# Broca's Region

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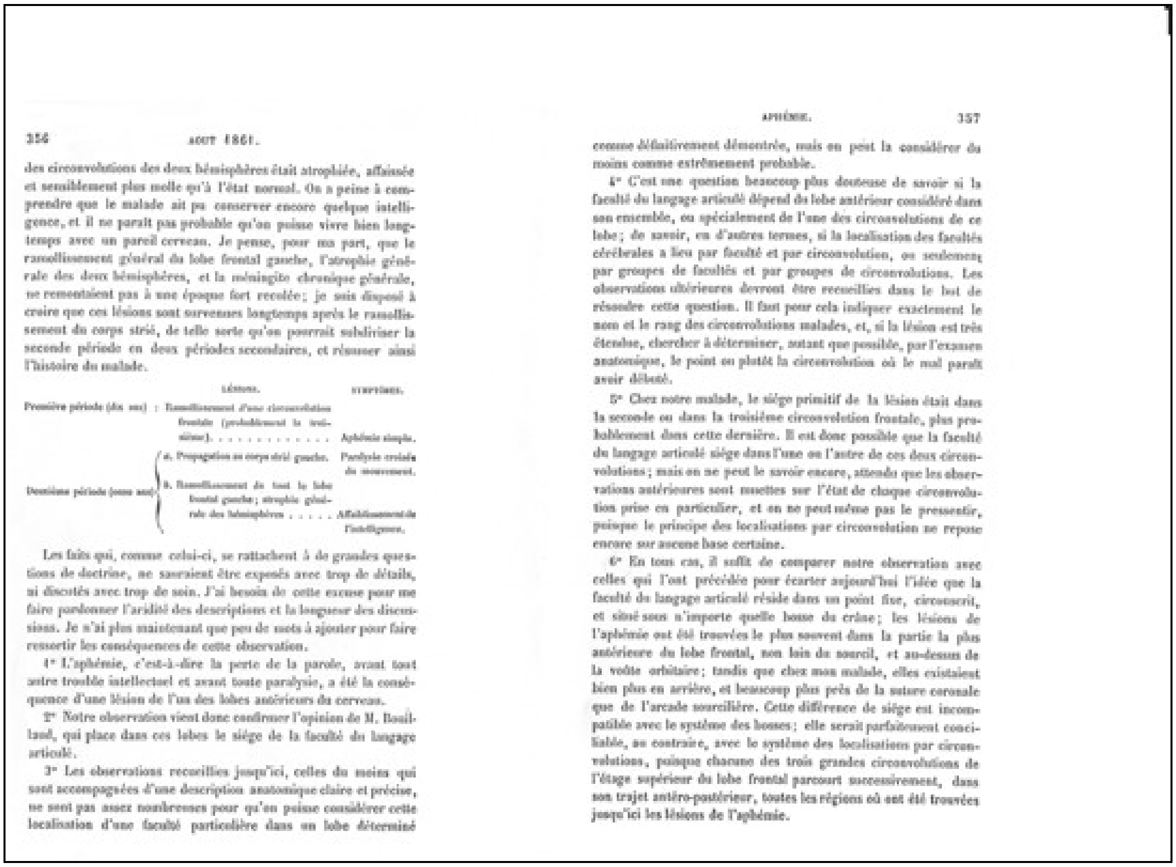
Broca's region was the first brain region to which a circumscribed function, i.e. language, was linked. Its discovery can be interpreted as the beginning of the scientific theory of the localization of cortical functions. The term originates from anatomo-clinical observations of patients with brain lesions and subsequent disturbances of articulated language, carried out by Pierre Paul Broca (1824-1880) in the middle of the 19th century (Broca, 1861a, b; 1863; 1865, Figure 1). A few years after Broca's first studies, Wernicke (1848-1904) proposed the first theory of language, which postulated an anterior, motor speech centre (Broca's region), a posterior, semantic language centre (Wernicke's region), as well as a fibre tract, the arcuate fasciculus, connecting both regions (Wernicke, 1874). Some decades later, Brodmann's famous maps (1903a, b; 1906; 1908; 1909; 1910; 1912) proposed that cytoarchitectonically defined cortical areas in the inferior frontal gyrus could be the anatomical correlates of Broca's region.


356 AOUT 1861.

des circonvolutions des deux hémisphères était atrophiée, affaissée et sensiblement plus molle qu'à l'état normal. On a peine à comprendre que le malade ait pu conserver encore quelque intelligence, et il ne paraît pas probable qu'on puisse vivre bien longtemps avec un pareil cerveau. Je pense, pour ma part, que le ramollissement général du lobe frontal gauche, l'atrophie générale des deux hémisphères, et la méningite chronique générale, ne remontaient pas à une époque fort reculée; je suis disposé à croire que ces lésions sont survenues longtemps après le ramollissement du corps strié, de telle sorte qu'on pourrait subdiviser la seconde période en deux périodes secondaires, et résumer ainsi l'histoire du malade.

| | LÉSIONS. | SYMPTÔMES. |
|---|---|---|
| Première période (dix ans) : | Ramollissement d'une circonvolution frontale (probablement la troisième). . . . . . . . . . . . . | Aphémie simple. |
| Deuxième période (onze ans) | a. Propagation au corps strié gauche. | Paralysie croisée du mouvement. |
| | b. Ramollissement de tout le lobe frontal gauche; atrophie générale des hémisphères . . . . . | Affaiblissement de l'intelligence. |

Les faits qui, comme celui-ci, se rattachent à de grandes questions de doctrine, ne sauraient être exposés avec trop de détails, ni discutés avec trop de soin. J'ai besoin de cette excuse pour me faire pardonner l'aridité des descriptions et la longueur des discussions. Je n'ai plus maintenant que peu de mots à ajouter pour faire ressortir les conséquences de cette observation.

1° L'aphémie, c'est-à-dire la perte de la parole, avant tout autre trouble intellectuel et avant toute paralysie, a été la conséquence d'une lésion de l'un des lobes antérieurs du cerveau.

