

Broca's Region: From Action to Language

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Abstract

Broca's region, classically considered a motor speech-production area, is involved in action understanding and imitation. It also seems to help in sequencing of actions. Broca's region might have evolved for interindividual communication, both by gestures and speech.

Key Words: Broca's region, BA 44 and 45, cytoarchitecture, dynamics, human, mirror-neuron system, gesture, imitation, magnetoencephalography, MEG, functional magnetic resonance imaging, fMRI, language

20-word summary for table of contents:

Broca's region, the classical speech-production region, has also other interesting functions, recently unraveled with noninvasive brain imaging.

Introduction

In his now classical report from 1861, Pierre Paul Broca described a man who was unable to speak although his tongue and lip movements were not impaired. The man, later called “Monsieur Tan”, was able to say only “tan” and utter a swear-word. He had a paralysis on the right side, but seemed to be intelligent and not impaired in other aspects. On autopsy, a fluid-filled cavity was found in his left frontal lobe, just anterior to the motor cortex of mouth and tongue (36). Lesions to what is nowadays called Broca’s region lead to non-fluent, sparse, dysprosodic, and agrammatical speech production (19). This deficit contrasts the “sensory” aphasia caused by a damage to the left parietotemporal (Wernicke’s) region.

In contrast to the early concept of Broca’s region as an exclusive speech-production area, today’s view comprises much wider language-related functions (14) and also other communication-related functions. Recent studies have shown that Broca’s region contains representations of hand actions and orofacial gestures. In this brief review we will focus on the motor functions of Broca’s region. We start by describing the anatomy and connections of Broca’s region, and then discuss its role in action execution, observation, and understanding, and the relationship of these functions to imitation. Finally we will speculate why Broca’s region is involved in so many different functions.

Structure and Connectivity of Broca’s Region

Anatomy and Histology

----- Figure 1 about here — location of Broca’s region -----
Broca’s region and its right-hemisphere homologue, schematically shown in Figure 1, includes Brodmann’s cytoarchitectonic areas (BA) 44 and 45, and occupies pars opercularis and pars triangularis of the inferior frontal gyrus (IFG) in the dominant hemisphere (the left in 95% of the population). The widely-used Brodmann map (16) represents a simplified drawing of only one typical brain, and later histological studies have indicated considerable individual variation in the size and extent of areas 44 and 45 with respect to the individual sulcal topography; for example, area 44 volumes may differ across individuals even by a factor of 10 (2, 4).

Broca’s region matures later than e.g. the primary sensorimotor cortices, as is evident from both the histological fine structure (3) and from cortical thickness maps based on magnetic resonance imaging (37).

Although areas 44 and 45 differ in their cytoarchitecture (2), they share e.g., the presence of very large pyramidal cells in deep layer III and in layer V, the lack of a clear border between layers II and III, and the low cell density in layer VI (2). However, while area 44 is “dysgranular” (containing a thin layer IV of small granular cells, and large pyramids in layer V, with pyramidal cells from deep layer III and upper layer V intermingled with those of layer IV), area 45 has densely-packed granular cells in layer IV (“granular” area) (2, 4, 65). Although Rizzolatti and Arbib (82) consider area 44 analogous to monkey area F5, the homology between the human area 44 and the monkey F5 has not yet been demonstrated in a strict sense.

Hemispheric Asymmetry

Areas 44 and 45 can be found in both hemispheres, but nearly all patients with Broca's aphasia have lesions in the *left* inferior frontal cortex. This clinical observation raises the question whether and how far Broca's region and its right-hemispheric counterpart differ anatomically and functionally.

Anatomical asymmetry. The volume of the histologically defined area 44 is larger in the left than the right hemisphere, whereas area 45 is more symmetrical (2, 30). Moreover, the cytoarchitecture of both areas shows significant interhemispheric differences (5).

In great apes, the inferior frontal region corresponding to human Broca's region is larger in the left than right hemisphere (18), suggesting that the neuroanatomical substrates for left-hemisphere dominance in vocalization developed already five million years ago, long before speech emerged. It has been suggested that vocalizations were gradually incorporated into the gestural system, and in the subsequent switch from manual gesture to vocal language, the left hemisphere could have taken dominance for both speech and manual action (21).

