WHITE MATTER FUNCTIONAL CONNECTIVITY AS AN ADDITIONAL LANDMARK FOR DOMINANT TEMPORAL LOBECTOMY

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Abstract

Dominant temporal lobectomy is classically performed according to two criteria: a perfect knowledge of the temporo-mesial microsurgical anatomy, and cortical landmarks laterally. However, the functional anatomy of the subcortical white matter tracts is less taken into account, despite the risk to induce a permanent deficit (especially aphasia) if damaged. Even if Klinger's technique allows to dissect fibers on cadaveric specimen, the exact 3D geometry of these fasciculi remains poorly described. Tractography, based on diffusion tensor imaging (DTI), is a powerful tool to build 3D images of several fasciculi, helping neurosurgeon to create a mental representation of their relationships. Moreover, intraoperative subcortical electrostimulation enables to map the function of these pathways. Here, we review the recent findings about the white matter anatomo-functional connectivity of dominant temporal lobe, based on combined anatomical data provided by DTI and functional information provided by intraoperative stimulation. Then, we discuss their implications for temporal lobectomy, by using white matter functional connectivity as an additional landmark.

Introduction

Since many decades, neurosurgeons perform temporal lobectomy in the dominant hemisphere, preserving the anterior part of the superior temporal gyrus as well as the mid part of the middle temporal gyrus, while resecting the anterior and mid part of the inferior temporal gyrus without any functional consequences, especially on language [1]. This usual view has been challenged since a major intervindividual anatomo-functional variability for language has been demonstrated at the level of the lateral temporal cortex, using both intraoperative electrostimulation [2] and functional neuroimaging [3]. Indeed, the anterior part of the superior temporal gyrus and the mid part of the middle temporal gyrus may be involved in language. When evidenced intraoperatively, these areas have to be preserved [2]. In addition, temporo-basal areas can also play a role in language, even if their resection does not systematically cause definitive deficit [4].

Thus, preoperative as well as intraoperative cortical mapping techniques have been introduced in order to tailor the cortical resection of the dominant temporal lobe according to functional boundaries, initially for epilepsy surgery [2], and then for glioma surgery [5]. However, because glioma spread along white matter fasciculi, intraoperative subcortical stimulation has been proposed, about ten years ago, in order to stop the resection as close as possible to eloquent subcortical pathways [6]. Similarly, in epilepsy surgery, the resection of cortical foci is often associated with a disconnection of white matter tracts [1]. However, functional damage during this disconnection must be avoided, in order to preserve the quality of life [7].

Thus, the aim of this paper is not to describe the well known anatomical landmarks of a temporo-mesial lobectomy [8, 9], and neither to detail the limbic connectivity of temporo-mesial structures involved in memory processing. We will rather attempt to describe additional and reliable landmarks given by functional white matter pathways (with special emphasis on language), in order to make the resection of the dominant temporal lobe more reproducible and safer, not only for glioma surgery, but also for corticectomies in epilepsy surgery.

Methodological advances in subcortical mapping

Recent developments of diffusion tensor imaging (DTI) have enabled the non invasive study of white matter bundles, in particular those thought to be involved in language [10]. However, DTI gives only anatomical information, and cannot provide details regarding the function sustained by the fibers.

Interestingly, during brain surgery for resection of a tumor invading both cortical and subcortical structures, it is now a common clinical practice to awaken patients in order to assess the functional role of restricted brain regions, so that the surgeon can maximise the extent of the resection without generating neither motor, sensory nor cognitive (especially language) impairments. Patients continuously perform functional tasks, while the surgeon temporarily inactivates localized regions within the grey or white matter around the lesion, using electrical stimulations. If the patient stops speaking or produces wrong responses, the surgeon does not remove the stimulated region. Indeed, it has been demonstrated that resection too close to structures that are considered as eloquent on the basis of electrical mapping, induced postoperative deficit [5]. Therefore, intraoperative electrostimulation is able to identify, with a great accuracy (5 mm) and reproducibility, the structures that are essential for the brain function, not only at cortical but also at subcortical levels [11].

