Ventral Precentral Fiber Intersection Area: A Central Hub in the Connectivity of Perisylvian Associative Tracts

Sonia Gayoso, MD* Pedro Perez-Borreda, MD[‡] Antonio Gutierrez, MD[‡] Juan A. García-Porrero, MD, PhD[§]

Enrique Marco de Lucas, MD¹ Juan Martino, MD, PhD

*Department of Neurological Surgery, Complexo Hospitalario Universitario A Coruña, As Xubias, La Coruña, Spain; *Department of Neurological Surgery, Hospital La Fe, Valencia, Spain; §Department of Anatomy and Celular Biology, Cantabria University, Santander (Cantabria), Spain; [¶]Department of Hospital Radiology, Universitario Marqués de Valdecilla and Fundación Instituto de Investigación Marqués de Valdecilla (IDIVAL), Santander (Cantabria), Spain; Department of Neurological Surgery, Hospital Universitario Marqués de Valdecilla and Fundación Instituto de Investigación Marqués de Valdecilla (IDIVAL), Santander (Cantabria), Spain

Correspondence:

Juan Martino, MD, PhD. Department of Neurosurgery, Hospital Universitario Marqués de Valdecilla (HUMV) and Fundación Instituto de Investigación Marqués de Valdecilla (IDIVAL), Avinguda Valdecilla s/n, 39008, Pabellón 19 bajos, Santander (Cantabria), Spain. E-mail: juan.martino@hotmail.com

Received, March 31, 2018. Accepted, September 27, 2018. Published Online, November 10, 2018.

Copyright © 2018 by the Congress of Neurological Surgeons **BACKGROUND:** The ventral part of the precentral gyrus is considered one of the most eloquent areas. However, little is known about the white matter organization underlying this functional hub.

OBJECTIVE: To analyze the subcortical anatomy underlying the ventral part of the precentral gyrus, ie, the ventral precentral fiber intersection area (VPFIA).

METHODS: Eight human hemispheres from cadavers were dissected, and 8 healthy hemispheres were studied with diffusion tensor imaging tractography. The tracts that terminate at the ventral part of the precentral gyrus were isolated. In addition, 6 surgical cases with left side gliomas close to the VPFIA were operated awake with intraoperative electrical stimulation mapping.

RESULTS: The connections within the VPFIA are anatomically organized along an anteroposterior axis: the pyramidal pathway terminates at the anterior bank of the precentral gyrus, the intermediate part is occupied by the long segment of the arcuate fasciculus, and the posterior bank is occupied by the anterior segment of the arcuate fasciculus. Stimulation of the VPFIA elicited speech arrest in all cases.

CONCLUSION: The present study shows strong arguments to sustain that the fiber organization of the VPFIA is different from the classical descriptions, bringing new light for understanding the functional role of this area in language. The VPFIA is a critical neural epicenter within the perisylvian network that may represent the final common network for speech production, as it is strategically located between the termination of the dorsal stream and the motor output cortex that directly control speech muscles.

KEY WORDS: Arcuate fasciculus, DTI tractography, Fiber dissection, Precentral gyrus, Pyramidal pathway

Operative Neurosurgery 17:182–192, 2019

DOI: 10.1093/ons/opy331

■ he precentral gyrus has been divided into ventral and dorsal portions, based on anatomical and functional considerations. The dorsal part controls arm and hand movements, while the ventral part is involved in orofacial movements and language. The exact border between them is controversial, but most authors accept that it is located at the ventral margin of the omega zone (hand knob).¹⁻⁴ The ventral part of the precentral gyrus is considered one of the most eloquent cortical areas, with crucial roles in motor, language, and higher cognitive functions. 1,3,5-9

ABBREVIATIONS: DTI, diffusion tensor imaging; **VPFIA**, ventral precentral fiber intersection area

In recent years, numerous publications have demonstrated that this area is highly connected with the main associative tracts of the brain. In this sense, connections with the arcuate fasciculus, pyramidal pathway, frontal aslant tract, and inferior fronto-occipital fasciculus have been described. 10-15 However, there is significant discussion regarding the exact cortical terminations of these tracts within the frontal operculum, and the organization of all these connections within the precentral gyrus. 10,16-20

In the current anatomical study, the organization of white matter underlying the ventral part of the precentral gyrus has been analyzed applying cortex sparing fiber dissection and diffusion tensor imaging (DTI) tractography. We named this area the ventral precentral fiber

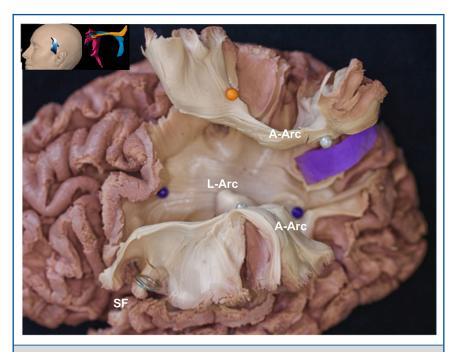


FIGURE 1. Fiber dissection of the tracts that terminate at the ventral precentral fiber intersection area (VPFIA) in a left hemisphere. The anterior segment of the arcuate fasciculus has been tilted superiorly and inferiorly to expose the long segment of the arcuate fasciculus. The dissection demonstrates that the terminations within the VPFIA are anatomically organized along an anterior-posterior axis. Anterior segment of the arcuate fasciculus terminates at the posterior part of the ventral precentral gyrus. The course of the long segment of the arcuate fasciculus within the parietal lobe is deep compared to the anterior segment of the arcuate fasciculus what determines a connection of the long segment of the arcuate fasciculus further anterior at the precentral gyrus. A-Arc: Anterior segment of the arcuate fasciculus; L-Arc: Long segment of the arcuate fasciculus; SF = Sylvian fissure.

intersection area (VPFIA) as it is a peculiar brain area crossed by numerous axons from 3 important tracts: anterior segment of the arcuate fasciculus, the long segment of the arcuate fasciculus, and pyramidal pathway. The specific cortical projections of these tracts within the precentral gyrus have been studied in detail. Our results show a renewed and elaborated description of the connectivity organization within the VPFIA that may help to have a better understanding of the functional role of this complex subcortical hotspot.