Functional asymmetry. The dominance of left-hemispheric area 44/45 in language-related functions is well established (14). It is far less clear whether area 44/45 is asymmetric in other communication-related functions (to be reviewed in the sections below, along with perception- and action-related functions in general). For example, the right IFG is activated during voluntary inhibition of imitative and overlearned responses (15) as well as during perceptual sequencing tasks (97). The right IFG is also activated when people try to make sense of ambiguous emotional expression in face images, but not when they view and judge pictures of ambiguous gender (73, 78). Both left and right IFG were activated during detection of errors in musical syntax (63). Furthermore, left and right IFG are essential for imitation (44). Finally, data of an imagery-of-movement study reported a left-hemispheric dominance of BA 44 for egocentric movements but a right-hemispheric dominance of the same area for movement characteristics in space (11). A systematic review of functional asymmetry is beyond the scope of this article. However, throughout this article, we will refer to findings about "Broca's region" in the left hemisphere and about its right-hemisphere counterpart separately. "Area 44/45" will refer to either hemisphere.

Connections of Broca's Region

The available data on connectivity derive mainly from tracing and electrophysiological experiments in the monkey brain and they have been extrapolated to the human brain. Some recent studies have applied diffusion tensor imaging (DTI) in the human brain to analyse connectivity. The major inputs and outputs of areas 44 and 45 differ to some extent, emphasizing the different functional roles of these areas..

According to the connections of monkey F5, the human IFG (bilaterally) is likely to be connected to the anterior intraparietal cortex (AIP), the superior temporal sulcus (STS), parietal cortex (area PF in monkeys), the cerebellum, and Wernicke's area (reviewed in ref. 6). In contrast to many other brain functions, conclusions based on primate research must be considered with particular caution when the anatomy and physiology of language processing are concerned. Electrophysiological experiments in primates have implicated both a dorsal and a ventral pathway connecting Wernicke's area to Broca's region (54, 89). This suggestion has been recently confirmed in the human brain using diffusion tensor imaging and tractography (80): A dorsal pathway, including the arcuate fasciculus, was distinguished from a more ventral route including the external capsule and the

uncinate fasciculus. Interestingly, the connections were stronger in the dominant than in the non-dominant hemisphere. Although studies on tractography in the human brain in general do not demonstrate the existence of anatomical, synaptic connectivity, they are indicators of the existence of anatomical pathways connecting one with the other brain region. The functional connectivity of Broca's area, evident e.g. in functional magnetic resonance imaging (fMRI), is task-specific and much more widely-spread than the anatomical connectivity would predict (42). However, as with any functional imaging studies, common activation does not necessarily imply a network of directly connected nodes.

Broca's Region with a Mosaic of Functions

Below we briefly discuss various functions that have been addressed to Broca's region and/or its right-hemisphere counterpart. It should be noted, however, that activation of Broca's region in a brain imaging study does not mean that the neural substrate of the mentioned functions would be seated only there; rather the activated area is involved in, or may be an important node in a widely distributed neuronal network. It is most likely that Broca's region consists of partly overlapping subsystems that support various functions ranging from motor imagery (11, 35), object manipulation and grasping (13), and motor preparation (59, 90) to motor planning (25).

We will proceed from the classical functions of Broca's region in speech production and language to more basic functions in perceptual sequencing, action understanding, and imitation.

Language and Speech

In her extensive review about fMRI studies of language areas, Bookheimer (14) showed that BA 44 and 45 subserve different functions. The IFG is often activated bilaterally, but with left-hemispheric dominance during tasks requiring naming (91), judgments of phonology (43, 100), semantics (4, 29, 101), and syntax (9, 28, 29, 43). Broca's region is also activated during acquisition of grammatical rules, discrimination of speech sounds, production of words, estimation of time intervals, and reproduction of rhythms (14). Consequently, Broca's region seems to be involved in both perception and production of speech. We will claim below that this role of Broca's region as an interface of action and perception can be generalized to non-verbal functions.

