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Isolated Ictal Aphasia

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Abstract

Isolated aphasia is an exceedingly rare presentation of epileptic activity. We present the case of a 70 year old woman who presented with language disturbance, which was initially misrecognized as altered mental status. After a finding of a left apical lung opacity, her presentation was attributed to pneumonia. Her symptoms did not improve after 2 days of antibiotic therapy and chest CT was consistent with a chronic process. Brain MRI with DWI failed to demonstrate restricted diffusion. An EEG was then obtained for her recurrent episodes of difficulty speaking and revealed left hemispheric slowing and left frontopolar sharp waves (maximum at Fp1>Fp2). She was started on levetiracetam, which improved her aphasic episodes, and a subsequent dose increase completely eliminated her aphasia. We discuss the etiopathology, diagnosis, and management of isolated ictal aphasia and the insights that this phenomenon provides into language network organization.

Keywords

Aphasia; Epileptic; Epilepsy; Language disturbance; Seizures

Introduction

Sudden-onset aphasia is a frequently-encountered problem by internists, neurologists, and neurosurgeons. The most concerning and frequent cause of this presentation is an occlusion compromising blood flow to the cerebrum. While stroke must remain at the top of the differential diagnosis, other causes are not infrequent, and include trauma and seizures (which may in turn be idiopathic, secondary to cerebrovascular disease, or trauma). These may present convulsively or non-convulsively and with or without associated symptoms, rendering epileptogenic activity the favored presumed diagnosis. Occasionally, though infrequently, aphasia is the sole manifestation of seizure activity [1-22].

Aphasia in the context of seizure activity represents either post-ictal activity [23], an aura [24], or, rarely, ictus proper. Ictal aphasia can in turn be idiopathic or secondary, the latter as a result of structural pathology, following tumor resection, or metabolic disturbances [20,21,25]. Importantly, absence of interictal activity frequently leads to misdiagnosis as psychogenic seizures [9]. Speech perturbations may also be the initial abnormality in kids with benign rolandic epilepsy [26]. This rare presentation has been reported in the literature in less than 30 cases. We present a case of a patient with isolated ictal aphasia and discuss this literature on this rather interesting topic.

Case report

A 70-year-old woman with history of hepatitis C, hepatocellular carcinoma, and stroke with residual right-sided weakness was brought to the emergency department by her daughter for a change in mental status starting on the day of admission. This was accompanied by fever and several episodes of vomiting. The daughter noted her mother was not responding to questions, but that at baseline she is appropriately conversant and completely independent, requiring the aid of a cane to ambulate.

The patient was admitted and initially suspected to have altered mental status given her language disturbance, which was attributed to possible pneumonia, for which she was started on antibiotics. Chest x-ray revealed a nodular opacity at the left lung apex and an ovoid, 5 cm opacity in the medial left lung apex. Her language failed to improve after 48 hours of antibiotic treatment. CT scan of the chest showed lobulated left apical pleural mass and subpleural masses measuring up to 7 cm and adjacent ground glass opacities and interstitial thickening of the left lung apex. The patient's clinical picture and the radiographic appearance of her lung pathology was inconsistent with an acute infectious etiology and interventional radiology recommended image-guided biopsy, but the patient refused.

She continued to experience episodes of speech arrest and language difficulty without disturbance in alertness. At this point, neurology was consulted. An MRI of the brain was obtained and showed no evidence of restricted diffusion to suggest acute ischemia. An electroencephalogram (EEG) was obtained for recurrent episodes of difficulty speaking with or without change in mental status. The EEG showed intermittent slowing in the left

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hemisphere at frequencies of 2-4 Hz of medium amplitude that is near continuous in the beginning of the record and decreases to intermittent by the conclusion of the record. Sharp waves were seen in the left frontopolar region with a maximum at Fp1>Fp2 seen abundantly and periodically in the early portions of the study but decreased in latter portions. The patient was started on levetiracetam 500 mg by mouth twice daily. Her symptoms improved significantly, but she continued to experience episodes of word finding difficulty, which resolved with an increase in her levetiracetam dose.

Discussion

Non-convulsive status epilepticus originating from the frontal foci may result in a myriad of behavioral manifestations [27]. Muteness absent specific speech or language signs may occur later in life in patients with frontal lobe complex partial status epilepticus [28,29]. However, a spectrum of language dysfunction encompassing stuttering, aphemia, aphasia, and global speech motor output failure, as in the case of our patient, is rarely seen as the isolated clinical manifestation of epileptic episodes. Given the typical absence of interictal activity, they are frequently attributed to psychogenic non-epileptic episodes [30].