METHODS

Cortex-Sparing Fiber Dissection

Eight human cerebral hemispheres were dissected with a methodology that has been previously described in detail, ie, cortex-sparing fiber dissection. 10,11,21,22 It was possible to completely isolate the fibers and cortical terminations of the anterior and long segments of the arcuate fasciculus, and pyramidal pathway within the VPFIA (Figures 1 and 2). The specimens were dissected between March 2017 and April 2017, and all dissections were performed by the same experienced author (J.M.). Specific cortical landmarks such as the anterior sylvian point or the hand knob were defined based in previous anatomical publications. 23,24

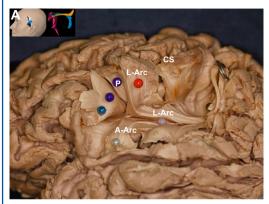
DTI Tractography Analysis

Four healthy volunteers (mean age = 36 yr) were studied with brain magnetic resonance imaging. The study was performed on a whole-body 3.0-T scanner (Achieva 3.0T; Philips Healthcare, Best, the Netherlands) with an 8-channel head coil. DTI tractography was performed using the same methodology previously described by our group. 25,26 The tractography analysis was performed between June 2017 and July 2017, and the reconstructions and measurements were performed by 2 experienced authors (A.G. and E.M.L.).

Surgical Technique

In order to analyze the functional anatomy of the VPFIA, 6 surgical cases with left side gliomas close to the VPFIA are presented. All patients were operated using intraoperative electrical stimulation mapping with an asleep-awake-asleep technique, a method previously described in detail by our group in previous reports. 27,28 All surgeries were performed between January 2015 and February 2017, and all surgeries were performed by the same surgeon (J.M.).

All participants signed a written informed consent to participate in the study. The study protocol (Protocol number 28/2016) was approved by the Hospital Committee of Human Research.



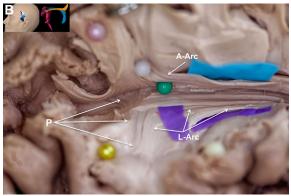


FIGURE 2. A, Fiber dissection of the tracts that terminate at the ventral precentral fiber intersection area (VPFIA) in a left hemisphere. The ventral part of the precentral gyrus has been splitted in order to isolate the termination of each tract. The anterior segment of the arcuate fasciculus terminates at the posterior portion of the VPFIA. The pyramidal pathway is connected to the anterior portion of the VPFIA. The long segment of the arcuate fasciculus terminates at the intermediate part of the VPFIA. B, Fiber dissection of the tracts that terminate at the VPFIA in another left hemisphere. The tracts organization within the VPFIA is similar to the hemisphere presented in A. A-Arc: Anterior segment of the arcuate fasciculus; CS = Central sulcus; CS = Central sulc

Statistical Analysis

The independent variable for the analysis was the side of the hemisphere (right vs left). The dependent variable was the distance measured at the VPFIA, and the identification or not of the different tracts at the VPFIA. For quantitative variables, a Mann-Whitney U test was used, and for qualitative variables the Fisher's exact test was used. A significance level of 5% (P < .05) was accepted in all cases. The analysis was performed with SPSS software version 20.0 (SPSS, IBM, Armonk, New York).

RESULTS

Table resumes the tracts identified at the VPFIA, cortical terminations of the different connections, and distances measured.

Tracts Identified at VPFIA

Three white matter tracts were identified at the VPFIA (arranged from posterior to anterior; Figures 1-5):

- 1. Anterior segment of the arcuate fasciculus. This pathway consists of anterior-posterior oriented fibers that run lateral to the long segment of the arcuate fasciculus and connect the inferior parietal lobe and posterior temporal lobe to the ventral part of the precentral gyrus.
- Long segment of the arcuate fasciculus. This long and large pathway, located deeply to the anterior segment of the arcuate fasciculus, connects the posterior temporal lobe with the ventral part of the precentral gyrus and the posterior frontal lobe.
- 3. Ventral part of the pyramidal tract. This tract consists of a well-defined group of fibers that are connected to the ventral part of the precentral gyrus, then run within the stem of this gyrus anterior and parallel to the terminations of the long segment

of the arcuate fasciculus, and finally course within the white matter of the central core.

The posterior cortical terminations of the different portions of the arcuate fasciculus were dissected and studied. Connections of the inferior fronto-occipital fasciculus and frontal aslant tract to the VPFIA were not identified.

Tracts Organization Within the VPFIA

The fibers projecting to the ventral part of the precentral gyrus are segregated in separated columns that terminate in specific cortical areas of the precentral gyrus (Figures 1-5). Three basic columns organized along an anteroposterior disposition were identified at the white matter of the VPFIA (Figures 1-5):

- *Posterior Column*: Contains fibers of the anterior segment of the arcuate fasciculus that terminates at the posterior part of the ventral precentral gyrus, with connections to the cortex of the central sulcus and the posterior part of the precentral gyrus.
- Intermediate Column: The fibers of the long segment of the arcuate fasciculus run within the precentral gyrus, immediately anterior to the fibers of the anterior segment of the arcuate fasciculus. These fibers are connected to the cortex of the ventral precentral gyrus, immediately anterior to the terminations of the anterior segment of the arcuate fasciculus.
- Anterior Column: The pyramidal pathway runs in the anterior part of the ventral precentral gyrus, immediately anterior to the fibers of the long segment of the arcuate fasciculus. The pyramidal pathway terminates in the cortex of the precentral sulcus and the anterior part of precentral gyrus. Anterior to the pyramidal pathway, U fibers connecting the posterior part of the inferior frontal gyrus with the precentral gyrus were encountered.