Language production and understanding also involves prosody, one of the few language-related processes with right-hemisphere dominance (68, 70). The interaction of the two hemispheres, however, seems to be more complex than assumed previously. Integrating evidence from neuroimaging, psycholinguistics, neurology, and neurophysiology, Friederici and Alter (27) proposed that segmental, lexical, and syntactic information is processed in different fronto-temporal networks in the left hemisphere (including the temporo-parieto-occipital junction, parts of the inferior frontal gyrus, and the superior temporal lobe). In contrast, the processing of intonation is supported by a temporo-frontal circuit in right hemisphere, consisting mainly of the frontal operculum and regions in the superior temporal gyrus. The strict right-hemispheric lateralisation of the processing of intonational information can be modulated by stimulus or task demands via the corpus callosum. The authors suggest that single regions within the described networks obtain their specific role for the processing of particular aspects of language via the interaction with other areas (27).

Perception–Action Link for Communication: Mirror Neurons

Communication, both verbal and non-verbal, requires the communicating individuals to “stay tuned”. Because the conspecifics certainly are very similar in their main characteristics, it is then also mandatory that each subject’s action and perception rely on closely linked neuronal circuitries—one individual’s output is the other (similar) individual’s input.

Interestingly, “mirror neurons” were discovered some years ago in frontal area F5 of the monkey cortex. These neurons are active during execution of object-related hand actions but also, importantly, when the monkey is just observing similar acts (23, 31, 84-86). For example, the neurons were activated when the monkey took a raisin from a tray and also when he viewed another monkey or the human experimenter doing the same. Mirror neurons have visuomotor properties, coding goal-related motor acts but they can also be activated by sounds that imply actions (55, 57). Importantly, the mirror neurons do not only react to visual input and then project, via some transformation step, to motor-output-related neurons but they are part of a system that forms a neuronal representation of the observed motor acts. They are sensitive to the goal of the act, and thereby can go beyond the information given (102). Similar to F5, the rostral part of inferior parietal cortex contains neurons that are active during action observation and execution (32). This parietal region receives input from STS, which is known to contain neurons responding to biological motion (for a review, see 1). However, the STS neurons are not activated when the subject makes movements herself, and thus can be considered only as contributing to the motor MNS.

In total, mirror neurons, as important parts of larger neuronal circuitries, can be considered to transfer action-related information (be it visual or auditory) to knowledge. Until now it is not known whether the monkey mirror neurons show any hemispheric lateralization.

In search of a human mirror-neuron system (MNS), human counterparts of the monkey mirror neurons were first searched for with positron emission tomography (PET) which follows oxygen consumption in the brain (40, 59, 86). Broca's region was activated when the subject observed, imagined, and imitated the examiner using a precision grasp to enclose an object or hand movements. These results implied that Broca’s region could contain neurons similar to the monkey mirror neurons. The activation sequence associated with online imitation and with observation of other person’s movements also included STS (77, 88). The monkey F5 mirror neurons are also activated by orofacial gestures. A recent magnetoencephalographic (MEG) study (77) applied still pictures of verbal and nonverbal lip forms that the subject had to observe, imitate, or make in a self-paced manner (Figure 2). In all conditions and in both hemispheres, the activation spread from occipital cortex (peak activation 120 ms after the picture onset) in 20–60 ms steps to the superior temporal region (STS, the strongest activation), the inferior parietal lobule, the inferior frontal lobe (Broca’s region), and, 80–100 ms later, to the primary motor cortex. In an earlier study (76), signals from Broca’s region and motor cortex were significantly stronger during imitation than observation or execution.

Assuming that the observed MNS activation sequence would have something to do with the link between a sender and a receiver of an action-related message, some abnormalities could be expected in subjects who have abnormal imitation skills and difficulties in understanding motor-act-based intentions of other subjects. Such deficits are observed in high-functioning autistic (Aspergers’) subjects, who in fact displayed delayed (by 45–60 ms) and diminished activation in Broca’s region (75) in the imitation condition (Figure 3). Moreover, activation was in many subjects absent in the right hemisphere.

----- Figure 2 about here (MEG & action sequence) -----

----- Figure 3 about here (Asperger subjects) -----

Within the MNS, the close link between perception and action seems to be realized in functions of Broca's region. Such a link may well be important in facilitating communication between an agent and an observer due to shared sensory and motor representation. Along similar lines, Liberman and Mattingly (62) strongly advocated a motor theory of speech, meaning that the listener perceives the speech sounds in terms of how they are articulated rather than in terms of their acoustic characteristics.

In line with left-hemisphere control for speech, orofacial gestures show a right hemimouth dominance in babies during babbling, as opposed to smiling (45). Corresponding results have been observed in humans (McGurk effect attenuated when the speakers's right hemimouth is covered, ref. 74)) and in marmosets (right hemimouth dominance for social contact calls as opposed to expressions of negative emotion, ref. 46).