Mechanism of ictal speech arrest

Speech arrest during ictus may either be the consequence of positive or negative motor responses [3,31]. In the former situation, this is accompanied by facial twitching and tends to be more prolonged [7,25,32,33], which may be misidentified as post-ictal activity. In the latter case, speech arrest is transitory and of shorter duration. Our patient did not have associated facial twitching during her episodes.

Ictal speech arrest most typically arises from a left hemispheric focus, as demonstrated by the EEG findings of our patient, though crossed aphasia has been reported [34-36]. A phenomenon which may underlie ictal aphasia is cortical spreading depression. This is a slowly-advancing depolarization wave followed by regional hypoperfusion as a consequence of vasoconstriction [37,38]. This has been shown to be poorly responsive to potent antiepileptic drugs, such as carbamazepine and levetiracetam [39], but highly-responsive to topiramate and magnesium [40-43] (Table 1).

Clinical diagnosis

Diagnostic criteria for ictal aphasia were first proposed in the 1980's [4]. Clinical evidence favoring the diagnosis of isolated ictal aphasia includes epileptiform activity in the EEG corresponding to predicted language localization and reversal of aphasia and EEG abnormalities in response to intravenous benzodiazepines. The diagnosis may prove more challenging in those individuals in whom the aphasic episodes are of short duration, given the typical absence of identifying interictal activity. Isolated ictal aphasia can be prolonged and represent nonconvulsive status epilepticus, which is defined clinically and electrocorticographically as persistence of low-voltage (delta) discharge and improvement in symptoms or the EEG pattern with the administration of benzodiazepines intravenously [44]. Nonconvulsive status epilepticus with aphasia has been reported secondary to diabetes and its complications [3,10,11] as hyperglycemia can lower the seizure threshold [45], demyelinating disease [46], cefepime encephalopathy [47], and in immunocompromised individuals [48].

Diagnostic modalities for ictal aphasia include standard EEG, continuous EEG [49] 56% sensitivity), depth electrode EEG [50], real-time spectra EEG, FDG-PET imaging [51], and CT perfusion. As standard EEG may be poorly sensitive for isolated ictal aphasia, the latter subsume greater importance when the diagnosis is highly suspected, but remains unconfirmed following typical work-up. As seizure activity is associated with ictal hyperperfusion and post-ictal (or prolonged ictal) hypoperfusion, additional useful adjunctive diagnostic modalities include diffusion-weighted imaging MRI [52-55] and CT perfusion studies.

Author	Age, gender	EEG findings	Speech impairment type
Herskovitz and Schiller, 2012, pt 1	76, F	PLEDS	Global
Herskovitz and Schiller, 2012, pt 2	20, F	Electrographic seizure	Global
Herskovitz and Schiller, 2012, pt 3	54, F	PLEDS	Motor
Herskovitz and Schiller, 2012, pt 4	44, F	PLEDS	Sensory
Herskovitz and Schiller, 2012, pt 5	48, F	PLEDS	Global
Herskovitz and Schiller, 2012, pt 6	47, M	Electrographic seizure	Motor
Commondoor et al., 2009	13, F	Left frontotemporal slowing	Motor
DeToledo et al., 2000	Unknown age, F	R frontal and parasagittal slowing	Motor
Flügel et al., 2015	62, F	Left frontotemporal slowing	Global
Kaplan and Stagg, 2011	Elderly, M	L frontal continuous discharges followed by bifrontal activity	Anarthria
Patil and Oware, 2012	60, F	L mid/post temporal (focal status transforming into fast rhythm)	Sensory
Riecker et al., 2004	59, F	R temporal (delta focus maximum in temporal leads) epileptiform activity	global
Sadiq et al., 2012	67, M	L temporal epileptiform activity	Motor
Shah and Adams, 2016	67, M	no change in EEG during events	Motor
Wells et al., 1992	45, M	EEG sharp waves from L hemisphere	Global

Table 1: Mechanism of Ictal Speech Arrest

Toledo et al. [56], demonstrated DWI hyperintensity in the parieto-temporal region and pulvinar in patients with aphasic status epilepticus and hyperperfusion in another subset of their patients. While MRI and MRA may be useful to exclude the possibility of a stroke, multiparametric CT was found to be the best modality in distinguishing the two diagnoses in a small series of patients with stroke alerts called later found to have epilepsy [14]. The most useful metric was time to peak, which if increased in multiple cerebral lobes with absence of large vessel occlusion or involvement of deep

gray matter, was highly predictive of epileptiform activity rather than cerebrovascular disease.