Moreover, combining the precise functional disturbances elicited by stimulations with the anatomical data provided by pre- and post-operative magnetic resonance imaging (in particular DTI), has enabled to perform reliable anatomo-functional correlations, especially with regard to the subcortical pathways [12-14]. In comparison to the voxel-based lesion – symptom mapping, which analyzes the relationship between tissue damage and behavior in patients with a neurological deficit [15], electrical mapping offers the possibility to study the relationship between brain and behavior in subjects with no or only very slight neurological disorder – since stimulation generates the effects of a transient virtual lesion [15].

On the basis of this methodological progress, it is now possible to integrate the better knowledge of the subcortical connectivity in the surgical planning of temporal lobectomy within the dominant hemisphere. To this end, we will study successively the different fasciculi which will be encounter during a resection of the temporal lobe, from anterior to posterior (Fig 1).

White matter (functional) landmarks in temporal lobectomy

Uncinate fasciculus

This pathway connects the anterior part of the temporal pole, the uncus, amygdale and hippocampal gyrus to the orbital and polar frontal cortex [16]. A reduced left-greater-than right asymmetry of uncinate fasciculus has been linked to schizophrenia by in vivo DTI study [17, 18], altought post-mortem studies failed to confirm this hypothesis [19]. Moreover, this tract is regularly sectioned in epilepsy surgery, without inducing major personality disorders. Thus, to the present date, the functional role of the dominant uncinate fasciculus remains speculative, and its resection is widely admitted.

Inferior longitudinal fasciculus

This tract, first described by K.F. Burdach in 1822, connects the anterior part of the temporal lobe to the occipital lobe, and runs laterally and inferiorly to the lateral wall of the temporal horn. Recent DTI studies [20] have demonstrated the existence of both a direct and indirect pathway (constituted by U-shaped fibers of the occipito-temporal projection system). Interestingly, while the inferior longitudinal fasciculus was supposed to play a role in emotional processing – likely through a wide network also involving the uncinate fasciculus –, a recent brain stimulation study has demonstrated that this tract was not essential for cognitive function, especially for language [21]. As a consequence, its disconnection or resection can be performed with no ecological consequence on the quality of life, even in the dominant hemisphere, as for the uncinate fasciculus. These findings are in accordance with the classical view concerning the temporal lobectomy, i.e. that it is possible to remove the inferior temporal gyrus and the fusiform gyrus (in addition to the temporal pole), without generating permanent deficit. Interestingly, some studies have also proposed that this resection might be performed very posteriorly, even if the existence of cortical eloquent areas have been suspected – namely that language disturbances have been elicited by cortical electrostimulation at the level of the so-called postero-basal temporal areas [4].

Inferior occipito-frontal fasciculus

This tract comes from the occipital lobe and postero-lateral temporal areas, then runs laterally and superiorly to the lateral wall of the temporal horn, and continues antero-superiorly to the orbito-frontal and dorso-lateral prefrontal cortices via the anterior floor of the external capsule under the insular lobe [22, 23]. Recently, using intraoperative subcortical mapping, it has been demonstrated that direct electrostimulation of this pathway induced semantic paraphasias (i.e. errors with regard to the meaning of the word target) with a high reproducibility [24]. These observations have provided strong arguments in favour of the fact that the inferior occipito-frontal fasciculus was a subcortical pathway underlying the “ventral stream”, crucial for language semantic processing, and able to compensate the inferior longitudinal fasciculus – thus explaining why this latter can be removed without deficit [21].

As a consequence, the inferior occipito-frontal fasciculus has absolutely to be preserved at the end of surgical resection in the depth of the dominant temporal lobe [24]. Interestingly, in the anterior floor of the external capsule, this pathway is located immediately medially and above the uncinate fasciculus [22]. Therefore, since the uncinate fasciculus can be resected, the inferior occipito-frontal fasciculus represents the postero-superior and deep limit of the resection of the temporal pole, at the level of the "pli falciforme de Broca". More posteriorly, the temporal part of this pathway represents the supero-mesial and deep boundary of the resection, above the roof of the temporal horn of the ventricle [24]. Indeed, the roof of the ventricle is a good anatomical landmark to distinct the inferior lateral fasciculus (below) and the inferior occipito-temporal fasciculus (above).