Speech production seems especially important during language acquisition: when the child listens to a new word, (s)he automatically tries to imitate it, thereby forming a close temporal link between sensing (hearing) and acting (articulating). Language acquisition through imitation of speech sounds could well be supported by the acoustical mirror neurons in F5/Broca's region (57, 83). The close connection between speech perception and imitation/production becomes manifest also in adults when they modify their accent and syntax according to the speaker with whom they are interacting.

In a combined TMS (transcranial magnetic stimulation) and PET study, auditory speech activated the left IFG, suggesting that this area primes the motor system to respond to heard speech (103), one more hint for a role of Broca's area as an interface between perception and action.

A role of area 44/45 as an interface between perception and action is also suggested by the *inhibitory* influence of right IFG on certain imitative and overlearned responses (15) – see also more general inhibitory functions of right IFG in (7).

The sum of these studies is in line with the view that the MNS supports communicative functions. This tentative statement may not extend to the MNS *in toto* since the STS neurons that are "strictly related" to the MNS (83) do not possess motor functions. STS and inferior parietal cortex, however, provide essential input to F5 where the communicative function of the MNS becomes manifest.

Action Understanding

Rizzolatti and coworkers (reviews 83, 87, 88) consider Broca's area essential for action understanding. Support for such an idea comes from studies where monkey F5 neurons react also when the end part of the movement is obscured and the monkey only knows what is going to happen (102). Furthermore, a part of the F5 mirror neurons are also activated by sounds provided that the sounds are related to actual motor acts and that the monkey understands this relationship (57).

Observation of different types of mouth actions activates several areas including the pars opercularis of the IFG and the adjacent ventral premotor cortex, with different patterns, likely via different mechanisms based on knowledge of the observed action (12, 17). Interestingly, Broca's area was not activated when the human subjects watched a dog barking, i.e. an action that is not in the observer's motor repertoire (17). In addition to Broca's area and premotor cortex, also the primary motor cortex shows differential activation dependent on action understanding: MEG results about the motor-cortex part of the human MNS suggest that the motor cortex

differentiates natural and artificially presented movements (52). Moreover, a recent study of observation of chopstick use demonstrated in the motor cortex the stronger activation the more often the subjects had used chopsticks during the last year. In other words, a dependence on experience was demonstrated in the motor-cortex part of the MNS (53).

We most likely understand other persons' actions, and also their motor-act-based intentions, by mapping observed actions, postures, and gaze onto our own motor representations of similar actions. The observed motor patterns may evoke memories and experiences of motor patterns that we have performed earlier. If the observed motor sequence contains recognizable parts that already are included in the observer's own motor vocabulary, it is far more easy to both understand and imitate the new sequence.

Imitation

As a part of the human MNS, Broca's region seems to have an important role in imitation, a capability different from direct copying, in which the observer copies the action precisely without understanding its goal. "True" imitation relies on perception-action coupling and allows the imitator to perform motor actions that (s)he has never earlier performed, thereby forming the basis for skill learning (67). In true imitation, the observed motor patterns are directly matched on the observer's own internal motor representations; this is a fundamentally different mechanism from detailed visual analysis, followed by matching of the visual and motor reference frames. A recent study criticized the role of Broca's region for imitation, claiming that most of the previous studies have had too little variability in the imitated actions so that the imitator could have just kept in mind the limited set of movement patterns, repeating them equally well as they would have been coded with numbers (64). Another possible contaminating factor could be covert verbalization ("internal speech") during the motor acts.

In an fMRI study, imitation of action involved strongly the left IFG (49). Imitation of goal-directed actions (as compared with non-goal-directed actions) led to more intense activation of the bilateral IFG (58). In an extensive analysis of 7 fMRI studies, Molnar-Szakacs et al. (71) concluded that Broca's region is functionally parcellated so that imitation-related activation occurs at the dorsal and ventral part of the pars opercularis; whereas pars triangularis is activated only during observation, and not during imitation. Accordingly, MEG recordings showed stronger responses of Broca's region and primary motor cortex during imitation than action observation or execution (75-77); the reason may be either facilitation/enhancement of responses by imitation or the co-activation and sum-up of two different neuronal populations.