2° Notre observation vient donc confirmer l'opinion de M. Bouillaud, qui place dans ces lobes le siège de la faculté du langage articulé.

3° Les observations recueillies jusqu'ici, celles du moins qui sont accompagnées d'une description anatomique claire et précise, ne sont pas assez nombreuses pour qu'on puisse considérer cette localisation d'une faculté particulière dans un lobe déterminé

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comme définitivement démontrée, mais on peut la considérer du moins comme extrêmement probable.

4° C'est une question beaucoup plus douteuse de savoir si la faculté du langage articulé dépend du lobe antérieur considéré dans son ensemble, ou spécialement de l'une des circonvolutions de ce lobe; de savoir, en d'autres termes, si la localisation des facultés cérébrales a lieu par faculté et par circonvolution, ou seulement par groupes de facultés et par groupes de circonvolutions. Les observations ultérieures devront être recueillies dans le but de résoudre cette question. Il faut pour cela indiquer exactement le nom et le rang des circonvolutions malades, et, si la lésion est très étendue, chercher à déterminer, autant que possible, par l'examen anatomique, le point ou plutôt la circonvolution où le mal paraît avoir débuté.

5° Chez notre malade, le siège primitif de la lésion était dans la seconde ou dans la troisième circonvolution frontale, plus probablement dans cette dernière. Il est donc possible que la faculté du langage articulé siège dans l'une ou l'autre de ces deux circonvolutions; mais on ne peut le savoir encore, attendu que les observations antérieures sont muettes sur l'état de chaque circonvolution prise en particulier, et on ne peut même pas le pressentir, puisque le principe des localisations par circonvolution ne repose encore sur aucune base certaine.

6° En tous cas, il suffit de comparer notre observation avec celles qui l'ont précédée pour écarter aujourd'hui l'idée que la faculté du langage articulé réside dans un point fixe, circonscrit, et situé sous n'importe quelle bosse du crâne; les lésions de l'aphémie ont été trouvées le plus souvent dans la partie la plus antérieure du lobe frontal, non loin du sourcil, et au-dessus de la voûte orbitaire; tandis que chez mon malade, elles existaient bien plus en arrière, et beaucoup plus près de la suture coronale que de l'arcade sourcilière. Cette différence de siège est incompatible avec le système des bosses; elle serait parfaitement conciliable, au contraire, avec le système des localisations par circonvolutions, puisque chacune des trois grandes circonvolutions de l'étage supérieur du lobe frontal parcourt successivement, dans son trajet antéro-postérieur, toutes les régions où ont été trouvées jusqu'ici les lésions de l'aphémie.

**Figure 1:** Part of the original publication of Paul Broca, 1861 (M. P. Broca. Remarques sur le siège de la faculté du langage articulé, suivies d'une observation d'aphémie, Perte de la Parole. *Bulletins et mémoires de la Société Anatomique de Paris* 36:330-357, 1861) in which he reported that the region is located in the posterior third of the left frontal convolution.

It can therefore be concluded that the anatomical variability of this regions is twofold: it includes the variability in the location, presence and shape of sulci, and the relationship of the architectonic borders to these sulci. A "simple" anatomical definition of Broca's region is, therefore, not possible.

However, when looking at these cortical areas in more detail, they cannot be unambiguously defined with respect to different cytoarchitectonic (microstructural) observations. Whereas some authors agreed that the cytoarchitectonic correlates of Broca's region comprise Brodmann's (Brodmann, 1909) areas (BA) 44 and 45 (Kononova, 1949; Aboitiz and Garcia, 1997; Amunts et al., 1999; Lieberman, 2002), other authors used this term either for BA 45 (Hayes and Lewis, 1992), or for area 44 only (Galaburda, 1980), or they even identified the frontal areas BA 44, 45 and 47 as Broca's region (Riegele, 1931). For an overview of the different meanings of the term "Broca's region" see Uylings et al. (1999). Finally, a Broca region in the "strict sense" was distinguished from a region in a "broader sense" (Hervé, 1888; Riegele, 1931; Strasburger, 1938).

Where does this rather confusing situation come from and, even more importantly, what is the appropriate usage of the term "Broca's region"? In this context, the following points seem to be important:

1. The historical definition of Broca's region: how did Broca define "Broca's region"?
2. The anatomy of Broca's region: what is known about its micro- and macrostructure?
3. The function of Broca's region: in which brain functions (speech or non-speech related) is Broca's region involved, both in normal subjects and in patients?
4. Structural–functional analysis in the same spatial reference system.

## Paul Broca and Tan's famous brain lesion

The concept of Broca's region was introduced after Pierre Paul Broca had published two papers claiming the existence of a centre for articulated speech on the basis of an anatomo-clinical observation (1861a, b). The papers described the brain of a neurological patient, Leborgne, who was transferred to the "Hôpital Bicêtre" because of a phlegmon. Leborgne had lost speech, and could no longer pronounce more than a single syllable, "tan" (for that reason, he became famous as "Monsieur Tan"). In addition to his inability to speak, he had a paralysis of the right side. He seemed to be normal in all other aspects.

Before Broca met Leborgne, he had participated in several meetings of the "Société d'Anthropologie" in Paris, where a great debate between Ernest Aubertin (1825-1893) and Pierre Gratiolet (1815-1865) took place about the sense or nonsense of a language centre in the frontal lobe. Whereas Gratiolet was convinced that the brain works as a whole, Auburtin declared that he would renounce the idea of cerebral localization if a single case could be demonstrated in which the loss of the faculty of articulate language is found without a lesion in the anterior lobes. Broca knew that an anatomo-clinical correlation would be possible if a patient's brain could be studied and that this correlation would solve the dispute. He therefore asked Aubertin to confirm that Leborgne had lost articulated speech (Stookey, 1954). Tan died a few days later on April 17, 1861. Broca performed the autopsy, and found a lesion at the predicted location in the inferior frontal lobe. He concluded that the location of the centre for articulate language ("faculté de langage articulé") was the third frontal convolution of the left hemisphere. Just one day after the autopsy, Leborgne's case was briefly presented by Broca before the Anthropological Society in Paris (Broca, 1861a). Four months later, he described it in more detail (Broca, 1861b).

