftward asymmetry for all fiber tracts when considering the mean FA.
Discussion: Using DTI methods, we confirm that the MdLF connects the angular gyrus and the superior temporal gyrus. On the basis of these findings, the role of the MdLF is discussed.
Conclusion: The middle longitudinal fasciculus, connects the angular gyrus and the superior temporal gyrus and its course can be systematically differenciated from those of other fascicles composing both ventral and dorsal routes (IFOF, IFL, AF and UF).

1. Introduction

In the human brain, white-matter tracts can be classified into 5 categories [1] depending on their location and function: brainstem fascicles, limbic system fascicles, projection fascicles linking the cortex to the brainstem, commissural (interhemispheric) fascicles linking one hemisphere to the other and finally association (intrahemispheric) fascicles connecting cortical regions together.

These tracts have initially been described using dissecting techniques. Diffusion tensor imaging (DTI) is a novel method allowing indirect investigation of brain microstructure determined by the directionality of water molecules' movements. Diffusion-weighted images are used to generate, non-invasively, three-dimensional representations of the white matter tracts. For water diffusion is oriented along fiber tracts' direction, fascicles are reconstructed by using this directional property of water diffusion in each voxel. White matter pathways are delineated using this information by inferring the continuity of fibre paths from voxel to voxel. Therefore, DTI allows the specific examination of the integrity of white matter pathways, which are altered by numerous diseases such

---

Abbreviations: AF, arcuate fasciculus; EmC, extreme capsule; DTI, diffusion tensor imaging; FA, fractional anisotropy; fMRI, functional magnetic resonance imaging; IFOF, Inferior fronto-occipital fasciculus; ILF, inferior longitudinal fasciculus; LI, lateralization index; MdLF, middle longitudinal fasciculus; MRI, magnetic resonance imaging; SLF, superior longitudinal fascicle; SLF III, third subcomponent of the superior longitudinal fasciculus; STG, superior temporal gyrus; UF, uncinate fasciculus.

* Corresponding author at: Department of Neuroradiology, University Hospital Center, Gui de Chauliac Hospital, 80 Avenue Augustin Fliche, 34295 Montpellier Cedex 5, France Tel.: +33 467 337276; fax: +33 4 67 33 68 38.
E-mail address: nicolasdechampfleur@orange.fr (N. Menjot de Champfleur).

0720-048X/$ – see front matter © 2012 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.ejrad.2012.05.034

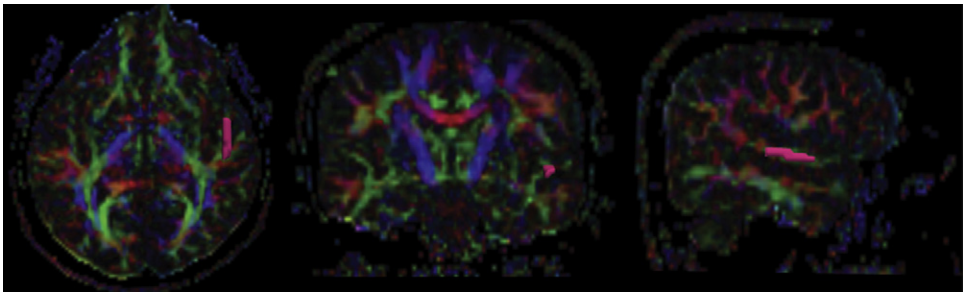

Fig. 1. Segmentation if the stem portion of the MdLF. The seed ROI's are delineated within the white matter of the STG, considering voxel with anterior–posterior diffusion properties (green on FA-color map).

as brain tumors [2], traumatic injuries or demyelinating diseases. More recently DTI, has permitted a precise delineation of white-matter tracts in vivo, non-invasively [3,4].

The middle longitudinal fasciculus was initially described in the macaque monkey where it connects the caudal part of the inferior parietal lobule to the white matter of the superior temporal gyrus. With the use of radiographic isotopic methods, it has been shown to be distinct from other long association fiber pathways such as the superior longitudinal fasciculus [5,6] and these findings were confirmed with the use of DTI imaging techniques in the human brain [7].

Due to its location, connecting the inferior parietal lobule and the superior temporal gyrus, one can speculate that the MdLF belongs to the language pathway, even if its function remains unclear. Modern comprehension into neurobiological basis of language suggest that language's network is distributed in a «dorsal» and «ventral» route [8–11]. In this model, the «dorsal» route is proposed for speech perception and the «ventral» route for semantic processing and speech comprehension.