TABLE. Tracts Identified, Posterior Cortical Terminations and Distances Measured at the Ventral Precentral Fiber Intersection Area **Posterior cortical VPFIA** tracts terminations VPFIA distances (mm) FD vs No Side DTI A-Arc PT A-Arc L-Arc D1 D4 L-Arc D₂ **D3** FD Yes Yes Yes SM mT3 40 47 55 8 R 2 FD Yes Yes Yes SM mT3 65 53 70 17 3 FD Yes Yes Yes SM mT2, mT3 25 57 48 9 R SM pT2, PT3 4 FD Yes Yes Yes 22 58 60 2 5 FD SM pT3 45 55 58 3 1 Yes Yes Yes 6 R FD Yes Yes Yes SM mT2, mT3 38 57 50 7 FD Yes Yes Yes SM pT1, pT2 62 62 67 5 8 R FD Yes Yes Yes SM mT2 45 60 51 9 9 DTI Yes Yes Yes SM pT2 37 47 65 18 10 R DTI Yes Yes SM, ANG pT2,pT3 36 66 53 13 Yes 11 DTI 38 68 1 Yes Yes Yes SM mT2 50 18 12 R DTI Yes Yes Yes SM, ANG mT2, mT3 37 55 60 5 SM, ANG 13 DTI 45 72 55 17 Yes Yes Yes pT2 14 R DTI Yes Yes Yes SM. ANG mT2 37 65 57 8 15 DTI Yes Yes Yes SM pT2 37 60 57 3 pT2 R DTI SM 38 58 62 16 Yes Yes Yes 4 100% Mean 40.4 Mean 9.1 Total 50% L 50% FD 100% 100% 100% SM 25% 43.8% pT2 Mean 58.8 Mean 57.4 50% R 50% DTI ANG 37.5% mT2 (22-65)(47-72)(48-70)31.3% mT3 18.8% pT3 1Ta %8.6

A-Arc: anterior segment of the arcuate fasciculus; ANG: angularis gyrus; DTI: diffusion tensor imaging tractography; FD: fiber dissection; IPS: intraparietal sulcus; L-Arc: long segment of the arcuate Fasciculus; mT2: middle portion of middle temporal gyrus; mT3: middle portion of inferior temporal gyrus; pT1: posterior portion of superior temporal gyrus, pT2: posterior portion of middle temporal gyrus, pT3: posterior portion of inferior temporal gyrus; PT; pyramidal tract; SM; supramarginal gyrus; VPFIA; ventral precentral fiber intersection area; D1: distance from the anterior sylvian point to the dorsal limit of the anterior segment of the arcuate fasciculus; D2: distance from the anterior sylvian point to the dorsal limit of the long segment of the arcuate fasciculus; D3: distance from the anterior sylvian point to the ventral limit of the hand knob; D4: distance from the inferior limit of the hand knob to the dorsal limit of the long segment of the arcuate fasciculus.

Distances Measured at the VPFIA

Distances were measured at the ventral premotor area (Figure 6 and Table). All distances were compared between both sides. The differences observed were not statistically significant (P > .05).

Surgical Findings

Stimulation of the VPFIA elicited speech arrest in all cases (Figures 7-9). In 2 cases, 1 cortical area related to speech arrest was found. In 4 cases, 2 cortical areas related to speech arrest were found. The histopathological diagnosis revealed low-grade glioma in 4 cases, anaplastic glioma in 2 cases, and glioblastoma in 1 case. The VPFIA defined a functional unresectable limit in all cases, as reorganization of function was never outside the ventral part of the precentral gyrus.

DISCUSSION

The present study revealed that the VPFIA is a central hub in the frontoparietal connectivity as it is connected to 3 important perisylvian bundles: anterior segment of the arcuate fasciculus, the long segment of the arcuate fasciculus, and pyramidal pathway. Importantly, the connections within the VPFIA appear to be anatomically organized along an anterior-posterior disposition. The most posterior connections are the fibers projecting from the anterior segment of the arcuate fasciculus, and the most anterior connection is the pyramidal pathway. The termination of the long segment of the arcuate fasciculus lies in between the anterior and posterior connections. The present findings can be explained based on the disposition of the dorsal stream within the frontoparietal operculum, and the pyramidal pathway within the precentral gyrus. The dorsal stream, composed by the long segment of the arcuate fasciculus and anterior segment of the arcuate fasciculus, is connected posteriorly to a wide area in the parietal and posterior temporal lobes, then runs in a posterior to anterior direction converging at the frontoparietal operculum. 10,16,29-31 Then, the stream enters in the frontal operculum through the posterior margin of the precentral gyrus. Within the precentral gyrus, the dorsal stream encounters the pyramidal pathway that consists of long axons that directly project from the motor cortex via de cortico-bulbar tract to the brainstem, ie, to the orofacial motor nuclei. 32,33 It is worth