Finally, it is worth noting that, since this tract connects the frontal lobe to the postero-lateral temporal cortex, the posterior limit of the resection at the cortical level (superior and middle temporal cortices) depends on the individual distribution of the language sites detected using brain mapping techniques. However, the subcortical postero-lateral boundary of the resection has also to be determined. The temporal part of the arcuate fasciculus may represent this limit.

Superior longitudinal fasciculus

The superior longitudinal fasciculus (or arcuate fasciculus) is a fiber tract stemming from the caudal part of the posterior and superior temporal cortex (mainly Wernicke's area) that arches around the insula and projects forward to end within the frontal lobe (mainly prefrontal and premotor gyri, especially Broca's area) [25]. With regard to functional aspects, Wernicke and then later Geschwind postulated that lesions of this tract would produce conduction aphasia. Recently, the different parts of the arcuate fasciculus have been identified using intraoperative subcortical stimulations, by eliciting reproducible phonemic paraphasias, namely disorders that affect the phonological form of the words [26]. As a consequence, it is mandatory to preserve this pathway, which subserves the “dorsal phonological stream”. Thus, the anterior wall of the temporal part of the arcuate fasciculus, running vertically at the outer surface of the ventricle, represents the subcortical postero-lateral boundary of the resection [26].

Optic radiations

The optic pathways are located just medially and above the inferior longitudinal fasciculus, whereas the inferior occipito-frontal fasciculus runs medially and above them [22, 27-29]. Interestingly, it was recently demonstrated that it was possible to identify these visual tracts intraoperatively, by eliciting transient shadow during their direct electrostimulation [26]. It is very important to preserve the optic radiations at this level, to avoid a permanent postoperative hemianopsia, a deficit which prevents to lead a normal life (e.g. for driving) – conversely to a single quadrantanopsia, frequently induced following a temporal lobectomy, but which has no ecological consequence on the quality of life. As a consequence, this tract has to represent the postero-superior and deep limit of a temporal lobectomy.

Finally, in the depth, the pyramidal pathway [30], running within the posterior limb of the internal capsule, and easily detectable using intraoperative stimulation, has to be preserved: this tract constitutes the most posterior mesial boundary of the resection.

Conclusion

The better knowledge of the anatomo-functional organization of the subcortical pathways may provide additional and reliable landmarks to perform temporal lobectomy in the dominant hemisphere. Indeed, while it is currently well-known that slow-growing lesion may induce functional cortical reshaping, due to cerebral plasticity mechanisms [31], such reorganization is negligible within the white matter [6]. As a consequence, the subcortical landmarks here detailed are very reproducible, and can be useful to optimize the benefit/risk ratio of temporal lobectomy, that is to perform a large resection of pathological tissue (during glioma as well as epilepsy surgery) without postoperative impairment of language function. Intraoperative stimulation is still the gold standard to map these functional pathways, but in a near future, intraoperative MRI combined with pre-operative DTI could allow their intraoperative identification with a great accuracy [32, 33].

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References

1. Spencer, D.D., Spencer, S.S., Mattson, R.H., et al., Access to the posterior medial temporal lobe structures in the surgical treatment of temporal lobe epilepsy. *Neurosurgery*, 1984. 15(5): p. 667-71.
2. Ojemann, G., Ojemann, J., Lettich, E., et al., Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. *J Neurosurg*, 1989. 71(3): p. 316-26.
3. Vigneau, M., Beaucousin, V., Herve, P.Y., et al., Meta-analyzing left hemisphere language areas: phonology, semantics, and sentence processing. *Neuroimage*, 2006. 30(4): p. 1414-32.
4. Luders, H., Lesser, R.P., Hahn, J., et al., Basal temporal language area. *Brain*, 1991. 114 (Pt 2): p. 743-54.
5. Haglund, M.M., Berger, M.S., Shamseldin, M., et al., Cortical localization of temporal lobe language sites in patients with gliomas. *Neurosurgery*, 1994. 34(4): p. 567-76; discussion 576.
6. Duffau, H., Intraoperative cortico-subcortical stimulations in surgery of low-grade gliomas. *Expert Rev Neurother*, 2005. 5(4): p. 473-85.
7. Smith, J.R., VanderGriff, A., and Fountas, K., Temporal lobotomy in the surgical management of epilepsy: technical report. *Neurosurgery*, 2004. 54(6): p. 1531-4; discussion 1534-6.
8. Sindou, M. and Guenot, M., Surgical anatomy of the temporal lobe for epilepsy surgery. *Adv Tech Stand Neurosurg*, 2003. 28: p. 315-43.