Activity was stronger during imitation than simple observation of facial expressions in premotor areas, including the inferior frontal cortex, as well as in the superior temporal cortex, insula, and amygdala (20). Moreover, imitation—but not execution—of finger-movements was impaired during repetitive transcranial magnetic stimulation applied over the left and right pars opercularis (44).

Some action patterns are highly contagious. For example, watching another person yawn may trigger us to do the same. In an fMRI study where subjects watched videotaped yawns vs non-nameable non-yawn facial gestures, no yawn-specific activation was observed in Broca's region. Thus activation associated with yawn contagiousness seems not to rely on essential parts of the MNS, in line with the nature of contagious yawns as automatically released behavioural acts – rather than truly imitated motor patterns that would require detailed action understanding (98).

Proponents of the ideomotor theory noted already in the 19th century that an idea leads into an action, unless we suppress it. Although some of us can view a cold beer on the table without drinking it, patients with frontal lesions may display echoing behaviour so that perception leads in an automatic response (61). In healthy subjects, some spinal mechanisms are inhibited at the same time as facilitation occurs at the cortical level (8).

Forward and Inverse Models

Planning an action, for example reaching for an object, includes expectation of sensory consequences of the action. "Forward models", considered to underlie such prediction, are thought to involve efference copies that inform the sensory areas about the forthcoming sensory input which then would be compared with the predictions. For example, utterances deviating infrequently from the frequently produced vowels do not elicit change-related responses in the human auditory cortex although the same sounds presented externally (from tape) do so (22). "Inverse models", on the other hand, refer to (e.g. visual) feedback from movements that are needed to reach the object.

Broca's region has been suggested as an interface between inverse and forward models (48), coding the goal of an action (in the dorsal part) and also sending efference copies to STS (in the ventral part). According to such an "interface hypothesis", Broca's region receives visual input from STS via the parietal cortex and processes it into action plans. A competing hypothesis stresses the role of the posterior parietal cortex as such an interface between inverse and forward models (69).

It is interesting that the inverse and forward models propose activation sequences very similar to those which have already been demonstrated (for the inverse model case) with MEG; for example, Figure 2 pinpointed dynamical activation from STS to inferior parietal cortex, Broca's region, and finally to the primary motor cortex (77). The forward and inverse models are useful in thinking about brain activation during online imitation of another person's actions.

Motor and Perceptual Sequencing

Parsing is essential for understanding any observed actions and for their consequent imitation. Think for example about learning a new language in which we first face great difficulties in segmenting the message into single words. Broca's region could have a role in action segmentation (on the sensory side) and in action sequencing (on the motor side). As a support of such an interpretation of Broca's region supporting representation of sequential information, be it perceptual or serial, Broca's region is activated during auditory and visual rhythm monitoring tasks (93) and during attention to timing and speed of moving objects, as opposed to attention to properties of the objects (94-96). Interestingly, IFG is activated by sequences of biological stimuli (such as goal-directed motion) but not during completion of geometrical figure sequences (97). Deviation from expected sequences may also be the reason why Broca's region and its right-hemisphere counterpart are activated when musical syntax is violated (63).

The hemispheres might have different roles in sequencing: Left hemisphere lesions affect verbal sequencing and right-hemisphere lesions nonverbal sequencing (14, 56).

Hand Gestures and Their Relation to Speech

Speech production and speech-related gestures are connected to a degree that they have been considered as outlets of the same thought process (39), a view supported by the finding that hand and orofacial gestures are supported by the speech production area.

Speech-related gestures may occur even when the speaker-gesturer knows that others cannot see the gestures, e.g. during a phone call. Similarly congenitally blind persons may gesture, even when speaking with other blind people (38, 50). The close connections between speech production and hand gestures are also supported by studies of hearing babies born to deaf parents: the infants' hand actions display a similar rhythm as does babbling (81). In stutterers, speech-related hand gestures freeze at the same time as the speech is disturbed; instead the non-speech-related hand movements can continue normally (66). Along similar lines, observation of grasping movements can influence the observer's simultaneous mouth movements and syllable pronunciation (33, 34).