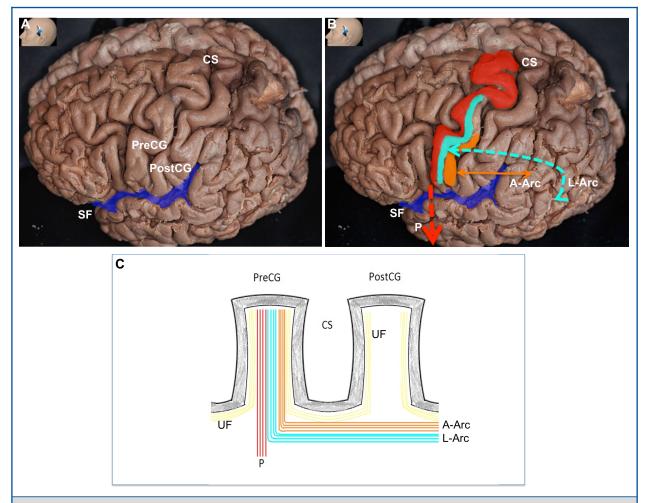


FIGURE 3. A, Left hemisphere where the sylvian fissure (SF) and the ventral part of the precentral gyrus (PreCG) and postcentral gyrus (PostCG) are marked. B, Schematic representation of the tracts that terminate at the ventral part of the precentral gyrus (VPFIA) in a left hemisphere. The tracts projecting to the VPFIA are organized in separated columns that terminate in specific cortical areas of the precentral gyrus. Three basic columns organized along an anteroposterior disposition were identified at the white matter of the VPFIA. The posterior column contains the anterior segment of the arcuate fasciculus (orange), the intermediate column contains the long segment of the arcuate fasciculus (blue), and the anterior column contains the pyramidal pathway (red). C, Schematic representation of the tracts that terminate at the VPFIA. A-Arc: Anterior segment of the arcuate fasciculus; CS = Central sulcus; L-Arc: Long segment of the arcuate fasciculus; P = Pyramidal pathway; PreCG = Precentral gyrus; PreCG = Precentral gyrus connecting adjacent gyrus.

to note that the pyramidal pathway conforms a vertical barrier within the precentral gyrus for the passage of axons of the dorsal stream. Consequently, it seems logical that the dorsal stream connects to the posterior bank of the precentral gyrus, as it enters the frontal lobe passing underneath the central sulcus, while the pyramidal pathway occupies the anterior bank as it is displaced by the projections of the dorsal stream. In the same way, the terminations of the anterior and long segments of the arcuate fasciculus have an anteroposterior organization. The course of the long segment of the arcuate fasciculus within the parietal lobe is deep compared to the anterior segment of the arcuate fasciculus what determines a connection of the long segment of the arcuate fasciculus further anterior at the precentral gyrus.

The VPFIA connectivity map presented here apparently conflicts with the established neuroanatomical cortical maps. The most widely used cortical map is that of Brodmann, in which the cortex is parcellated based in cytoarchitectonic criteria. In Brodmann's cortical atlas, the primary motor cortex is located in the posterior part of the precentral gyrus, just anterior to the central sulcus (Brodmann area 4), and the ventral premotor cortex is situated anterior to the primary motor cortex (Brodmann area 6).³⁴ This is just the opposite of what we have found at the ventral part of the precentral gyrus: pyramidal pathway connected to the

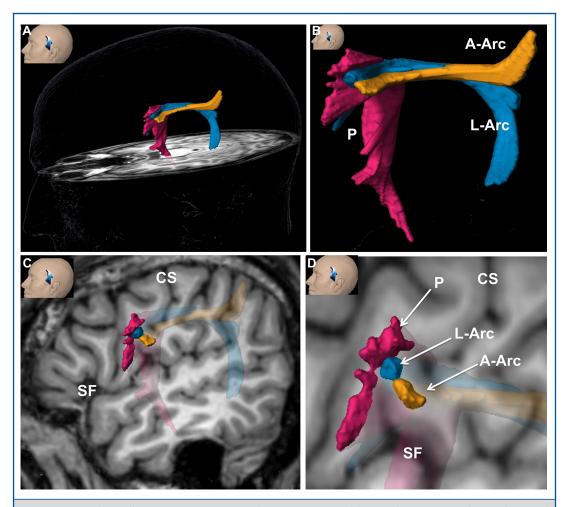


FIGURE 4. A and B, Diffusion tensor imaging tractography 3D reconstruction of the tracts that terminate at the ventral precentral fiber intersection area (VPFIA). C, T1 sagittal weighted magnetic resonance imaging with diffusion tensor imaging tractography reconstruction of the arcuate fasciculus, and pyramidal pathway terminating at the VPFIA. The anterior segment of the arcuate fasciculus terminates at the posterior portion of the VPFIA. The intermediate part of the VPFIA is occupied by the long segment of the arcuate fasciculus. The pyramidal pathway terminates at the anterior portion of the VPFIA. D, Detailed view of the image presented in C. A-Arc: Anterior segment of the arcuate fasciculus; CS = Central sulcus; L-Arc: Long segment of the arcuate fasciculus; P = Pyramidalpathway; SF = Sylvian fissure.

anterior part of the precentral gyrus, and dorsal stream connected to the posterior bank. The following arguments may help to better understand these apparently contradictory results: (1) cytoarchitectonic and myeloarchitectonic maps reflect different aspects of connectivity. Brodmann divided the cerebral cortex into distinct cytoarchitectonic areas based on differences in cell types, and in the organization of neurons in specific cortical layers.³⁴ On the other hand, the current study presents a myeloarchitectonic map that reflects the organization of axons, terminating at the cortex.³⁵ (2) The borders of the Brodmann's cytoarchitectonic areas are more disperse than classical maps suggested. In this sense, the margin between the premotor and motor cortex is still rather unclear, and it has been described at the precentral sulcus,

within the anterior precentral gyrus, and posterior part of inferior, middle, and superior frontal gyrus.³⁶ (3) The giant pyramidal cells of Betz are considered a landmark of the primary motor cortex. However, Betz cells are not the only main output from the motor area to the spinal cord and brainstem, with numerous corticospinal connections distributed at numerous motor planning areas and sensory cortex.³⁷