Findings in human using DTI techniques as well as intraoperative electrical stimulations had been compared to radioactive anterograde tract tracing method in the Rhesus monkeys in order to identify white matter pathways composing «ventral» and «dorsal» route and clarify their role. These studies have supported the model of language network detailed earlier. The «dorsal» route involved in phonological and articulatory processes, appears to be comprised of the arcuate fasciculus (AF) and the third subcomponent of the superior longitudinal fasciculus (SLFIII) [12]. The «ventral» route, involved in semantic processes would be comprised of the inferior longitudinal fasciculus (ILF), the uncinate fasciculus (UF) and the inferior fronto-occipital fasciculus (IFOF) [13]. Saur et al. [11] suggest that the MdLF participate in both dorsal and ventral

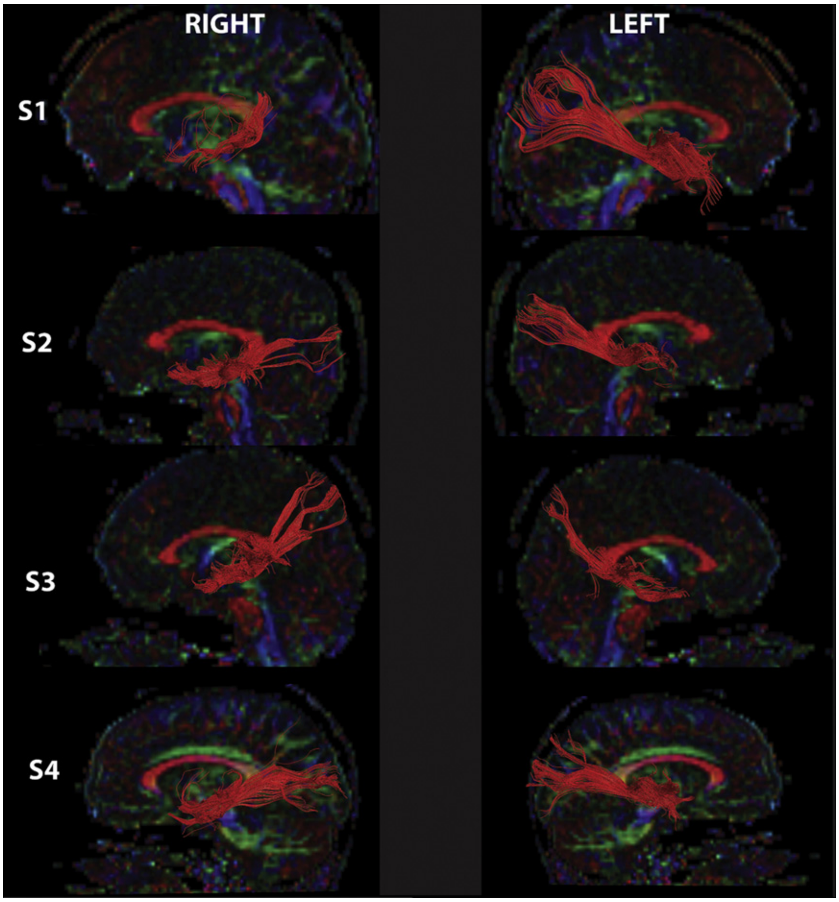

Fig. 2. Trajectory of the MdLF.

Table 1
Results of FA, volumetry and lateralization index of the stem portion of the MdLF.

Parameter	Side	Subject 1	Subject 2	Subject 3	Subject 4	Groupe	std-dev	lateralization index
FA ROI	G	0.36	0.41	0.43	0.38	0.40	0.03	−0.002
	D	0.38	0.43	0.37	0.38	0.40	0.04	
Number of voxels	G	89	41	31	99	65	33.98	−0.14
	D	81	54	81	82	74.5	13.67	

L = left; *R* = right; std-dev = standard deviation; lateralization index = (*L* − *R*)/(0.5(*L* + *R*)).

routes involved in language processing, thus, De Witt Hamer et al. [14] recently found intraoperatively no interference with picture naming by electrostimulation of the middle longitudinal fascicle, nor permanent post-operative language deficit when resection includes a large part of the fascicle and therefore, the fasciculus might not be essential for language.

In the present work, we aim (1) to confirm that this fascicle is found constantly in control subjects and (2) to delineate the MdLF from the other fiber bundles that constitute the language pathways, especially the ventral pathway (i.e. IFOF, ILF, and UF).

2. Materials and methods

2.1. Subjects

Four right-handed healthy volunteers were enrolled in this study, 2 males and 2 females, mean age: 28.5-year-old (max.: 34, min.: 23, SD: 4.9). This study was approved by the local Ethics Committee and informed consent was obtained from all participants.