It has to be noted, however, that the lesion of Leborgne's brain was huge (Figure 2). In addition to the involvement of the anterior speech region, Broca observed that the brain of Leborgne showed more posterior lesions, but he interpreted these lesions as occurring after the onset of Leborgne's aphasia and not being relevant for his speech disturbances. As shown by post mortem functional imaging of Leborgne's brain, large parts of the subcortical white matter, as well as parts of the middle frontal convolution, the insula and the temporal pole of the left hemisphere, were lesioned. The lesion even reached the parietal lobe (Signoret et al., 1984). During the following years, Leborgne's brain was supplemented by other brains of patients, e.g. that of Lelong, which lost speech after a more focused brain lesion (Broca, 1863).

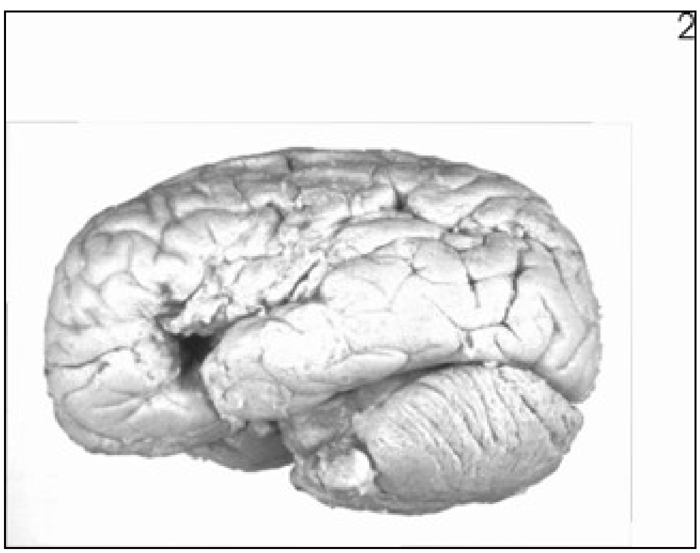


**Figure 2:** Photograph of the lateral view of the brain of Leborgne, the patient for which Broca introduced the concept of the motor speech region. This speech region was called Broca's area (or region) and the syndrome that results from its damage was called Broca's aphasia.

Broca's publication was not the first that suggested a language centre in the left frontal lobe, and he was not the first to hypothesize left hemispheric dominance. Several studies had been published since the early 18th century, which reported loss of language in patients after brain lesion. Earlier evidence on the localization of language was provided, e.g. by Franz Josef Gall (1758-1828) and Jean Baptiste Bouillaud (1796-1881), who was Aubertin's father-in-law. Marc Dax (1770-1837), e.g., suggested as early as 1836, that disorders of speech were constantly associated with a lesion of the left hemisphere, thus introducing the principle of cerebral dominance. For the historical background, see Stookey (1954), Deneke (1985), Kolb and Whishaw (1996), Finger (1994; 1996), and Greenblatt (1995). Broca's paper of 1865 has been translated into English (1986). The same is true for some other papers (see Green's translation at http://psychclassics.yorku.ca/Broca). Broca acknowledged these earlier contributions. He was, however, the person who focused not on language in general, but on a particular aspect of language, i.e. articulate language, and he enabled the breakthrough of the theory of localization of function and of clinical descriptions of brain-damage effects (Kolb and Whishaw, 1996). Broca never processed this or one of the following brains of patients with brain lesions and loss of speech for histological analysis. Thus, he did not make any conclusions concerning the cortical microstructure of the lesioned region. This is not surprising considering that one of the very first papers describing regional differences in the microstructure, i.e. the cytoarchitecture, in the central region of the brain was published by Vladimir Betz only in 1874 (Betz, 1874). Brodmann's famous map showing the microstructural, cytoarchitectonic parcellation of the human cerebral cortex as well as several other cortical maps were published 40 years later (Campbell, 1905; Elliot Smith, 1907; Brodmann, 1909). Thus, Broca's observations were based on macroscopical and clinical observations, but they did not contain references to microscopically defined cortical areas.

The brain of Broca's patient was deposited in the Dupuytren Museum, Paris. It was re-evaluated macroscopically, e.g. by Pierre Marie Pierre (1906), Schiller (1979), Castaigne (1979) and Signoret et al. (1984). It has not been processed histologically.

### Macroscopy and microstructure of Broca's region

Is it possible to identify the underlying cortical areas exclusively on the basis of the macroscopical descriptions of Broca? When referring to Brodmann's map (1909, Figure 3), it seems that areas 44 and 45, which occupy the posterior portion of the inferior frontal gyrus (opercular and triangular parts), are good candidates for being the microstructural correlates of Broca's region. It is not clear, however, whether the most ventral part of BA 6 is also part of Broca's region, nor can it be excluded, that parts of the cortex hidden in the depths of the Sylvian fissure or the orbital part of the inferior frontal gyrus (BA 47) also belong to Broca's region. Brodmann himself as well as the authors of other classical cortical maps, e.g. von Economo and Koskinas (1925), Sarkissov et al. (1949), and the Vogts (Vogt and Vogt, 1919) did not mention the term "Broca's region", and thus did not define this region with respect to their microstructural parcellation of the cortex.

**Figure 3:** Cytoarchitectonic maps of the lateral surface of a human brain adapted from Brodmann (1909). Cytoarchitectonic areas are marked by different hatches and classified according to Brodmann's nomenclature by Arabic numerals. The approximated location of Broca's region in the posterior part of the inferior frontal gyrus is marked.