The language network: insights into basic organization and clinical implications

Language lateralization has been a subject of intense interest and fruitful investigation for over a century. It is believed that the overwhelming majority of right-handed individuals exhibit language dominance in the left hemisphere, with 1-5% having paradoxical ipsilateral language dominance. The converse is true for left-handed individuals, but crossed language dominance (ipsilateral hemisphere dominance) is more common in such individuals. It appears to be dependent on a host of variables, including both hereditary factors (i.e., genetics, family history of left-handedness, gender) and environmental factors (e.g, multilingualism) [57].

The classic model of language network organization includes cortical areas mediating the motor and sensory aspects of language – Broca's and Wernicke's areas, respectively – with subcortical white matter tracts linking cortical regions for language representation, programming, and articulation – for example, the arcuate fasciculus. These are based on early studies dating back to the mid-20th century. Penfield and Rasmussen [58] demonstrated speech arrest as a consequence of intraoperative electrical stimulation in the dominant frontal and parietal opercula [59] and the precentral gyri bilaterally, providing the first direct electrophysiological evidence for the existence of discrete language centers and their localization. Involvement of the precentral gyri in language programming was later shown by PET studies [60,61]. Luders et al. [31], showed that stimulation of a discrete number of areas were capable of resulting in speech arrest and suggested that this phenomenon is distinct from true aphasia. Lecours and Lhermitte argue that speech arrest, representing perturbed articulatory programming, represents a subset of aphasia.

While showing interindividual variability, language centers are discrete and defined for any given individual [36]. For example, stimulation of the posterior aspects of the superior, middle, and inferior frontal gyri effected speech arrest in 75, 55, and 77% of individuals, respectively [36]. This explains the frequent discordance between seizure focus and type of language disturbance [18], which may also be explained by surrounding seizure spread, complexity of the language network, and involvement of subcortical fasciculi. For example, temporal epileptiform activity, which usually results in sensory aphasia, may also underlie the clinical expression of a pure motor aphasia, representing spread of epileptiform activity. Also, crossed spreading of epileptiform activity has been shown from the left to right hemisphere [44].

More recent studies suggest greater complexity, as well as a different model for language organization. Analogous to the visual pathway, language appears to be processed by dorsal and ventral streams, the former responsible for phonemic, and the latter for semantic, processing, respectively. Stimulation of contralateral right ventral premotor cortex has been shown to produce speech arrest in both right and left-handed individuals. Stimulation of the inferior fronto-occipital and arcuate fasciculi in the language-dominant hemisphere has been shown to effect paraphasias of the semantic and phonemic type, respectively [62]. This suggests that IFOF and AF may represent the anatomic substrates for the ventral and dorsal pathways processing meaning and phonemes, respectively [63,64].

Vassal et al. [65], 2010 present evidence for paradoxical crossed language dominance in the hemisphere ipsilateral to hand dominance. They report on three right-handed patients in whom intraoperative cortical stimulation elicited transient speech arrest, known as crossed aphasia. These areas included both cortical regions, such as the inferior frontal gyrus and posterior aspect of the superior temporal gyrus, as well as subcortical regions corresponding to the well-known language-transmitting white matter tracts. Stimulation in the right hemispheric areas corresponding to Broca's and Wernicke's areas (IFG and pSTG) resulted in anomic aphasia. Stimulation in regions corresponding to IFOF (roof of the left ventricular temporal horn) and AF (superoposterior to IFOF) in these patients with crossed language dominance also resulted in similar speech disturbances. This suggests that in right-handed individuals with crossed right hemispheric language dominance, the language network is organized in mirror fashion to the well-described left hemispheric network.

Conclusion

Isolated aphasia can be the sole manifestation of seizure activity and it is critical for clinicians to recognize this. EEG should be performed in all patients with aphasia in whom a standard work-up fails to reveal the diagnosis.Diagnosis is made with concordant EEG findings and improvement/resolution of aphasia with antiepileptic therapy. Cases of isolated ictal aphasia in conjunction with more specific intraoperative cortical stimulation studies also provide us with powerful insights and understanding into cortical and subcortical and atypical variation of language network organization. This helps from a diagnostic perspective, in correlating symptomatology with corresponding EEG, fMRI, PET, and SPECT abnormalities, as well as for therapeutic planning, in cases of perisylvian and insular tumor resections where language centers must be preserved.