MRI data were acquired using echo-planar imaging at 1.5T scan (Philips Medical Systems, Best, the Netherlands) with a standard head coil. High resolution T1-weighted anatomical images were acquired (gradient-echo sequence, repetition time 7 ms, echo time 3.5 ms, flip angle = 9°, matrix 256 × 256, slice thickness 2 mm). DTI axial slices were obtained using the following parameters: repetition time 10,785 ms, echo time 70 ms, flip angle 90°, matrix 96 × 96, slice thickness 2.5 mm, voxel size 1.88 × 1.88 × 2.5 mm). Diffusion MR images were obtained from 15 independent noncolinear directions with a *b*-value of 1000 s/mm^2 and with one $b = 0$ image with no diffusion gradients.

Raw diffusion data were corrected for distortion secondary to eddy currents by using FSL (FMRIB (The Oxford Centre for Functional Magnetic Resonance Imaging of the Brain) Software Library, http://www.fmrib.ox.ac.uk/fsl). FA maps were calculated in native space using the Diffusion toolkit software [15].

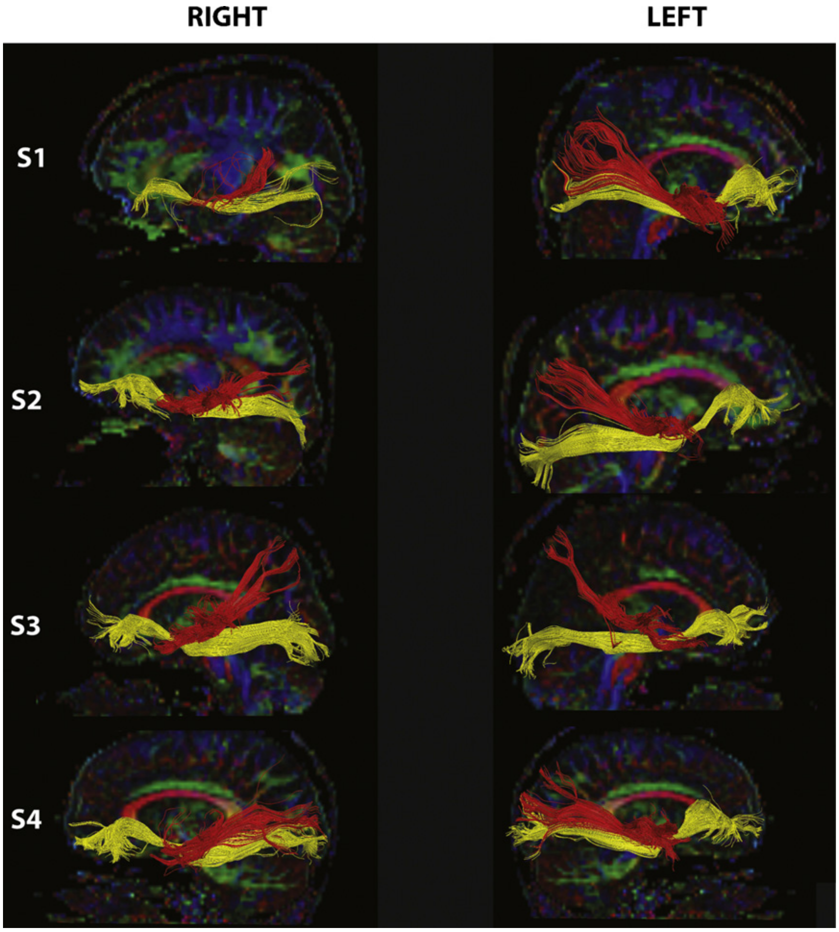

Fig. 3. Comparison of the trajectories of the MdLF and IFOF. Grey: MdLF; white: IFOF.