A reference to Brodmann's schematic drawing (1909) or any other classical cortical map, however, does not take into account the intersubject variability in the gyri and sulci of the frontal lobe, such as between the brains studied by Brodmann and Broca. This variability includes the presence or absence of sulci, the shape of sulci and gyri and their size (Ono et al., 1990; Duvernoy, 1991). E.g., the opercular part of the inferior frontal gyrus may consist of two small convolutions, whereas in other brains only one is present. Additionally, one of the two convolutions may lie on the surface of the brain, whereas the other may be hidden in the depth of the inferior precentral sulcus (Tomaiuolo et al., 1999). The same is true for the sulci, e.g. the vertical branch of the Sylvian fissure and the diagonal sulcus, which may differ in shape, or may even be absent. Data on the presence of the diagonal sulcus, e.g., vary between 12.5% in the right hemispheres (Geschwind and Levitsky, 1968) to 72% in the left hemispheres (Ono et al., 1990). Our own studies showed that this sulcus was present in half of the 20 observed hemispheres (Amunts et al., 1999). Thus, there is considerable intersubject variability in the macroscopical anatomy of the inferior frontal lobe, which makes a sulcus-based definition of Broca's region problematic, to say the least.

Furthermore, intersubject variability of the anatomy of Broca's region also includes the location of the borders of cortical areas with respect to the surrounding sulci. The border between BA 44 and BA 6 is an example for this type of intersubject variability. The analysis of ten human postmortem brains showed that the location of the border between BA 44 and BA 6 varied between the rostral and caudal walls of the precentral sulcus. It differed therefore with respect to the fundus of the sulcus by approximately 1-2 cm (Amunts et al., 1999). The ventro-rostral border of BA 45 was, in most of these brains, located dorsally from the fundus of the horizontal branch of the lateral fissure and its continuation. In four (of 20) hemispheres, however, the border was found on the ventral wall of the horizontal branch. In these cases, BA 45 extended onto the orbital surface of the inferior frontal gyrus. Sometimes, the border between BA 44 and 45 was located in the surrounding of the ascending branch of the lateral fissure in some hemispheres, but in others was close to the diagonal sulcus, or interposed between both sulci. Finally, the location of the cytoarchitectonic borders with respect to the sulci also differed between the two hemispheres of a single brain (Figure 4).

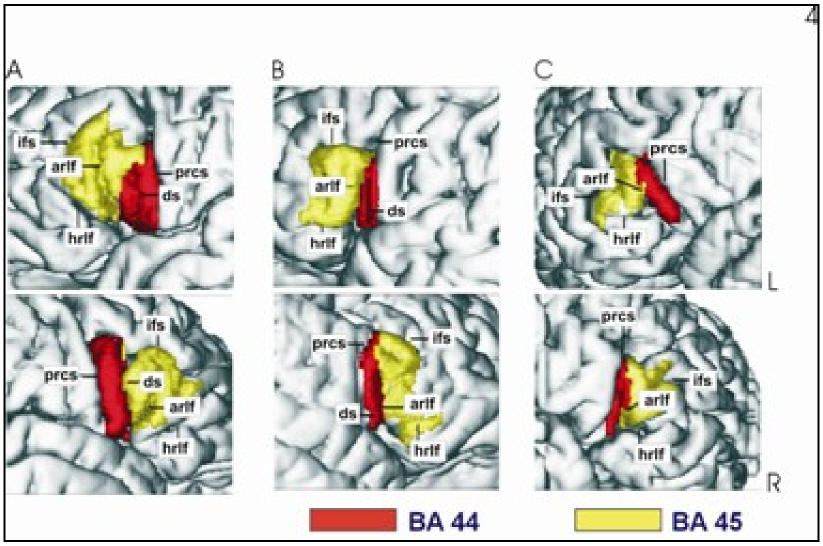


**Figure 4:** Lateral views of 3D reconstructions (surface rendering) of three individual postmortem brains (A-C) with BA 44 (red) and 45 (yellow) of the left (L) and the right (R) hemispheres after cutting of the brain into histological sections, staining for cell bodies, and observer-independent definition of cytoarchitectonic borders on serial histological sections (Amunts et al., 1999). arlf – ascending branch of the lateral fissure, ds – diagonal sulcus, hrlf – horizontal branch of the lateral fissure, ifs – inferior frontal sulcus, prcs – precentral sulcus. Note the high intersubject variability with respect to (i) differences in shape and size of both areas, (ii) variability in the sulcal pattern, and (iii) in the relationship of areal borders to surrounding sulci. E.g., whereas the diagonal sulcus marks the border between BA 44 and BA 45 in the right hemisphere of brain B, this sulcus is inside BA 44 in the left hemisphere of brain A, and is absent in brain C.

The first approach was introduced by Broca, who studied behavioural deficits of aphasic patients after frontal lobe lesions. The second approach became available only during the last decades, and allowed the functional analysis of Broca’s region in healthy subjects as well. Both approaches of studies have significantly improved our understanding of language in general, and the contribution of Broca’s region in particular. They also have added complexity: it has been shown that infarcts affecting Broca’s region and its immediate surrounding may cause mutism, which can be followed by a rapidly improving dyspraxic and effortful articulation, and, finally, no persisting significant alteration of language function. On the other hand, the more complex syndrome traditionally referred to as Broca’s aphasia, including Broca’s original case, is characterized by protracted mutism, verbal stereotypes, and agrammatism. It is associated with a considerably larger infarct that encompasses the operculum, insula and adjacent cortex (Mohr et al., 1978). It has also been reported that articulatory speech disorders may be related not to Broca’s region, but to the insula (Dronkers, 1996). Finally, whereas the focus of the first reports on functional deficits in Broca’s aphasics was on articulation, it is now shifted to more specific deficits, e.g. in comprehension and application of grammatical rules (Grodzinsky, 2000). Disadvantages of the anatomo-clinical approach for studying language-related cortical regions are the considerable variability in lesion size, side and development, as well as brain plasticity.