All these findings suggest an intimate connection between speech-related hand and face gestures and speech production. The co-representation of speech and gestures in Broca's region may reflect shared evolutionary roots. Accordingly, Rizzolatti and Arbib (82) suggested that hand and orofacial gestures — rather than primate vocalizations — are the precursors of human language; their proposal links earlier gestural theories to recent neurophysiological results about the MNS. The close connection between gestures and speech/language is also evident from the spontaneous emergence of sign languages in isolated societies of deaf persons (99), and of the brain imaging findings that sign language activates very similar brain regions than does speech (47, 60). Interestingly, Horwitz et al. (47) showed an extensive involvement of area 45 for spoken and signed language, suggesting representation of modality-independent aspects of language generation in the inferior frontal cortex.

Broca's Region – Conclusions and Speculations

Broca's region in the lateral, ventral part of the frontal lobe, with representations of face, head, and hands—but not of foot—may have evolved to a special communication area relying on orofacial gestures and hand movements. That function requires representation and segmentation of rapidly changing motor and sensory patterns, and a close matching of these two to form an action–perception interface.

Far beyond its classical language functions, Broca's region, encompassing Brodmann's cytoarchitectonic areas 44 and 45 in the left hemisphere, contributes to action planning, action observation, action understanding, and imitation. Speech-production and comprehension can be considered as one highly developed form of action execution/observation matching (cf. motor theory of speech, ref. 62). The new concepts of “motor cognition” (51) and “sequential cognition” (24) may be useful as first approximations of the wide range of functions subserved by Broca's region.

The role of Broca's region in action understanding, derived from findings of mirror-neuron research, is also supported by the following observations: (1) When subjects view audiovisual speaking faces, activation of Broca's region is stronger during incongruent than congruent stimuli (79), (2) when dyslexic subjects passively view words, they show stronger Broca's region activation than do normal-reading subjects (92), and (3) when patients with cochlear prosthesis listen to their native language they show stronger Broca's region activation than do normal-hearing subjects (72). In all these conditions, Broca's region seems to be more activated when the task requires much effort for understanding the sensory stimulus.

As a likely interface for sensory and motor sequencing, Broca's region is at a good position to support action understanding in general. True imitation can follow only when the action is first parsed and understood. Strong effort for action understanding also recruits top-down influences based on the subject's previous experience, and thus predictive behaviour can result (26).

The studies reviewed here converge on a central role of Broca's region as an orchestrator of time-sensitive perceptual and motor functions underlying verbal and non-verbal communication. However, several questions still remain open, for example whether and how specific language components (e.g., transformational components as part of syntactic abilities (10, 41)) do have common evolutionary roots with perceptual and motor functions supported by Broca's region, and whether their neuronal correlates are identical. Once the basic functions and neuronal substrates are identified, information is also needed about temporal activation sequences and connectivity to fully unravel the multitude of brain functions to which Broca's region contributes.

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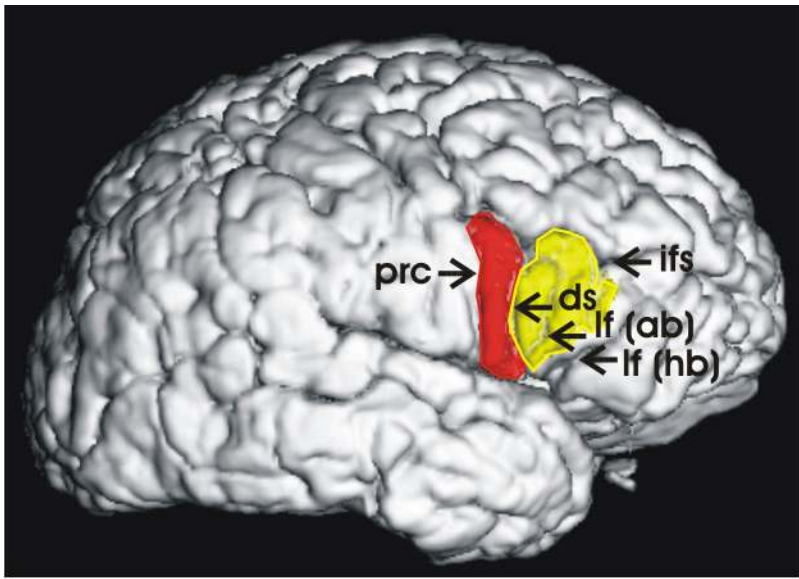
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Figure legends