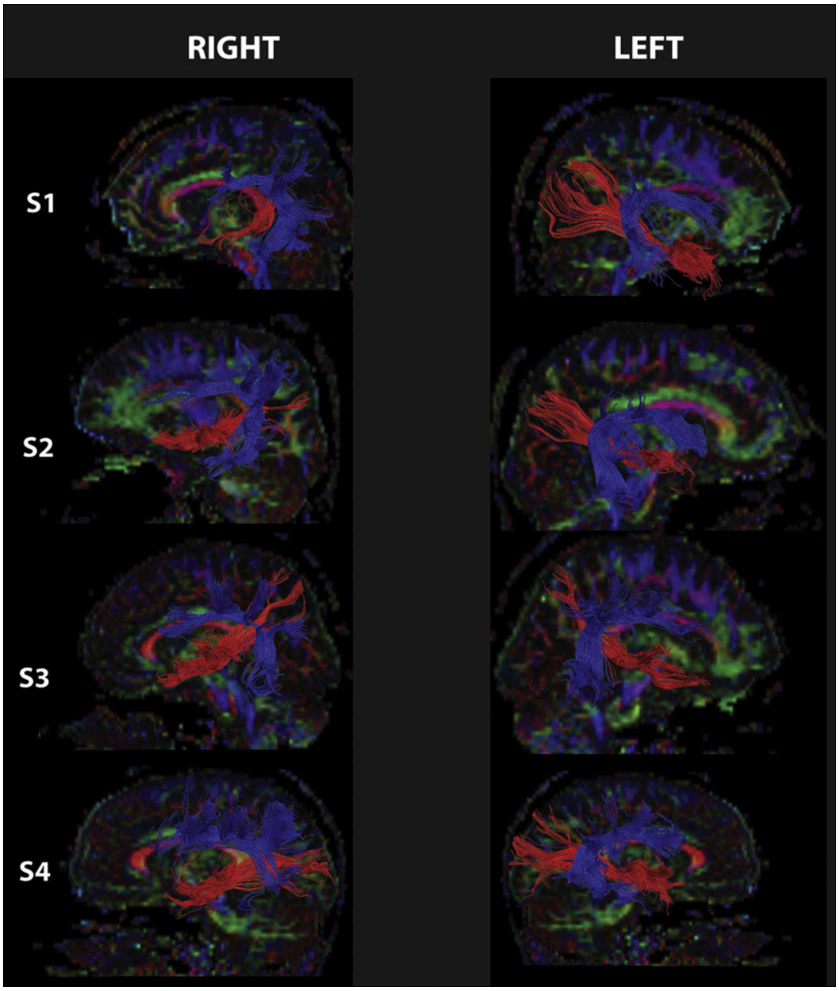

Fig. 4. Comparison of the trajectories of the MdLF and AF. Red: MdLF; blue: AF.

Tractography data were analyzed using TrackVis software [15]. DTI tractography was performed based on an algorithm based on streamlined method. Tractography parameters were set as follows: angle threshold 30°, FA threshold 0.2.

We used the TrackVis 3D tool software to delineate the seed ROI's. They were selected on FA color maps, according to previously described methods for the AF, UF, IFOF, ILF [16]. In order to realize the middle longitudinal fascicle (MdLF) tractography, we manually segmented the stem portion of the MdLF on coronal slices of the FA map as described by Makris et al. [7]. The selected voxels were considered as being part of the MdLF if they were located within the white matter of the superior temporal gyrus (STG) and if the orientation of diffusion properties of the tissue was anterior–posterior (green on FA-color map).

Each ROI and each fiber tract were characterized for their size and mean FA. Additionally, fiber tracts were characterized for their length and number of streamlines. Then, we calculated lateralization index based upon the following formula: $(L-R)/(0.5(L+R))$ considering these parameters.

Each individual fiber tracts were normalized in the Montreal Neurological Institute Space (MNI http://www.bic.mni.mcgill.ca/). The T1 images of each subject were normalized using the T1 template provided in SPM8 (http://www.fil.ion.ucl.ac.uk/spm/). Then the transformation matrix obtained from the T1 normalization was applied to b0 images, FA parametric maps and fiber tracts of each subject. Finally, cortical boundaries of MdLF tract were characterized for each subject in MNI space.

3. Results

In this study, (1) we segmented the seed ROI of the MdLF in 4 healthy volunteers, and made volumetric and FA measurements; (2) we characterized the MdLF using tractographic techniques; (3) we differenciated the MdLF from the putative fasciculi comprising both «dorsal» and «ventral» route; (4) we calculated lateralization index for each fiber tract and for the stem portion of the MdLF; (5) we characterized the cortical boundaries of the MdLF in the MNI space.

3.1. Segmentation observations

Seed ROI for the MdLF, delineated on the basis of anatomical knowledge were traced within the white matter of the STG,

Table 2
Caudal cortical boundaries of the MdLF.

	Left caudal	Right caudal
Subject 1	IPL (angular gyrus), lateral occipital cortex	NA
Subject 2	IPL (angular gyrus)	IPL (angular gyrus), occipital pole
Subject 3	IPL (angular gyrus)	IPL (angular gyrus)
Subject 4	IPL (angular gyrus), occipital pole	IPL (angular gyrus), occipital pole

IPL: inferior parietal lobule.