Conflicts of Interest

The authors have no conflicts of interest to disclose.

References

1. De Pasquet EG, Gaudin ES, Bianchi A, De Mendilaharsu SA. Prolonged and monosymptomatic dysphasic status epilepticus. Neurology. 1976 Mar;26(3):244-247.
2. Hamilton NG, Matthews T. Aphasia: the sole manifestation of focal status epilepticus. Neurology. 1979 May;29(5):745-748.
3. Dinner DS, Lueders H, Lederman R, Gretter TE. Aphasic status epilepticus: a case report. Neurology. Neurology. 1981 Jul;31(7):888-891.
4. Rosebaum DH, Siegel M, Barr WB, Rowan AJ. Epileptic aphasia. Neurology. 1986 Jun;36(6):822-825.
5. Primavera A, Bo GP, Venturi S. Aphasic status epilepticus. Eur Neurol. 1988;28(5):255-257.
6. Wells CR, Labar DR, Solomon GE. Aphasia as the sole manifestation of simple partial status epilepticus. Epilepsia. 1992 Jan-Feb;33(1):84-87.
7. Herskovitz M, Schiller Y. Prolonged ictal aphasia: a diagnosis to consider. J Clin Neurosci. 2012 Nov;19(11):1605-1606.
8. Commondoor R, Eisenhut M, Fowler C, Kirollos RW, Nathwani N. Transient Broca's aphasia as feature of an extradural abscess. Pediatr Neurol. 2009 Jan;40(1):50-53.
9. De Toledo JC, Minagar A, Lowe MR. Persisting aphasia as the sole manifestation of partial status epilepticus. Clin Neurol Neurosurg. 2000 Sep;102(3):144-148.
10. Flügel D, Kim OC, Felbecker A, Tettenborn B. De novo status epilepticus with isolated aphasia. Epilepsy Behav. 2015 Aug;49:198-202.
11. Huang LC, Ruge D, Tsai CL, Wu MN, Hsu CY, et al. Isolated aphasic status epilepticus as initial presentation of nonketotic hyperglycemia. Clin EEG Neurosci. 2014 Apr;45(2):126-128.
12. Kaplan PW, Stagg R. Frontal lobe nonconvulsive status epilepticus: a case of epileptic stuttering, aphemia, and aphasia--not a sign of psychogenic nonepileptic seizures. Epilepsy Behav. 2011 Jun;21(2):191-195.
13. Kirshner HS, Hughes T, Fakhoury T, Abou-Khalil B. Aphasia secondary to partial status epilepticus of the basal temporal language area. Neurology. 1995 Aug;45(8):1616-1618.
14. López Ruiz R, Quintas S, Largo P, de Toledo M, Carreras MT, et al. Usefulness of multiparametric computerized tomography findings in the differential diagnosis of stroke mimics of epileptic origin: A preliminary study. Neurologia. 2019 Mar;34(2):73-79.

15. Patil B, Oware A. De-novo simple partial status epilepticus presenting as Wernicke's aphasia. Seizure. 2012 Apr;21(3):219-222.

16. Racy A, Osborn MA, Vern BA, Molinari GF. Epileptic aphasia. First onset of prolonged monosymptomatic status epilepticus in adults. Arch Neurol. 1980 Jul;37(7):419-422.

17. Riecker A, Gerloff C, Wildgruber D, Nägele T, Grodd W, et al. Transient crossed aphasia during focal right-hemisphere seizure. Neurology. 2004 Nov 23;63(10):1932.

18. Sadiq SB, Hussain SA, Norton JW. Ictal aphasia: an unusual presentation of temporal lobe seizures. Epilepsy Behav. 2012 Apr;23(4):500-502.

19. Shah NH, Adams D. Episodic Aphasia Associated With Cortical Spreading Depression After Subdural Hemorrhage Evacuation. Neurohospitalist. 2016 Jan;6(1):NP1-4.

20. Sperli F, Placidi F, Izzi F, Marciani MG, Floris R, et al. ICTAL aphasia as manifestation of partial status epilepticus in a long-lasting misdiagnosed symptomatic epilepsy: an emblematic case. Int J Neurosci. 2009;119(4):531-537.

21. Wells CR, Labar DR, Solomon GE. Aphasia as the sole manifestation of simple partial status epilepticus. Epilepsia 1992;33:84–87.

22. Sakai K, Hidari M, Fukai M, Okamura T, Asaba H, et al. A chance SPECT study of ictal aphasia during simple partial seizures. Epilepsia. 1997 Mar;38(3):374-376.