The application of functional imaging to the analysis of language in healthy subjects has opened new ways in cognitive science. Models have been developed which provide a more detailed picture of the components of language and relate these components to a more distributed network instead of one or two language centres. For reviews see, e.g., Friederici (1997), Brown & Hagoort (1999), Gazzaniga (2000), Grodzinsky (2000), Marantz et al. (2000), Price (2000) and Bookheimer (2002). Language studies are based on a variety of different concepts. Whereas some studies analyse language in perceptual or motor terms, e.g. fluency, reading, rhyming (Zatorre et al., 1992; Price et al., 1994; Paulesu et al., 1997; Gurd et al., 2002), others focus on language as governed by special rules (Zurif et al., 1993; Friederici and Mecklinger, 1995; Heim et al., 2002; Ben-Shachar et al., 2003; Meyer et al., 2003). A third focus comes from comparative neuroscience and brain evolution, e.g. the mirror neuron hypothesis (Rizzolatti and Arbib, 1998), or the hypothesis of Aboitiz and Garcia (1997). These different approaches are not mutually exclusive, but rather seem to be complementary. Consequently, the question of the function of Broca's region may lead to different answers.

**Structural–functional relationship of Broca's region**

The analysis of both brain lesions and functional activations during language tasks depends on the precision of the localization of lesion sites or activated cortical areas. It has been shown, that neurones with similar receptive fields and response properties lie within the same cytoarchitectonic area. Response properties of neurones change across cytoarchitectonic borders (Tanji and Kurata, 1989; Matelli et al., 1991; Luppino et al., 1991). Considering these data as well as the considerable intersubject variability in the macrostructure of the brain, it follows that cortical areas, not sulci and gyri, represent the anatomical correlates of brain function.

The anatomical interpretation of functional activations is often based on the stereotaxic atlas of Talairach and Tournoux (1988). Talairach and Tournoux used Brodmann's schematic surface drawing of an architectonic map (Brodmann, 1909) as the basis for the architectonic parcellation in their atlas. They simply transferred Brodmann's areas to their own atlas brain by trying to identify corresponding sulcal patterns in both brains, assuming a strong association between the sulcal pattern and the borders of cortical areas. Such an association, however, was already doubted by Brodmann (1908), and does not exist for Broca's region, in particular (see above).

Therefore, three-dimensional, cytoarchitectonic probability maps of Brodmann's areas 44 and 45 (Amunts et al., 1999) have been applied for the structural-functional analysis of language (Indefrey et al., 2001; Horwitz et al., 2003; Amunts et al., 2002), motor imagery (Binkofski et al., 2000) and attention (Herath et al., 2001). Probability maps are based on the observer-independent definition of the cortical borders (Schleicher et al., 1999; Zilles et al., 2002) of BA 44 and 45 in cell body stained sections of ten human brains, subsequent 3D-reconstruction and alignment of the postmortem brains and their cytoarchitectonically defined areas to a standard reference brain. The superimposition of the cortical areas within one reference brain enabled determination of overlap of each individual cortical areas in each voxel of the reference brain, i.e. to quantify intersubject variability in size and location of the cytoarchitectonic areas.

These maps were also applied in an fMRI study, in which we enquired whether and to which extent both areas 44 and 45 of the left hemisphere are involved in a verbal fluency task in healthy volunteers. The experiment was motivated by the original definition of Broca's aphasics, that is, the presence of disturbances in fluency, thus attributing fluency to Broca's region in healthy human subjects as well. This hypothesis, however, has never been rigorously tested. Therefore, verbal fluency was investigated in 11 healthy volunteers, who were asked covertly to produce words (Gurd et al., 2002; Amunts et al., 2002). A factorial design was used which contrasted semantic categories against overlearned fluency. These data were compared with probabilistic cytoarchitectonic maps of BA 44 and 45 (Amunts et al., 1999). Both in vivo and postmortem MR data as well as the cytoarchitectonic maps were warped to a common reference brain using a new elastic warping tool. The superimposition of activations during the fluency task and the maps of BA 44 and 45 showed the involvement of left BA 44 and 45 when verbal fluency was compared with rest (Figure 5).