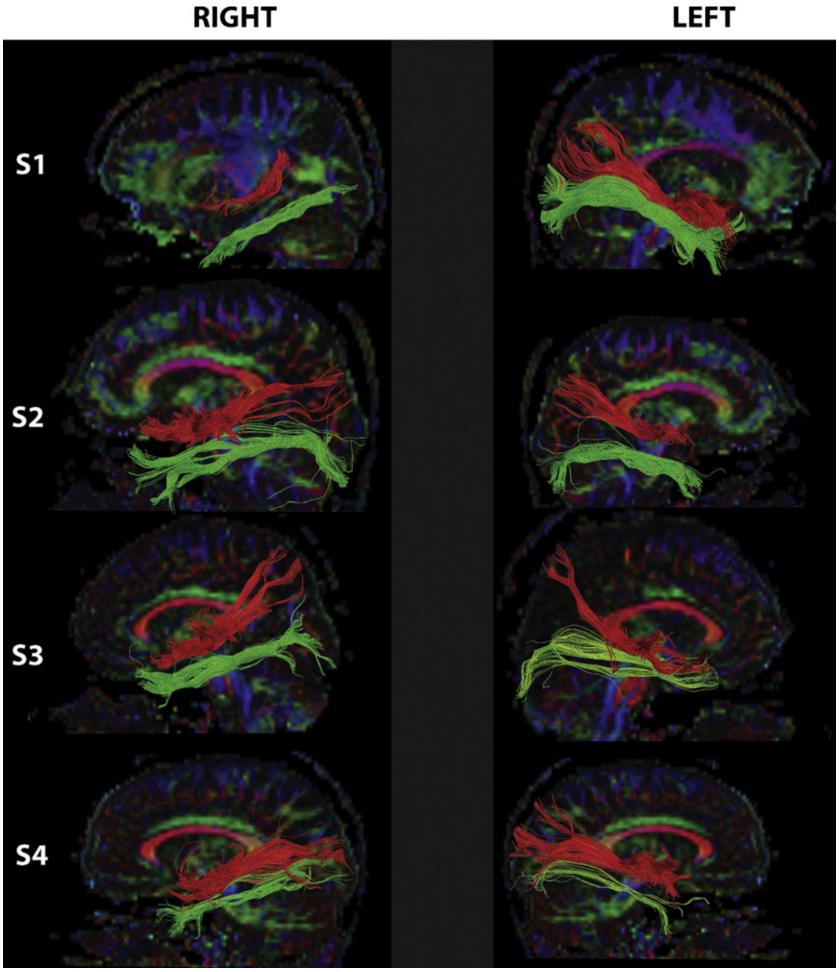

Fig. 5. Comparison of the trajectories of the MdLF and ILF. Red: MdLF; green: ILF.

Table 3
Quantitative assessment of each tract.

	measurement	Side	subject 1	subject 2	subject 3	subject 4	mean	std-deviation	LI
MdLF	FA	G	0.45	0.46	0.42	0.41	0.43	0.02	0.10
		D	0.38	0.43	0.37	0.38	0.39	0.03	
	Number of streamlines	G	503	310	280	482	393.75	115.0	−0.09
		D	410	388	553	371	430.5	83.21	
	Lenght (mm)	G	62.43	62.82	44.45	57.19	56.72	8.57	0.08
		D	40.41	52.45	55.45	61.74	52.51	8.95	
AF	FA	G	0.44	0.46	0.43	0.43	0.44	0.01	0.1
		D	0.40	0.41	0.38	0.40	0.40	0.01	
	Number of streamlines	G					2507.5	745.24	−0.2
		D					3033	595.55	
	Lenght (mm)	G					59.39	6.51	
		D					58.86	6.33	
IFOF	FA	G	0.49	0.50	0.48	0.46	0.49	0.02	0.02
		D	0.48	0.47	0.48	0.47	0.47	0.05	
	Number of streamlines	G					315.25	114.93	−0.38
		D					461.75	322.89	
	Lenght (mm)	G					165.21	10.92	
		D					158.20	6.58	
ILF	FA	G	0.51	0.50	0.48	0.45	0.49	0.03	0.14
		D	0.46	0.45	0.40	0.38	0.42	0.035	
	Number of streamlines	G					199.25	237.78	0.49
		D					120.75	78.67	
	Lenght (mm)	G					114.24	4.14	
		D					104.13	11.78	

FA, volume and length are calculated for each tract and each subject, then mean value for these parameters are calculated for the entire group, considering each fiber tract separately. FA = fractional anisotropy; LI = lateralization index; std-deviation = standard deviation.

taking into account voxels with anterior–posterior orientation of diffusion properties (i.e. green on FA-color map as shown on Fig. 1). Considering FA and volume of both left and right seed ROI's for the entire group, we found a rightward lateralization index for both parameters (Table 1). On the one hand, FA showed a minor rightward lateralization (LI = −0.002) whereas, on the other hand, ROI volume showed a pronounced rightward lateralization (LI = −0.14).