23. Privitera M, Kim KK. Postictal language function. Epilepsy Behav. 2010 Oct;19(2):140-145.

24. Kanemoto K, Janz D. The temporal sequence of aura-sensations in patients with complex focal seizures with particular attention to ictal aphasia. J Neurol Neurosurg Psychiatry. 1989 Jan;52(1):52-56.

25. Grimes DA, Guberman A. De novo aphasic status epilepticus. Epilepsia. 1997 Aug;38(8):945-949.

26. Deonna TW, Roulet E, Fontan D, Marcoz JP. Speech and oromotor deficits of epileptic origin in benign partial epilepsy of childhood with rolandic spikes (BPERS). Relationship to the acquired aphasia-epilepsy syndrome. Neuropediatrics. 1993 Apr;24(2):83-87.

27. Kaplan PW. Behavioral manifestations of nonconvulsive status epilepticus. Epilepsy Behav. 2002 Apr;3(2):122-139.

28. Kaplan PW. Nonconvulsive status epilepticus. Semin Neurol 1996;16(1):33-40.

29. Thomas P, Beaumanoir A, Genton P, Dolisi C, Chatel M. "De novo" absence status: report of 11 cases. Neurology. 1992 Jan;42(1):104-110.

30. Rösche J, Schley A, Schwesinger A, Grossmann A, Mach H, et al. Recurrent aphasic status epilepticus after prolonged generalized tonic–clonic seizures versus a special feature of Todd's paralysis. Epilepsy & Behavior 2011;20:132–137.

31. Luders H, Lesser RP, Dinner DS, Morris HH, Wyllie E, et al. Localization of cortical functions: new information from extraoperative monitoring of patients with epilepsy. Epilepsia. 1988;29 Suppl 2:S56-S65.

32. Scholtes FB, Renier WO, Meinardi H. Simple partial status epilepticus: causes, treatment and outcome in 47 patients. J Neurol Neurosurg Psychiatry. 1996 Jul;61(1):90-92.

33. Chung PW, Seo DW, Kwon JC, Kim H, et al. Nonconvulsive status epilepticus presenting as a subacute progressive aphasia. Seizure. 2002 Oct;11(7):449-454.

34. Ojemann G. Localization of language in frontal cortex. In: Chavel P, Delgado-Escueta AG, Halgren E, Bancaud J, editors. Frontal Lobe Seizures and Epilepsies. Adv Neurol. New York(NY): Raven Press;1992,P.361–368.

35. Hecaen H, Maxurs G, Ramier A, et al. Aphasiecroisse chez un sujetdroitierbilingue. Rev Neurol 1971;1:319–23.

36. Albert ML, Goodglass H, Helm NA, Rubens AB, et al. In: Arnold GE, Winckel F, Wyke BD, editors. Clinical Aspects of Dysphasia. New York (NY):Springer-Verlag;1981:121–122.

37. Leao AA. Further observations on the spreading depression of activity in the cerebral cortex. J Neurophysiol. 1947 Nov;10(6):409-414.

38. Ayata C. Spreading depression and neurovascular coupling. Stroke. 2013 Jun; 44(6 suppl 1):S87-S89.

39. Costa C, Tozzi A, Rainero I, et al. Cortical spreading depression as a target for anti-migraine agents. J Headache Pain. 2013 Jul;14:62.

40. Akerman S, Goadsby PJ. Topiramate inhibits cortical spreading depression in rat and cat: impact in migraine aura. Neuroreport. 2005 Aug;16(12):1383-1387.

41. Unekawa M, Tomita Y, Toriumi H, Suzuki N. Suppressive effect of chronic peroraltopiramate on potassium-induced cortical spreading depression in rats. Cephalalgia. 2012 May;32(7): 518-527.

42. Van der Hel WS, van den Bergh WM, Nicolay K, Tulleken KA, Dijkhuizen RM. Suppression of cortical spreading depressions after magnesium treatment in the rat. Neuroreport. 1998 Jul;9(10): 2179-2182.

43. Tepe N, Filiz A, Dilekoz E, Akcali D, Sara Y, et al. The thalamic reticular nucleus is activated by cortical spreading depression in freely moving rats: prevention by acute valproate administration. Eur JNeurosci. 2015 Jan;41(1):120-128.

44. Al-Qahtani M, Khan SA, Kabiraj M, Khoja WA. Non-convulsive status epilepticus presenting with Wernicke's aphasia. Neurosciences (Riyadh). 2009 Jul;14(3):284-286.