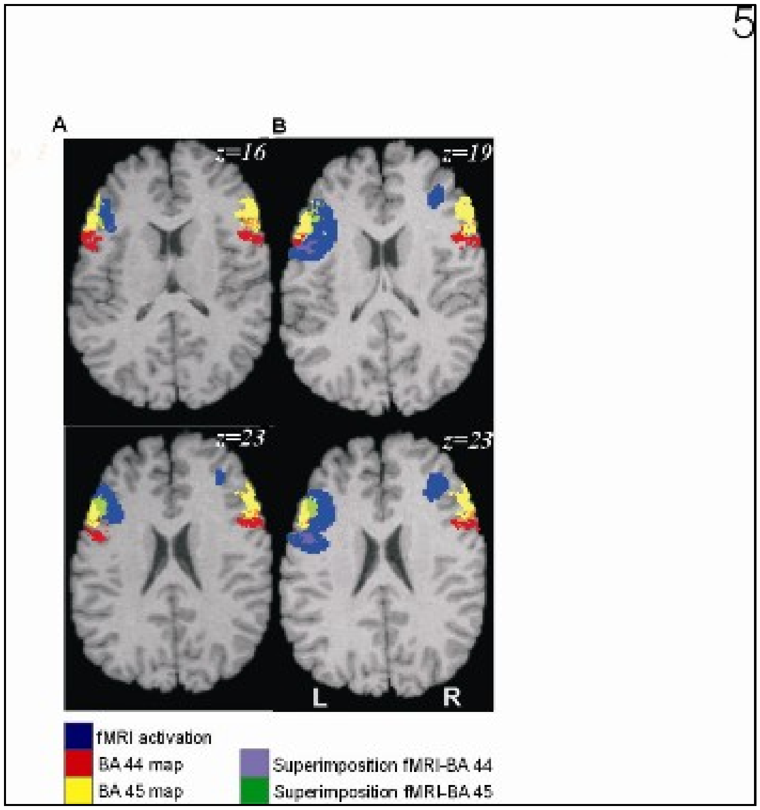


**Figure 5:** Superimposition (violet and green) of cytoarchitectonically defined BA 44 (red) and 45 (yellow) with relative differential increases in neural activity during a verbal fluency task (Gurd et al., 2002) for 11 subjects (blue) as shown on representations of the standard reference brain in stereotactic space (Roland and Zilles, 1994). A: semantic vs. over-learned fluency, B: all conditions vs. rest. The local maxima of the areas of significant relative increase ($p<0.05$, corrected for multiple comparisons) in neural activity were superimposed on horizontal sections of the standard reference brain. R – right, L – left hemisphere. The cytoarchitectonic maps of BA 44 and 45 (Amunts et al., 1999) were obtained by (i) superimposing the individual cytoarchitectonic maps in the format of the reference brain, and (ii) selecting only those voxels, which were present in 4 or more out of 10 brains of each area. Orange pixels mark the overlap between the maps of BA 44 and BA 45, i.e. show those regions, in which both BA 44 and BA 45 were found with a probability of 40% and more. Note, that if semantic fluency was compared with over-learned fluency (A), left BA 45 was activated, whereas the comparison of all conditions versus low level baseline activated both BA 44 and 45 (B).

The comparison of semantic with overlearned fluency showed the participation of left BA 45, but not 44. In conclusion, although both areas participate in verbal fluency, they do so in different ways. Left BA 45 seems to be more involved in semantic aspects of language processing than BA 44, while the latter is probably involved in high-level aspects of programming speech production per se (Amunts et al., 2002).

The combination of cytoarchitectonic probabilistic maps and functional activations increases the precision of the topographical interpretation of fMRI data as well as of lesion data. This precision is necessary since neurolinguistic and neuropsychological approaches test more and more specific, detailed aspects of language processing in contrast to the historical concept of language. It may be hypothesized that these detailed aspects of language do not "occupy" a whole cytoarchitectonically defined area, e.g. BA 44 or 45, but parts of them. It may also be hypothesized that several of these aspects share networks within the same cortical region considering the very different tasks that cause an activation of one of these two areas. As compared to the motor, somatosensory, auditory, and visual systems, where function converges with the anatomy of certain cortical areas and fiber tracts, the structural–functional analysis of language seems to be less well established.

In summary, the concept of Broca’s region and its role in language has changed from a centre of language production and articulation to a center which is involved in the processing of syntax, semantics, phonology as well as in non-language related tasks, e.g. motion. Such diversity may suggest a subparcellation of Broca’s region for which evidence has been provided both in functional imaging studies (Zatorre et al., 1996; Friederici, 2002; Koski et al., 2002) and in architectonic observations (Vogt, 1910; Riegele, 1931; Kononova, 1935; Petrides and Pandya, 1994; Amunts et al., 1999). And/or as an alternative, it may suggest that the function of Broca’s region can only be defined on a more abstract level. Finally, it might be the case that the concept of Broca’s region is not yet appropriate, and that Broca’s region represents rather a historical concept, than a functionally and anatomically defined brain region. Anatomical probability maps may help to solve this question.

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**Bibliography**

Aboitiz F and Garcia GL. 1997. The evolutionary origin of language areas in the human brain. A neuroanatomical perspective. *Brain Research Reviews* 25:381-396.

Amunts K, Schleicher A, Bürgel U, Mohlberg H, Uylings HBM, and Zilles K. 1999. Broca's region revisited: Cytoarchitecture and intersubject variability. *J Comp Neurol* 412:319-341.

Amunts K, Weiss PH, Mohlberg H, Pieperhoff P, Gurd J, Marshall JC, Fink GR, and Zilles K. 2002. Analysis of verbal fluency in microstructurally defined stereotactic space: The role of Brodmann's areas 44 and 45. *Neuroimage* 16:176.

Ben-Shachar M, Hendler T, Kahn I, Ben-Bashat D, and Grodzinsky Y. 2003. The neural reality of syntactic transformation: Evidence from fMRI. *Psychol Sci* 14:433-440.

Berker EA, Berker AH, and Smith A. 1986. Translation of Broca's 1865 report. *Arch Neurol* 43:1065-1072.

Betz W. 1874. Anatomischer Nachweis zweier Gehirncentra. *Centralblatt für die medizinischen Wissenschaften* 37/38.

Binkofski F, Amunts K, Stephan KM, Posse S, Schormann T, Freund H-J, Zilles K, and Seitz RJ. 2000. Broca's region subserves imagery of motion: A combined cytoarchitectonic and fMRI study. *Human Brain Mapping* 11:273-285.

Bookheimer SY. 2002. Functional MRI of language: New approaches to understanding the cortical organization of semantic processing. *Ann Rev Neurosci* 25:151-188.

Broca MP. 1861a. Perte de la parole, ramollissement chronique et desstruction partielle du lob antérieur gauche de cerveau. *Bulletins de la Société d'Anthropologie* 62:235-238.

Broca MP. 1861b. Remarques sur le siége de la faculté du langage articulé, suivies d'une observation d'aphemie (Perte de la Parole). *Bulletins et mémoires de la Société Anatomique de Paris* 36:330-357.

Broca MP. 1863. Localisation des fonctions cérébrales. Siège du langage articulé. *Bulletins de la Société d'Anthropologie.* Séance du 2 Avril 1863:200-204.

Broca MP. 1865. Sur la siege de la faculté langage articulé. *Bulletin of the Society of Anthropology* 6:377-396.

Brodmann K. 1903a. Beiträge zur histologischen Lokalisation der Grosshirnrinde. I: Die Regio Rolandica. *Beiträge zur Lokalisation der Grosshirnrinde* II:79-107.

Brodmann K. 1903b. Beiträge zur histologischen Lokalisation der Grosshirnrinde. II: Der Calcarinustyp. *J Psychol Neurol* II:133-159.