3.2. Tractographic observations

DTI tractography was used to characterize the course of the MdLF in 4 healthy subjects (8 hemispheres). In 7 cases, it seems to connect the IPL to the superior temporal gyrus. Additional fibers connecting the occipital lobe (lateral occipital cortex and occipital pole) were seen in 4 cases (3 subjects) (Table 2) (Fig. 2). It runs within the STG white matter from the temporal pole to the caudal part of the STG. Then it extends caudally in the upper part of the sagittal stratum and the posterior part of the corona radiata, to reach the IPL. We were not able to determine the caudal cortical boundaries of the MdLF in one case (subject 1, right hemisphere), thus the proximal portion of the fasciculi was still found within the core of the STG white matter with a caudal extend in the lateral part of the sagittal stratum.

Figs. 3–6 compare the course of the MdLF with that of the other fiber tracts composing the "dorsal" route (Fig. 4: arcuate fasciculus) and "ventral" (Fig. 3: inferior fronto-occipital fasciculus; Fig. 5: inferior longitudinal fasciculus; Fig. 6: uncinate fasciculus). At the level of the sagittal stratum (Fig. 7), the MdLF runs medially to that of the superior longitudinal fasciculus and above the course of the IFOF and the ILF. It has a global ascending orientation reaching the cortex of the IPL, thus some of its fibers course horizontally to reach the occipital pole.

We were able to clearly distinguish the rostral extend of the fasciculus from those of the other tracts of both ventral and dorsal route. The rostral extent of the MdLF is located in the temporal pole, at the level of the STG, whereas the ILF is located underneath, in the inferior and middle temporal gyrus. The inferior portion of the AF is located laterally and posteriorly to the MdLF, within the posterior part of the STG and in the temporal lobe. The temporal projections of the UF are located in the temporal pole, medially and anteriorly to that of the MdLF.

We also extracted several measurements from the DTI tractography, such as mean FA and mean volume for each tract. These findings are summarized in Table 3. Considering FA, we found a leftward asymmetry for all fiber tracts, whereas the lateralization index suggested a rightward asymmetry when considering the number of streamlines for the MdLF, AF, IFOF and a leftward asymmetry for the ILF.

4. Discussion

In this study, (1) we confirmed that the MdLF is found constantly in 8 hemispheres of four healthy volunteers and (2) we clearly delineate the MdLF from the other fascicles that constitute the language pathways, especially the ventral pathway (i.e. inferior longitudinal fascicle, inferior longitudinal fascicle, and arcuate fascicle).

With the use of DTI, several language pathways have been identified, including the arcuate fasciculus [4], the inferior frontooccipital fasciculus [4], and the inferior longitudinal fasciculus. The Middle longitudinal fascicle has been initially described in non-human primates [5], and its identification in the human brain was made feasible with the use of DTI [7].

Our observation, supply its existence, thus, the role of the MdLF remains unclear. Due to its location between the inferior parietal lobule (angular gyrus) and the superior temporal gyrus, Makris et al. [7] hypothesize that it has a role in cognitive functions such as attention in the right hemisphere and language in the left hemisphere. This assumption is based on previous observations relating lesions in the right IPL to attentional impairment [17] and lesions in the left IPL to language deficits [18]. The role of the parietal cortex in the non-dominant hemisphere in cognitive tasks such as spatial attention, attention processing and episodic memory is supported by functional neuroimaging observations [19]. Considering the language network, Makris et al. [7] conceive the MdLF as an alternative route between the angular gyrus ("Geschwind's territory") and the superior temporal gyrus ("Wernicke's territory"), in this way being a substitute for the role traditionally devoted to the arcuate fascicle in the dorsal route [9].

Combining DTI and fMRI, Saur et al. [11] suggest that the MdLF participate in both dorsal and ventral routes involved in language processing.