The functional anatomy of language processing implicates multiple cortical and subcortical areas that are organized in 2 processing streams: a dorsal stream (composed by the arcuate fasciculus) involved in sensory motor mapping of acoustic language signals to articulatory networks at the frontal lobe and a ventral stream (composed by the inferior fronto-occipital

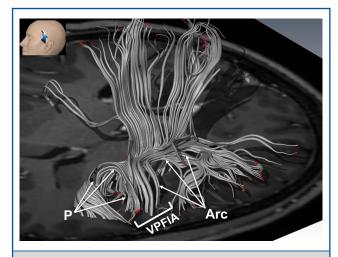


FIGURE 5. Diffusion tensor imaging tractography 3D reconstruction of the tracts that terminate at the ventral precentral fiber intersection area (VPFIA). The pyramidal pathway terminates at the anterior portion of the VPFIA, while the arcuate fasciculus terminates posteriorly. P = Pyramidal pathway; Arc = Arcuate fasciculus.

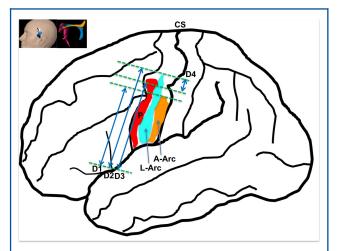


FIGURE 6. Schematic representation of the tracts that terminate at the ventral part of the precentral gyrus (VPFIA) in a left hemisphere. The following distances were measured at the VPFIA: D1 = minimal distance from the anterior sylvian point to the dorsal limit of the anterior segment of the arcuate fasciculus. D2 = minimal distance from the anterior sylvian point to the dorsal limit of the long segment of the arcuate fasciculus. D3 = minimal distance from the anterior sylvian point to the ventral limit of the hand knob. D4 = minimaldistance from the inferior limit of the hand knob to the dorsal limit of the long segment of the arcuate fasciculus. A-Arc: Anterior segment of the arcuate fasciculus; CS = Central sulcus; L-Arc: Long segment of the arcuate fasciculus; P = Pyramidal pathway.

fasciculus, uncinated fasciculus, middle longitudinal fasciculus, and inferior longitudinal fasciculus) involved in processing speech signals for comprehension. 38,39 Our results revealed that the VPFIA is mainly connected with the dorsal stream (posteriorly), with only few connections through U fibers with the ventral stream and the Broca's area anteriorly. In the last decades, numerous authors have questioned the classical view of Broca's area as the main language production center. 40-42 In the same way, stimulation studies demonstrated that, in brain tumors cases and using mapping techniques, it is possible to remove the Broca's area completely, without generating language deficits. 43,44 At a fundamental level, our results support this hypothesis as the small number of connections between Broca's area and the motor speech output center would greatly hamper Broca's control over speech muscles.

A comprehensive understanding of the anatomical organization within the VPFIA is capital to infer its function. The VPFIA has been proposed as the final pathway for speech production. Our results support this hypothesis, as ventral part of the VPFIA is strategically located between the termination of the dorsal stream and the motor output cortex that directly control speech muscles. This area may integrate the information that has been processed at the dorsal pathway, and send the final outputs to coordinate the complex movements of the tongue, lips, and larynx necessary for speech production.⁶⁻⁹ Interestingly, previous studies had demonstrated that the plastic potential of the VPFIA is very low as reorganization of function never occurred outside the precentral gyrus, despite the infiltration of a glioma.⁴⁵ These stimulation results are entirely in accordance with the surgical cases presented here, as we detected function in all cases within the precentral gyrus despite the fact that the tumor was infiltrating or immediately in contact with the VPFIA. The authors of the previous study interpreted these observations based on the limited subcortical plastic potential, and the necessity for the VPFIA to be connected to the anterior segment of the arcuate fasciculus. We raise here an alternative hypothesis, and focus the attention on the importance for the VPFIA to be connected to the pyramidal pathway. The neurons of the pyramidal pathway form a unique and long connection between the cortex and the motor nucleus of the nerves that control language muscles (one connection - one function). Therefore, such neurons are irreplaceable as it is not possible to rebuild new connections if they are damaged. Contrary, the plastic potential of other associative perisylvian areas is very high, including the so-called Broca's and Wernicke's areas. 43,44,46 These associative areas, unlike the VPFIA, have multiple and redundant connections (multiple connections - one function), so if one network is damaged another is activated and the global function is not affected.

Limitations

The results presented here are subject to some limitations. First, the number of subjects studied with fiber dissection and

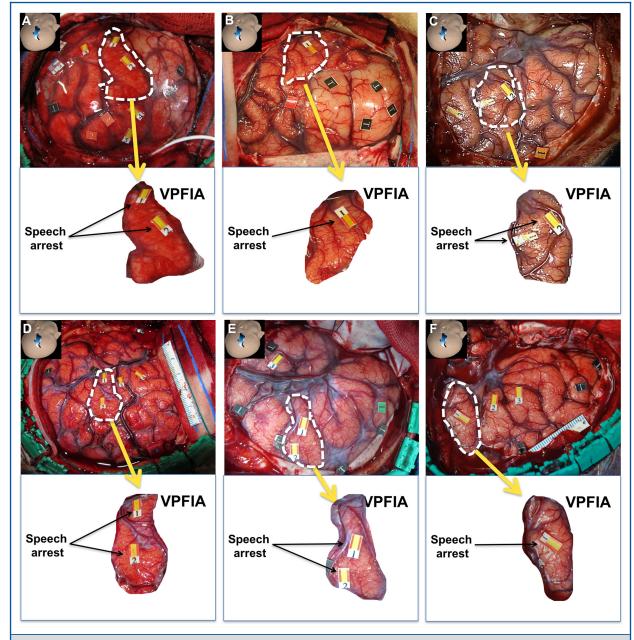


FIGURE 7. A-F, Schematic representation of the 6 surgical cases presented. The VPFIA has been marked in every case with a dotted line. Stimulation of the VPFIA elicited speech arrest in all cases.