Brodmann K. 1906. Beiträge zur histologischen Lokalisation der Großhirnrinde. V: Über den allgemeinen Bauplan des Cortex pallii bei den Mammaliern und zwei homologe Rindenfelder im besonderen. Zugleich ein Beitrag zur Furchenlehre. *J Psychol Neurol* VI:275-303.

Brodmann K. 1908. Beiträge zur histologischen Lokalisation der Großhirnrinde. VI: Die Cortexgliederung des Menschen. *J Psychol Neurol* X:231-246.

Brodmann K. 1909. Vergleichende Lokalisationslehre der Großhirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues. Leipzig: Barth JA.

Brodmann K. 1910. Feinere Anatomie des Großhirns. In Lewandowsky M, editor. *Handbuch der Neurologie.* Berlin: Springer. pp. 206-307.

Brodmann K. 1912. Neue Ergebnisse über die vergleichende histologische Lokalisation der Großhirnrinde mit besonderer Berücksichtigung des Stirnhirns. *Anatomischer Anzeiger*, Ergänzungsheft zum 41. Band: 157-216.

Brown CM and Hagoort P. 1999. *The Neurocognition of Language*. Oxford: Oxford University Press.

Campbell AW. 1905. *Histological Studies on the Localisation of Cerebral Function*. Cambridge: Cambridge University Press.

Castaigne P. 1979. Photographies et tomodensitométrie des deux cerveaux sur lesquels Broca fonda sa conception anatomoclinique de l' "aphémie". *Bull Acad Nat Méd* 163:663-667.

Deneke JFV. 1985. Die Phrenologie als publizistisches Ereignis. Galls Schädellehre in der Tagespublizistik des 19. Jahrhunderts. *Medizinhistorisches Journal* 20:83-108.

Dronkers NF. 1996. A new brain region for coordinating speech articulation. *Nature* 384:159-161.

Duvernoy H. 1991. The *Human Brain: Surface, Three-dimensional Sectional Anatomy and MRI*. Wien, New York: Springer.

Elliot Smith G. 1907. A new topographical survey of the human cerebral cortex, being an account of the distribution of the anatomically distinct cortical areas and their relationship to the cerebral sulci. *J Anat* 41:237-254.

Finger S. 1994. *Origins of Neuroscience: A History of Explorations into Brain Function*. New York, Oxford: Oxford University Press.

Finger S. 1996. Gustave Dax and the early history of cerebral dominance. *Arch Neurol* 53:806-813.

Friederici AD. 1997. Neurophysiological aspects of language processing. *Clin Neurosci* 4:4-72.

Friederici AD. 2002. Neurobiologische Grundlagen der Sprache. In Karnath H-O and Thier P, editors. *Neuropsychologie*. Springer. pp. 367-377.

Friederici AD and Mecklinger A. 1995. Syntactic parsing as revealed by brain response. *J Psycholing Res* 25:157-176.

Galaburda AM. 1980. La region de Broca: Observations anatomiques faites un siecle apres la mort de son decoveur. *Rev Neurol (Paris)* 136:609-616.

Gazzaniga MS. 2000. *Cognitive Neuroscience: A Reader*. Malden, Massachusetts: Blackwell Publishers.

Geschwind N and Levitsky W. 1968. Human brain: left-right asymmetries in temporal speech region. *Science* 130:186-18

Greenblatt SH. 1995. Phrenology in the science and culture of the 19th century. *Neurosurgery* 37:790-805.

Grodzinsky Y. 2000. The neurology of syntax: language use without Broca's area. *Behav Brain Sci* 23:1-71.

Gurd J, Amunts K, Weiss PH, Zafiris O, Zilles K, Marshall JC, and Fink GR. 2002. Posterior parietal cortex is implicated in continous switching between verbal fluency tasks: an fMRI study with clinical implications. *Brain* 125:1024-1038.

Hayes TL and Lewis DA. 1992. Nonphosphorylated neurofilament protein and calbindin immunoreactivity in layer III pyramidal neurons of human neocortex. *Cereb Cortex* 2:56-67.

Heim S, Opitz B, and Friederici AD. 2002. Broca's area in the human brain is involved in the selection of grammatical gender for language production: evidence from functional magnetic resonance imaging. *Neurosci Lett* 328:101-104.

Herath P, Klingberg T, Young Y, Amunts K, and Roland P. 2001. Neural correlates of dual task interference can be dissociated from those of divided attention: an fMRI study. *Cereb Cortex* 11:796-805.

Hervé G. 1888. La Circonvolution de Broca. Etude de morphologie cerebrale. Paris: Davy,A.

Horwitz B, Amunts K, Bhattacharyya R, Patkin D, Jeffries J, Zilles K, and Braun AR. 2003. *Activation of Broca's area during the production of spoken and signed language: A combined cytoarchitectonic mapping and PET analysis*. Neuropsychologia, in press.

Indefrey P, Brown CM, Hellwig F, Amunts K, Herzog H, Seitz RJ, and Hagoort P. 2001. A neural correlate of syntactic encoding during speech production. *PNAS* 98:5933-5936.

Kolb B and Whishaw IQ. 1996. *Human Neuropsychology*. New York: W.H. Freeman and Company.

Kononova EP. 1935. *Structural variability of the cortex cerebri. Inferior frontal gyrus in adults* (Russian). In Sarkisov SA and Filimonoff IN, editors. Annals of the Brain Research Institute. Vol. I. Moscow-Leningrad: State Press for Biological and Medical Literature. pp. 49-118.

Kononova EP. 1949. The frontal lobe (Russian). In Sarkisov SA, Filimonoff IN, and Preobrashenskaya NS, editors. *The Cytoarchitecture of the Human Cortex Cerebri*. Moscow: Medgiz. pp. 309-343.

Koski L, Wohlschlager A, Bekkering H, Woods RP, Dubeau MC, Mazziotta JC, and Iacoboni M. 2002. Modulation of motor and premotor activity during imitation of target-directed actions. *Cereb Cortex* 12:847-855.