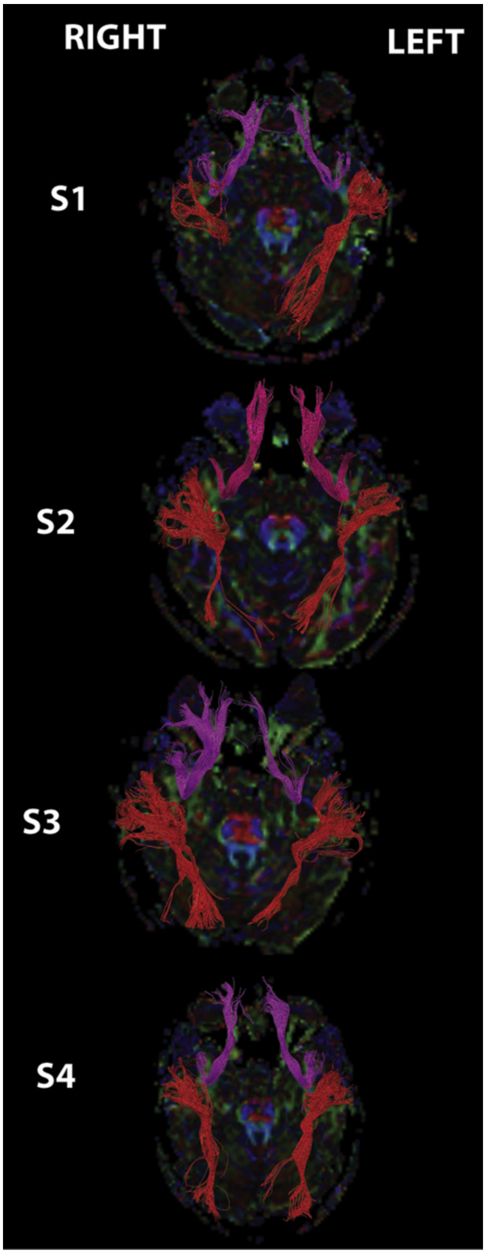

Fig. 6. Comparison of the trajectories of the MdLF and UF. Red: MdLF; pink: UF.

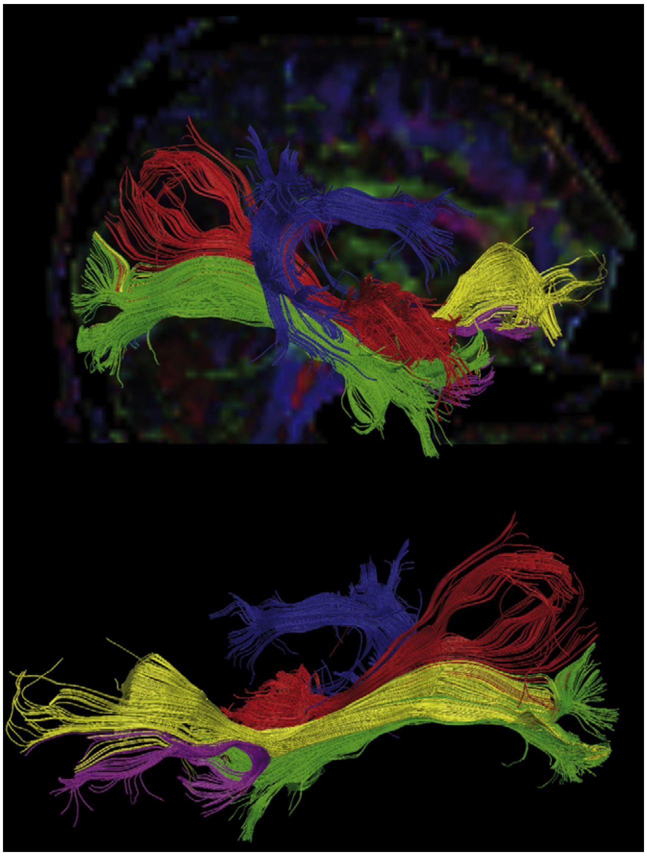

Fig. 7. Global view of the fiber tracts. Upper figure: lateral view and lower figure: medial view. Red: MdLF; yellow: IFOF; blue: AF; green: ILF, purple: UF. At the level of the sagittal stratum, the MdLF runs medially to the AF, and superiorly to the IFOF and the ILF.

The dorsal route involved in auditory-motor representation of speech sounds is associated with repetition of pseudoword and, according to these authors, this route is composed of the SLFIII, the AF and the MdLF. Repetition of pseudo-words contrasted with repetition of real words reveals activations located in the anterior part of the superior temporal gyrus as well as in the inferior frontal gyrus (pars opercularis) and the dorsal premotor cortex [11]. These regions being connected via the MdLF entering the AF in posterior part of the superior temporal gyrus, then the AF courses in the white matter of the parietal lobe and reaches the premotor cortex. Considering this dorsal route, in our observations, the MdLF, running from the STG to the IPL (AG), takes its courses medially to the AF and we systematically differentiate the posterior part of the MdLF from the AF.

As for the ventral route, associated with sentence comprehension, it should be comprised of the MdLF, the extreme capsule (EmC) and the ILF. Our findings are in contradiction with those previous observations for we found no clear connections between the MdLF and the other fascicles composing this route: the fascicle runs superiorly to the ILF and does not seem to reach the extreme capsule. Considering the IFOF as part of the ventral stream [13], using the Klingler fiber dissection technique, we have reported that the IFOF can be decomposed in two different components [20]: a superficial and dorsal subcomponent connecting the frontal lobe with the superior parietal lobe and the posterior portion of the superior and middle occipital gyri; and a deep and ventral subcomponent, which connects the frontal lobe with the posterior portion of the inferior occipital gyrus and the posterior temporo-basal area. In this study, we clearly distinguished the MdLF from both two subcomponents of the IFOF.