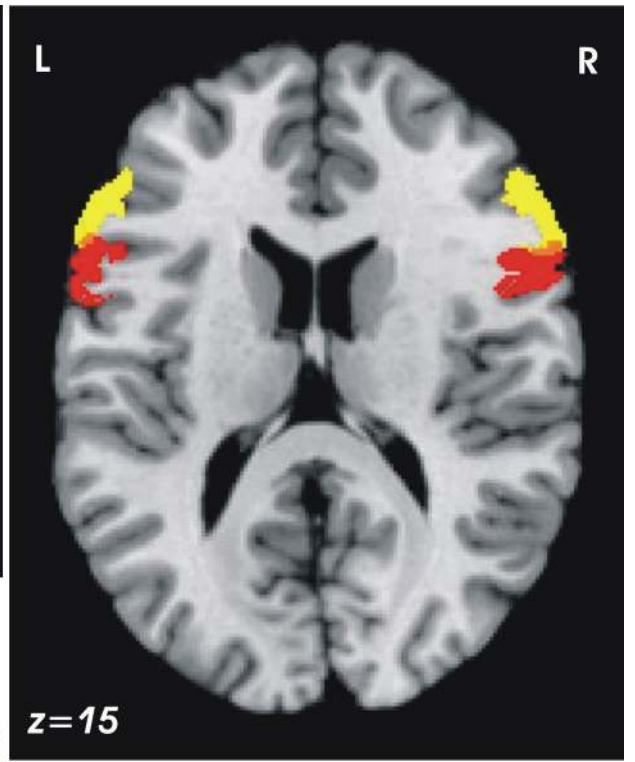
Figure 1: [A] Surface rendering of the right hemisphere of a 3D-reconstructed post-mortem brain. BA 44 (red) and 45 (yellow), the cytoarchitectonic correlates of the right-hemispheric homologue of Broca's region. Areas of both hemispheres have been delineated in histological sections of a total of ten brains and superimposed on a lateral view of the right hemisphere where the sulcal pattern is clearer than in the left hemisphere (2, 4). [B] 50% probabilistic maps of BA 44 (red) and 45 (yellow) after warping of the ten MR data sets of the post-mortem brains and their cytoarchitectonic areas to the "MNI reference brain" (http://www.fz-juelich.de/ime/ime_start, <http://www.bic.mni.mcgill.ca/>). L and R: left and right hemisphere. The maps show only those voxels of the reference space, which overlapped in five or more out of ten brains. Prc – precentral sulcus, ifs – inferior frontal sulcus, ds – diagonal sulcus, ab – ascending and hb – horizontal branch of the lf – lateral fissure.

Figure 2: *Left*: Magnetoencephalographic (MEG) recording with a 306-channel whole-head neuromagnetometer at the Brain Research Unit, Low Temperature Laboratory, Helsinki University of Technology. MEG picks up weak magnetic field produced by excitatory postsynaptic intracellular currents, arising in synchronously activated cortical pyramidal cells. These magnetic fields, mainly generated by neural currents in fissural cortex, are measured non-invasively outside the head. *Right*: Brain activation by imitation and observation of orofacial gestures. Upper panel shows nonverbal lip forms used as stimuli. Lower panel illustrates activation sequence during imitation (red) and observation (green) of nonverbal orofacial gestures. The responses recorded from 5 locations are indicated, and the cortical activations progress from the occipital visual area to the superior temporal sulcus, to the inferior parietal areas, then to Broca's region in the inferior frontal cortex, and finally to the primary motor cortex. Similar activation areas and temporal sequences were seen also in the right hemisphere. The blue traces refer to control stimuli (landscapes which activated only the two first steps). Modified from Nishitani & Hari *Neuron* 2002; 36: 1211–1220.

Figure 3: Mean (\pm SEM) peak latencies in the left hemisphere of control subjects (open circles) and Asperger subjects (filled circles; AS). There were no significant differences in the duration of the whole activation sequence from the occipital area to the primary motor cortex between both groups. The activation interval from the inferior parietal lobule to Broca's region was statistically significantly longer for Asperger subjects than control subjects; the statistically significant difference is marked with asterisks. Occ – occipital; STS –superior temporal sulcus; IPL – inferior parietal lobule; IFG – inferior frontal gyrus, M1 – primary motor cortex. Modified from Nishitani et al. *Ann Neurol* 2004; 55: 558–562.



A



B



— Imitation
— Observation
— Control