Lieberman P. 2002. On the nature and evolution of the neural bases of human language. *Yearbook of Physical Anthropology* 45:36-62.

Luppino G, Matelli M, Camarda RM, Gallese V, and Rizzolatti G. 1991. Multiple representations of body movements in mesial area 6 and the adjacent cingulate cortex: An intracortical microstimulation study in the macaque monkey. *J Comp Neurol* 311:463-482.

Marantz A, Miyashita Y, and O'Neil WO. 2000. *Image, Language, Brain*. Cambridge, Massachusetts: MIT Press.

Marie P. 1906. L'aphasie de 1861 à 1866. Essai de criticque sur la génèse de la doctrine de Broca. *Semaine Médicale* 26:565-571.

Matelli M, Luppino G, and Rizzolatti G. 1991. Architecture of superior and mesial area 6 and the adjacent cingulate cortex in the macaque monkey. *J Comp Neurol* 311:445-462.

Meyer M, Alter K, and Friederici AD. 2003. Functional MR imaging exposes differential brain responses to syntax and prosody. *J Neuroling*, in press.

Mohr JP, Pessin MS, Finkelstein S, Funkenstein HH, Duncan GW, and Davis KR. 1978. Broca aphasia: pathologic and clinical. *Neurol* 28:311-324.

Ono M, Kubik S, and Abernathey CD. 1990. *Atlas of the Cerebral Sulci*. Stuttgart, New York: Thieme.

Paulesu E, Goldacre B, Scifo P, Cappa SF, and Fazio F. 1997. Functional heterogeneity of left inferior frontal cortex as revealed by fMRI. *Neuroreport* 8:2011-2016.

Petrides M and Pandya DN. 1994. Comparative architectonic analysis of the human and the macaque frontal cortex. In Boller F and Grafman J, editors. *Handbook of Neuropsychology*. New York: Elsevier. pp. 17-58.

Price CJ. 2000. The anatomy of language: contributions from functional neuroimaging. *J Anat* 197:335-359.

Price CJ, Wise RS, Watson JDG, Patterson K, Howard D, and Frackowiak RSJ. 1994. Brain activity during reading. The effects of exposure duration and task. *Brain* 117:1255-1269.

Riegele L. 1931. Die Cytoarchitektonik der Felder der Broca'schen Region. *J Psychol Neurol* 42:496-514.

Rizzolatti G and Arbib MA. 1998. Language within our grasp. *Trends Neurosci* 21:188-194.

Roland PE and Zilles K. 1994. Brain atlases - a new research tool. *Trends Neurosci* 17:458-467.

Sarkisov SA, Filimonoff IN, and Preobrashenskaya NS. 1949. *Cytoarchitecture of the Human Cortex Cerebri* (Russian). Moscow: Medgiz.

Schiller F. 1979. *Paul Broca*. Berkeley: University of California Press.

Schleicher A, Amunts K, Geyer S, Morosan P, and Zilles K. 1999. Observer-independent method for microstructural parcellation of cerebral cortex: a quantitative approach to cytoarchitectonics. *Neuroimage* 9:165-177.

Signoret J-L, Castaigne P, Lhermitte F, Abelanet R, and Lavorel P. 1984. Rediscovery of Leborgne's brain: Anatomical description wit CT scan. *Brain Lang* 22:303-319.

Stookey B. 1954. A note on the early history of cerebral localization. *Bulletin of the New York Academy of Medicine* 30:559-578.

Strasburger EH. 1938. Vergleichende myeloarchitektonische Studien an der erweiterten Broca'schen Region des Menschen. *J Psychol Neurol* 48:477-511.

Talairach J and Tournoux P. 1988. *Coplanar Stereotaxic Atlas of the Human Brain*. Stuttgart: Thieme.

Tanji J and Kurata K. 1989. Changing concepts of motor areas of the cerebral cortex. *Brain Dev* 11:374-377.

Tomaiuolo F, MacDonald B, Caramanos Z, Posner G, Chiavaras M, Evans AC, and Petrides M. 1999. Morphology, morphometry and probability mapping of the pars opercularis of the inferior frontal gyrus: an in vivo MRI analysis. *Europ J Neurosci* 11:3033-3046.

Uylings HBM, Malofeeva LI, Bogolepova IN, Amunts K, and Zilles K. 1999. Broca's language area from a neuroanatomical and developmental perspective. In Hagoort P and Brown C, editors. *Neurocognition of Language Processing*. Oxford: Oxford University Press. pp. 319-336.

von Economo C and Koskinas GN. 1925. *Die Cytoarchitektonik der Hirnrinde des erwachsenen Menschen*. Berlin: Springer.

Vogt C. 1910. Die myeloarchitektonische Felderung des menschlichen Stirnhirns. *J Psychol Neurol* 15:221-238.

Vogt C and Vogt O. 1919. Allgemeinere Ergebnisse unserer Hirnforschung. *J Psychol Neurol* 25:292-398.

Wernicke C. 1874. *Der aphasische Symptomencomplex. Eine psychologische Studie auf anatomischer Basis.* Berlin: Springer Verlag.

Zatorre RJ, Evans AC, Meyer E, and Gjedde A. 1992. Lateralization of phonetic and pitch discrimination in speech processing. *Science* 256:846-849.

Zatorre RJ, Meyer E, Gjedde A, and Evans AC. 1996. PET studies of phonetic processing of speech: review, replication, and reanalysis. *Cereb Cortex* 6:21-30.

Zilles K, Schleicher A, Palomero-Gallagher N, and Amunts K. 2002. Quantitative analysis of cyto- and receptor architecture of the human brain. In Mazziotta JC and Toga A, editors. *Brain Mapping: The Methods.* USA: Elsevier. pp. 573-602.

Zurif E, Swinney D, Prather P, Solomon J, and Bushell C. 1993. An on-line analysis of syntactic processing in Broca's and Wernicke's aphasia. *Brain Lang*