One the one hand, due to its location, the fascicle might not participate in the dorsal route as a main relay between the anterior part of the superior temporal gyrus (T1p) and both the pars opercularis of the inferior frontal gyrus (F3op) and the dorsal premotor cortex (PMd). On the other hand, its situation in the ventral route is still unclear and, in the present study, we were not able to distinguish any connection between the MdLF and other fascicles of the ventral stream (i.e. ILF, IFOF, UF, nor EmC).

Finally, as the MdLF is clearly distinguished from the other fascicle of the dorsal and ventral routes, and considering its relationship with them are not clearly defined, our observations support the hypothesis that the MdLF might not be a main pathway in language processing but rather, as suggested by De Witt Hamer et al., participate in a parallel transmodal neurocognitive network, that needs to be defined.

5. Conclusion

Using DTI methods, we confirm that the MdLF connects the AG and the STG and we supply evidence that its course can be systematically differenciated from those of other fascicles composing both ventral and dorsal routes (IFOF, IFL, AF and UF).

References

[1] Wakana S, Jiang H, Nagae-Poetscher LM, van Zijl PCM, Mori S. Fiber tract-based atlas of human white matter anatomy. Radiology 2004;230:77–87.
[2] Leclercq D, Delmaire C, de Champfleur NM, Chiras J, Lehericy S. Diffusion tractography: methods, validation and applications in patients with neurosurgical lesions. Neurosurgery Clinics of North America 2011;22:253–68.
[3] Makris N, Worth AJ, Sorensen AG, et al. Morphometry of in vivo human white matter association pathways with diffusion-weighted magnetic resonance imaging. Annals of Neurology 1997;42:951–62.
[4] Catani M, Howard RJ, Pajevic S, Jones DK. Virtual in vivo interactive dissection of white matter fasciculi in the human brain. NeuroImage 2002;17:77–94.
[5] Schmahmann JD, Pandya DN, Wang R, et al. Association fibre pathways of the brain: parallel observations from diffusion spectrum imaging and autoradiography. Brain 2007;130:630–53.
[6] Seltzer B, Pandya DN. Further observations on parieto-temporal connections in the rhesus monkey. Experimental brain research 1984;55:301–12.
[7] Makris N, Papadimitriou GM, Kaiser JR, Sorg S, Kennedy DN, Pandya DN. Delineation of the middle longitudinal fascicle in humans: a quantitative, in vivo, DT-MRI study. Cerebral Cortex 2009;19:777–85.
[8] Hickok G, Poeppel D. Towards a functional neuroanatomy of speech perception. Trends in Cognitive Sciences 2000;4:131–8.
[9] Hickok G, Poeppel D. Dorsal and ventral streams: a framework for understanding aspects of the functional anatomy of language. Cognition 2004;92:67–99.
[10] Hickok G, Poeppel D. The cortical organization of speech processing. Nature Reviews Neuroscience 2007;8:393–402.
[11] Saur D, Kreher BW, Schnell S, et al. Ventral and dorsal pathways for language. Proceedings of the National Academy of Sciences of the United States of America 2008;105:18035–40.
[12] Makris N, Kennedy DN, McInerney S, et al. Segmentation of subcomponents within the superior longitudinal fascicle in humans: a quantitative, in vivo, DT-MRI study. Cerebral Cortex 2005;15:854–69.
[13] Duffau H, Leroy M, Gatignol P. Cortico-subcortical organization of language networks in the right hemisphere: an electrostimulation study in left-handers. Neuropsychologia 2008;46:3197–209.
[14] De Witt Hamer PC, Moritz-Gasser S, Gatignol P, Duffau H. Is the human left middle longitudinal fascicle essential for language? A brain electrostimulation study. Human Brain Mapping 2010.
[15] Wang R, Wedeen VJ. Diffusion Toolkit and TrackVis. Proceedings of the International Society for Magnetic Resonance in Medicine 2007.
[16] Catani M, Mesulam M. The arcuate fasciculus and the disconnection theme in language and aphasia: history and current state. Cortex 2008;44:953–61.
[17] Mesulam MM. A cortical network for directed attention and unilateral neglect. Annals of Neurology 1981;10:309–25.
[18] Geschwind N. Disconnexion syndromes in animals and man. II. Brain 1965;88:585–644.
[19] Cabeza R, Ciaramelli E, Olson IR, Moscovitch M. The parietal cortex and episodic memory: an attentional account. Nature Reviews Neuroscience 2008;9:613–25.
[20] Martino J, Brogna C, Robles SG, Vergani F, Duffau H. Anatomic dissection of the inferior fronto-occipital fasciculus revisited in the lights of brain stimulation data. Cortex 2010;46:691–9.