tractography (16) is not enough to evaluate the potential variability of the connectivity of the VPFIA. Second, fiber dissection technique and DTI tractography have known limitations to analyze the fiber organization in areas where the trajectory of different axons intersects. Third, the limitation of intraoperative electrical stimulation mapping to evaluate the function of areas of tract intersection, due to the dispersion of current. Fourth, previous reports have demonstrated that, in the language nondominant side, a portion of the face motor cortex can be resected without causing a permanent language, articulatory, or motor deficit.⁴⁷ The most accepted view considers that the recovery is mediated by the contralateral side, as the ventral motor cortex is projected bilaterally to the brainstem nuclei. Consequently, further anatomical and functional studies about this area are necessary to analyze in more detail the difference in connectivity and function between the right and left VPFIA.

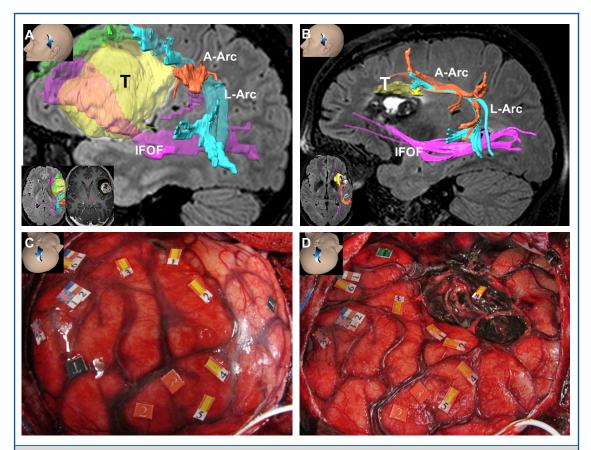


FIGURE 8. A 43-yr-old, trilingual (Spanish, English, and French), right-handed man with a left frontal glioblastoma. The patient had 2 partial seizures with dysphasia one week before admission. No preoperative neurological deficit was observed. A, Preoperative sagittal fluidattenuated inversion-recovery (FLAIR) magnetic resonance images with diffusion tensor imaging tractography reconstruction of the tracts terminating at the ventral precentral fiber intersection area (VPFIA). The tumor is anterior to the VPFIA, in direct contact with the anterior termination of the anterior and long segments of the arcuate fasciculus. B, Postoperative sagittal FLAIR magnetic resonance images with diffusion tensor imaging tractography reconstruction of the tracts terminating at the VPFIA. The residual tumor volume was 4.2 mL. C, Intraoperative photograph taken before tumor resection in which the frontal, parietal, and temporal left lobes are exposed. Intraoperative electric stimulation of the cortex and white matter immediately posterior to the tumor elicited speech arrest. These areas were located with neuronavigation corresponding to the VPFIA. Intraoperative cortical electric stimulation elicited the following responses: Spanish flags 1, 2, 4, and 5 = speech arrest; Spanish flag 3 = dysarthria; Spanish flag 6 = anomia; English flags 1 and 2 = phonemic paraphasia; French flags 1 and 2 = phonemic paraphasia; Red tag 2 and 3 = lower lip movement. D, Intraoperative photograph taken after tumor resection. Resection was pursued until eloquent structures were encountered around the surgical cavity. Intraoperative electric stimulation of the white matter elicited the following responses: Spanish flag 8= semantic paraphasia. The final pathology was glioblastoma.

CONCLUSION

The present anatomic study delineated the VPFIA, a capital neural center within the perisylvian language network connected to the pyramidal pathway, and 2 important associative tracts: anterior and long segments of the arcuate fasciculus.

The present study shows strong arguments to sustain that the fiber organization of the VPFIA is different from the classical descriptions, bringing new light for understanding the functional role of this area in language. The connections within the VPFIA are anatomically organized along an anteroposterior axis. The

pyramidal pathway is connected to the anterior bank of the precentral gyrus, as the posterior bank is occupied by the connections of the dorsal stream (anterior and long segments of the arcuate fasciculus). Therefore, this area is strategically located between the termination of the dorsal stream and the motor output cortex that directly control speech muscles. Consequently, this area may represent the final common pathway for speech production, as it may integrate the information that has been processed at the dorsal pathway, and send the final outputs to coordinate the complex movements of the tongue, lips, and larynx necessary for speech.