9. Wen, H.T., Rhoton, A.L., Jr., de Oliveira, E., et al., Microsurgical anatomy of the temporal lobe: part 1: mesial temporal lobe anatomy and its vascular relationships as applied to amygdalohippocampectomy. *Neurosurgery*, 1999. 45(3): p. 549-91; discussion 591-2.

10. Catani, M., Jones, D.K., and ffytche, D.H., Perisylvian language networks of the human brain. *Ann Neurol*, 2005. 57(1): p. 8-16.

11. Duffau, H., Lessons from brain mapping in surgery for low-grade glioma: insights into associations between tumour and brain plasticity. *Lancet Neurol*, 2005. 4(8): p. 476-86.

12. Kamada, K., Todo, T., Masutani, Y., et al., Visualization of the frontotemporal language fibers by tractography combined with functional magnetic resonance imaging and magnetoencephalography. *J Neurosurg*, 2007. 106(1): p. 90-8.

13. Thiebaut de Schotten, M., Urbanski, M., Duffau, H., et al., Direct evidence for a parietal-frontal pathway subserving spatial awareness in humans. *Science*, 2005. 309(5744): p. 2226-8.

14. Henry, R.G., Berman, J.I., Nagarajan, S.S., et al., Subcortical pathways serving cortical language sites: initial experience with diffusion tensor imaging fiber tracking combined with intraoperative language mapping. *Neuroimage*, 2004. 21(2): p. 616-22.

15. Bates, E., Wilson, S.M., Saygin, A.P., et al., Voxel-based lesion-symptom mapping. *Nat Neurosci*, 2003. 6(5): p. 448-50.

16. Crossby, E.C., Humphrey, T., and E.W., L., Correlative Anatomy of the Nervous System. 1962, New York: MacMillian.

17. Burns, J., Job, D., Bastin, M.E., et al., Structural disconnectivity in schizophrenia: a diffusion tensor magnetic resonance imaging study. *Br J Psychiatry*, 2003. 182: p. 439-43.

18. Kubicki, M., Westin, C.F., Maier, S.E., et al., Uncinate fasciculus findings in schizophrenia: a magnetic resonance diffusion tensor imaging study. *Am J Psychiatry*, 2002. 159(5): p. 813-20.

19. Highley, J.R., Walker, M.A., Esiri, M.M., et al., Asymmetry of the uncinate fasciculus: a post-mortem study of normal subjects and patients with schizophrenia. *Cereb Cortex*, 2002. 12(11): p. 1218-24.

20. Catani, M., Jones, D.K., Donato, R., et al., Occipito-temporal connections in the human brain. *Brain*, 2003. 126(Pt 9): p. 2093-107.

21. Mandonnet, E., Nouet, A., Gatignol, P., et al., Does the left inferior longitudinal fasciculus play a role in language? A brain stimulation study. *Brain*, 2007. 130(Pt 3): p. 623-9.

22. Kier, E.L., Staib, L.H., Davis, L.M., et al., MR imaging of the temporal stem: anatomic dissection tractography of the uncinate fasciculus, inferior occipitofrontal fasciculus, and Meyer's loop of the optic radiation. *AJNR Am J Neuroradiol*, 2004. 25(5): p. 677-91.

23. Catani, M., Howard, R.J., Pajevic, S., et al., Virtual in vivo interactive dissection of white matter fasciculi in the human brain. *Neuroimage*, 2002. 17(1): p. 77-94.