45. Schwechter EM, Veliskova J, Velisek L. Correlation between extracellular glucose and seizure susceptibility in adult rats. Ann Neurol. 2003 Jan;53:91-101.

46. Primavera A, Gianelli MV, Bandini F. Aphasic status epilepticus in multiple sclerosis. EurNeurol . 1996;36(6):374–377.

47. Kwon J, Choi JY, Bae EK. Cefepime-induced aphasic status epilepticus mimicking acute stroke. J Epilepsy Res. 2014 Dec;4(2):85–87.

48. Ozkaya G, Kurne A, Unal S, Oğuz KK, Karabudak R, et al. Aphasic status epilepticus with periodic lateralized epileptiform discharges in a bilingual patient as a presenting sign of"AIDS–toxoplasmosis complex". Epilepsy Behav. 2006 Aug;9(1):193-196.

49. Ericson EJ, Gerard EE, Macken MP, Schuele SU. Aphasic status epilepticus: electroclinical correlation. Epilepsia. 2011 Aug;52(8):1452–1458.

50. Hirsch LJ, Emerson RG, Pedley TA. Prolonged postictal aphasia: demonstration of persistent ictal activity with intracranial electrodes. Neurology. 2001 Jan;9(56(1)):134–136.

51. Dong C, Sriram S, Delbeke D, Al-Kaylani M, Arain AM, et al. Aphasic or amnesic status epilepticus detected on PET but not EEG. Epilepsia. 2009 Feb;50(2):251–255.

52. Wieshmann UC, Symms MR, Shorvon SD. Diffusion changes in status epilepticus. Lancet. 1997 Aug;350(9076):493–494.

53. Lansberg MG, O'Brien MW, Norbash AM, Moseley ME, Morrell M, et al. MRI abnormalities associated with partial status epilepticus. Neurology. 1999 Mar23;52(5):1021–1027.

54. Szabo K, Poepel A, Pohlmann-Eden B, Hirsch J, Back T, et al. Diffusion-weighted and perfusion MRI demonstrates parenchymal changes in complex partial status epilepticus. Brain. 2005 Jun;128(6):1369–1376.

55. Cianfoni A, Caulo M, Cerase A, Della Marca G, Falcone C, et al. Seizure-induced brain lesions: a wide spectrum of variably reversible MRI abnormalities. Eur J Radiol. 2013 Nov;82(11):1964–1972.

56. Toledo M, Munuera J, Sueiras M, Rovira R, Alvarez-Sabín J, et al. MRI findings in aphasic status epilepticus. Epilepsia. 2008 Aug;49(8):1465–1469.

57. Alexander MP, Annett M: Crossed aphasia and related anomalies of cerebral organization: case reports and a genetic hypothesis. Brain Lang. 1996 Nov;55(2):213–239.
58. Penfield W, Rasmussen T. Vocalization and arrest of speech. Arch Neurol Psychiatry. 1949 Jan;61(1):21-27.
59. Geschwind N. Specializations of the human brain. Sci Am. 1979 Sep;241(3):180-199.
60. Petersen SE, Fox PT, Posner MI, Mintun M, Raichle ME. Positron emission tomographic studies of the cortical anatomy of single-word processing. Nature. 1988 Feb 18;331(6157):585-589.
61. Petersen SE, Fiez JA. The processing of single words studied with positron emission tomography. Annu Rev Neurosci 199316:509-530.
62. Duffau H, Gatignol P, Mandonnet E, Peruzzi P, Tzourio-Mazoyer N, et al. New insights into the anatomo-functional connectivity of the semantic system: a study using cortico-subcortical electrostimulations. Brain. 2005 Apr;128(Pt 4):797–810.
63. Duffau H, Capelle L, Sichez N, Denvil D, Lopes M, et al. Intraoperative mapping of the subcortical language pathways using direct stimulations. An anatomo-functional study. Brain. 2002 Jan;125(Pt 1):199-214.
64. Duffau H, Peggy Gatignol ST, Mandonnet E, Capelle L, Taillandier L. Intraoperative subcortical stimulation mapping of language pathways in a consecutive series of 115 patients with Grade II glioma in the left dominant hemisphere. J Neurosurg. 2008 Sep;109(3):461-471.
65. Vassal M, Le Bars E, Moritz-Gasser S, Menjot N, Duffau H. Crossed aphasia elicited by intraoperative cortical and subcortical stimulation in awake patients. J Neurosurg. 2010 Dec;113(6):1251-1258.