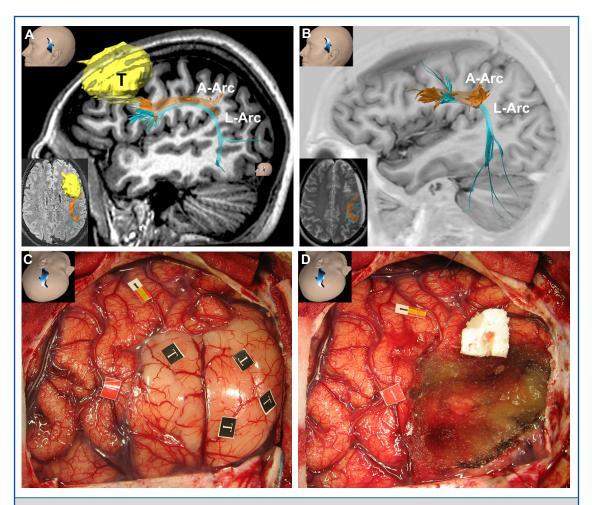


FIGURE 9. Magnetic resonance imaging (MRI) and surgical pictures of a 41-yr-old right-handed woman with a left frontal WHO grade II astrocytoma. The patient had a partial seizure with dysphasia 1 month before admission. No preoperative neurological deficit was observed. A, Preoperative sagittal fluid-attenuated inversion-recovery (FLAIR) magnetic resonance images with diffusion tensor imaging tractography reconstruction of the tracts terminating at the ventral precentral fiber intersection area (VPFIA). The tumor is located at the posterior part of the middle and inferior frontal gyrus. The tumor is anterior and superior to the VPFIA, in contact with the anterior termination of the anterior and long segments of the arcuate fasciculus. B, Postoperative sagittal FLAIR magnetic resonance images with diffusion tensor imaging tractography reconstruction of the tracts terminating at the VPFIA. Postoperative MRI revealed complete tumor resection. C, Intraoperative photograph taken before tumor resection in which the frontal, parietal, and temporal left lobes are exposed. Intraoperative electric stimulation of the cortex and white matter immediately posterior to the tumor elicited speech arrest. These areas were located with neuronavigation corresponding to the VPFIA. Intraoperative cortical electric stimulation elicited the following responses: Spanish flags 1 = speech arrest; Red tag 1 = thumb movement. D, Intraoperative photograph taken after tumor resection. Resection was pursued until eloquent structures were encountered around the surgical cavity. The final pathology was diffuse low-grade astrocytoma.

Disclosures

Dr Martino receives specific founding from the Instituto de Salud Carlos III (PI13/01249, grant entitled "Preservación de las áreas implicadas en la memoria de trabajo verbal para evitar secuelas en la cirugía de gliomas en áreas elocuentes") and Fundación Instituto de Investigación Marqués de Valdecilla (IDIVAL). The aid granted for this project is eligible for co-financing with Fondo Europeo de Desarrollo Regional (FEDER) funds. The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES

- 1. Rizzolatti G, Fogassi L, Gallese V. Motor and cognitive functions of the ventral premotor cortex. Curr Opin Neurobiol. 2002;12(2):149-154.
- 2. Preuss TM, Stepniewska I, Kaas JH. Movement representation in the dorsal and ventral premotor areas of owl monkeys: a microstimulation study. J Comp Neurol. 1996;371(4):649-676.
- 3. Penfield W, Boldrey E. Somatotopic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. Brain. 1937;60 4:389-

- 4. Conant D, Bouchard KE, Chang EF. Speech map in the human ventral sensorymotor cortex. Curr Opin Neurobiol. 2014;24(1):63-67.
- 5. Mayka MA, Corcos DM, Leurgans SE, Vaillancourt DE. Three-dimensional locations and boundaries of motor and premotor cortices as defined by functional brain imaging: a meta-analysis. Neuroimage. 2006;31(4):1453-1474.
- 6. Peeva MG, Guenther FH, Tourville JA, et al. Distinct representations of phonemes, syllables, and supra-syllabic sequences in the speech production network. Neuroimage. 2010;50(2):626-638.
- 7. Price CJ. The anatomy of language: a review of 100 fMRI studies published in 2009. Ann N Y Acad Sci. 2010;1191 (1):62-88.
- 8. Schubotz RI, Anwander A, Knosche TR, von Cramon DY, Tittgemeyer M. Anatomical and functional parcellation of the human lateral premotor cortex. Neuroimage. 2010;50(2):396-408.
- 9. Vigneau M, Beaucousin V, Herve PY, et al. Meta-analyzing left hemisphere language areas: phonology, semantics, and sentence processing. Neuroimage. 2006;30(4):1414-1432.
- 10. Martino J, De Witt Hamer PC, Berger MS, et al. Analysis of the subcomponents and cortical terminations of the perisylvian superior longitudinal fasciculus: a fiber dissection and DTI tractography study. Brain Struct Funct. 2013;218(1):105-121.
- 11. Martino J, De Witt Hamer PC, Vergani F, et al. Cortex-sparing fiber dissection: an improved method for the study of white matter anatomy in the human brain. J Anat. 2011;219(4):531-541.
- 12. Fernandez-Miranda JC, Rhoton AL Jr, Alvarez-Linera J, Kakizawa Y, Choi C, de Oliveira EP. Three-dimensional microsurgical and tractographic anatomy of the white matter of the human brain. Neurosurgery. 2008;62(6 Suppl 3):989-1026.
- Sarubbo S, De Benedictis A, Merler S, et al. Towards a functional atlas of human white matter. Hum Brain Mapp. 2015;36(8):3117-3136.
- 14. Rhoton AL Jr. The cerebrum. Neurosurgery. 2002;51(4 Suppl):S1-51.
- 15. Forkel SJ, Thiebaut de Schotten M, Dell'Acqua F, et al. Anatomical predictors of aphasia recovery: a tractography study of bilateral perisylvian language networks. Brain. 2014;137(7):2027-2039.
- 16. Wang X, Pathak S, Stefaneanu L, Yeh FC, Li S, Fernandez-Miranda JC. Subcomponents and connectivity of the superior longitudinal fasciculus in the human brain. Brain Struct Funct. 2016;221(4):2075-2092.
- 17. Bernal B, Altman N. The connectivity of the superior longitudinal fasciculus: a tractography DTI study. Magn Reson Imaging. 2010;28(2):217-225.
- 18. Barrick TR, Lawes IN, Mackay CE, Clark CA. White matter pathway asymmetry underlies functional lateralization. Cereb Cortex. 2007;17(3):591-598.
- 19. Catani M, Thiebaut de Schotten M. A diffusion tensor imaging tractography atlas for virtual in vivo dissections. Cortex. 2008;44(8):1105-1132.
- 20. Glasser MF, Rilling JK. DTI tractography of the human brain's language pathways. Cereb Cortex. 2008;18(11):2471-2482.
- 21. 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(5):691-699.
- 22. Martino J, Vergani F, Robles SG, Duffau H. New insights into the anatomic dissection of the temporal stem with special emphasis on the inferior frontooccipital fasciculus: implications in surgical approach to left mesiotemporal and temporoinsular structures. Neurosurgery. 2010;66(3 Suppl Operative):4-12.
- 23. Ono M, Kubik S, Abernathey CD. Atlas of the Cerebral Sulci. New York: Georg Thieme Verlag; 1990.
- Ribas GC, Ribas EC, Rodrigues CJ. The anterior sylvian point and the suprasylvian operculum. Neurosurg Focus. 2005;18(6B):E2.
- 25. Martino J, da Silva-Freitas R, Caballero H, Marco de Lucas E, Garcia-Porrero JA, Vazquez-Barquero A. Fiber dissection and diffusion tensor imaging tractography study of the temporoparietal fiber intersection area. Neurosurgery. 2013;72(1 Suppl Operative):ons87-ons98.
- 26. Martino J, Mato D, Marco de Lucas E, et al. Subcortical anatomy as an anatomical and functional landmark in insulo-opercular gliomas: implications for surgical approach to the insular region. J Neurosurg. 2015;123(4):1081-1092.
- 27. Martino J, Taillandier L, Moritz-Gasser S, Gatignol P, Duffau H. Re-operation is a safe and effective therapeutic strategy in recurrent WHO grade II gliomas within eloquent areas. Acta Neurochir. 2009;151(5):427-436.
- 28. Martino J, Gomez E, Bilbao JL, Duenas JC, Vazquez-Barquero A. Cost-utility of maximal safe resection of WHO grade II gliomas within eloquent areas. Acta Neurochir. 2013;155(1):41-50.
- 29. 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(3):630-653.