24. Duffau, H., Gatignol, P., Mandonnet, E., et al., New insights into the anatomo-functional connectivity of the semantic system: a study using cortico-subcortical electrostimulations. *Brain*, 2005. 128(Pt 4): p. 797-810.

25. Nieuwenhuys, R., Voogd, J., and van Huijzen, C., The human central nervous system. 1988, Berlin: Springer-Verlag.

26. Duffau, H., Capelle, L., Sichez, N., et al., Intraoperative mapping of the subcortical language pathways using direct stimulations. An anatomo-functional study. *Brain*, 2002. 125(Pt 1): p. 199-214.

27. Sincoff, E.H., Tan, Y., and Abdulrauf, S.I., White matter fiber dissection of the optic radiations of the temporal lobe and implications for surgical approaches to the temporal horn. *J Neurosurg*, 2004. 101(5): p. 739-46.

28. Rubino, P.A., Rhoton, A.L., Jr., Tong, X., et al., Three-dimensional relationships of the optic radiation. *Neurosurgery*, 2005. 57(4 Suppl): p. 219-27; discussion 219-27.

29. Ebeling, U. and Reulen, H.J., Neurosurgical topography of the optic radiation in the temporal lobe. *Acta Neurochir* (Wien), 1988. 92(1-4): p. 29-36.

30. Ebeling, U. and Reulen, H.J., Subcortical topography and proportions of the pyramidal tract. *Acta Neurochir* (Wien), 1992. 118(3-4): p. 164-71.

31. Desmurget, M., Bonnetblanc, F., and Duffau, H., Contrasting acute and slow-growing lesions: a new door to brain plasticity. *Brain*, 2006.

32. Nimsky, C., Ganslandt, O., and Fahlbusch, R., Implementation of fiber tract navigation. *Neurosurgery*, 2006. 58(4 Suppl 2): p. ONS-292-303; discussion ONS-303-4.

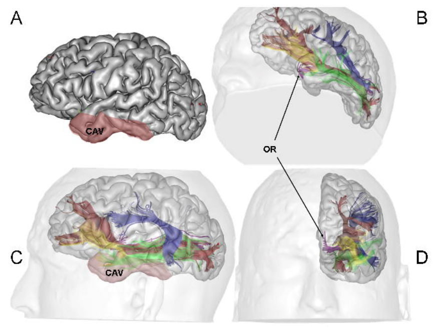
33. Nimsky, C., Ganslandt, O., Merhof, D., et al., Intraoperative visualization of the pyramidal tract by diffusion-tensor-imaging-based fiber tracking. *Neuroimage*, 2006. 30(4): p. 1219-29.

34. Basser, P.J. Fiber-Tractography via diffusion tensor MRI (DT-MRI). in Sixth Annual Meeting of the International Society for Magnetic Resonance in Medicine. 1998: ISMRM.

Figure Legend

Fig. 1: The Fiber tracking of the arcuate fasciculus (blue), inferior longitudinal fasciculus (green), inferior fronto-occipital fasciculus (red), uncinate (yellow), optic radiation (OR) was performed using the ROIs described by Catani et al. [23] A “two regions of interest” approach was used for each fasciculus tracking. The procedure, described by Basser et al. [34], consisted in defining a second ROI, at a distance from the first ROI, such that it contained at least a section of the desired fasciculus but did not contain any fibres of the undesired fasciculus that passed through the first ROI. DTI and high-resolution 3-D anatomical images (B, C, D) was registered using Brainvisa 3.0.2. The displaying of derived tracts was performed using Anatomist 3.0.2 (http://brainvisa.info).

We have drawn a virtual resection cavity (CAV) according to essential subcortical pathways (inferior fronto-occipital fasciculus and arcuate fasciculus), while removing the "non essential" tracts (uncinate, inferior longitudinal fasciculus and anterior part of the OR). By reporting this cavity on the 3-D surface reconstruction (A), we have obtained a resection similar to those classically reported in the literature - according to cortical boundaries.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