- 30. 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. Cereb Cortex. 2005;15(6):854-869.
- 31. Bucheli C, Mato D, Marco de Lucas E, Garcia-Porrero JA, Vazquez-Barquero A, Martino J. Insular-opercular associative tracts: Review of their anatomy and relevance for the trans-opercular approach to the insula. Neurocirugía. 2014;25(6):268-274.
- 32. Vulliemoz S, Raineteau O, Jabaudon D. Reaching beyond the midline: why are human brains cross wired? Lancet Neurol. 2005;4(2):87-99.
- Verstynen T, Jarbo K, Pathak S, Schneider W. In vivo mapping of microstructural somatotopies in the human corticospinal pathways. J Neurophysiol. 2011;105(1):336-346.
- 34. Brodmann K. Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues. Leipzig: Barch JA; 1909.
- 35. Amunts K, Zilles K. Architectonic mapping of the human brain beyond brodmann. Neuron. 2015;88(6):1086-1107.
- Geyer S, Zilles K. Functional Neuroanatomy of Human Motor Cortex in Higher Order Motor Disorders. Oxford: Oxford University Press; 2005.
- 37. Dum RP, Strick PL. The origin of corticospinal projections from the premotor areas in the frontal lobe. J Neurosci. 1991;11(3):667-689.
- Hickok G, Poeppel D. Dorsal and ventral streams: a framework for understanding aspects of the functional anatomy of language. Cognition. 2004;92(1-2):67-
- 39. Poeppel D, Hickok G. Towards a new functional anatomy of language. Cognition. 2004;92(1-2):1-12.
- 40. Turken AU, Dronkers NF. The neural architecture of the language comprehension network: converging evidence from lesion and connectivity analyses. Front Syst
- 41. Dronkers NF, Plaisant O, Iba-Zizen MT, Cabanis EA. Paul Broca's historic cases: high resolution MR imaging of the brains of Leborgne and Lelong. Brain. 2007;130(5):1432-1441.
- 42. Duffau H. The "frontal syndrome" revisited: lessons from electrostimulation mapping studies. Cortex. 2012;48(1):120-131.
- 43. Benzagmout M, Gatignol P, Duffau H. Resection of World Health Organization Grade II gliomas involving Broca's area: methodological and functional considerations. Neurosurgery. 2007;61(4):741-753.
- 44. Plaza M, Gatignol P, Leroy M, Duffau H. Speaking without Broca's area after tumor resection. Neurocase. 2009;15(4):294-310.
- van Geemen K, Herbet G, Moritz-Gasser S, Duffau H. Limited plastic potential of the left ventral premotor cortex in speech articulation: evidence from intraoperative awake mapping in glioma patients. Hum Brain Mapp. 2014;35(4):1587-
- 46. Sarubbo S, Le Bars E, Moritz-Gasser S, Duffau H. Complete recovery after surgical resection of left Wernicke's area in awake patient: a brain stimulation and functional MRI study. Neurosurg Rev. 2012;35(2):287-292.
- LeRoux PD, Berger MS, Haglund MM, Pilcher WH, Ojemann GA. Resection of intrinsic tumors from nondominant face motor cortex using stimulation mapping: report of two cases. Surg Neurol. 1991;36(1):44-48.

COMMENT

The authors present an interesting and complete research about the main white-matter fiber bundles found at the "ventral precentral fiber intersection area", collecting data from anatomical fiber dissection, diffusion tensor imaging tractography, and surgeries. Their results add significant information for the understanding of the complex connectivity of the brain, clarifying the position of fiber bundles related to motor and language functions at this region. Deep knowledge of the subcortical fiber architecture is essential for neurosurgeons, particularly in brain mapping procedures where finding the location of the main white matter fiber bundles is mandatory to define functional boundaries. Congratulations to the authors for the good work.

> Eduardo Carvalhal Ribas São Paulo, Brazil