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Language evolution: neural homologies and neuroinformatics☆

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Abstract

This paper contributes to neurolinguistics by grounding an evolutionary account of the readiness of the human brain for language in the search for homologies between different cortical areas in macaque and human. We consider two hypotheses for this grounding, that of Aboitiz and García [Brain Res. Rev. 25 (1997) 381] and the Mirror System Hypothesis of Rizzolatti and Arbib [Trends Neurosci. 21 (1998) 188] and note the promise of computational modeling of neural circuitry of the macaque and its linkage to analysis of human brain imaging data. In addition to the functional differences between the two hypotheses, problems arise because they are grounded in different cortical maps of the macaque brain. In order to address these divergences, we have developed several neuroinformatics tools included in an on-line knowledge management system, the NeuroHomology Database, which is equipped with inference engines both to relate and translate information across equivalent cortical maps and to evaluate degrees of homology for brain regions of interest in different species.

Keywords: Brain evolution; Broca's area; Cortical maps; Homologies; Neural; Language; Neural mechanisms; Mirror neurons; NeuroHomology Database; Neuroinformatics; Neurolinguistics; Wernicke's area

1. Introduction

We define *neuroinformatics* to include not only the use of databases, the World Wide Web, and visualization for the storage and analysis of neuroscience data but also the use of computational models in structuring masses of possibly diverse neuroscientific data (Arbib & Grethe, 2001). The challenge here is to integrate insights from synthetic data obtained from running a model with empirical data obtained from studying the animal or human brain. The present paper will exemplify this approach within the context of neurolinguistics by grounding an evolutionary account of the readiness of the human brain for language in the search for homologies between different cortical areas in macaque and human. We consider two hypotheses for this grounding, that of Aboitiz and García (1997) and the Mirror System Hypothesis (MSH) of Rizzolatti and Arbib (1998). The promise of computational modeling of neural circuitry of the macaque and its linkage to analysis of human brain imaging data is indicated by a brief discussion of two fully implemented models of neural circuitry involved in grasping and recognition of grasping. We also examine a conceptual model of neurolinguistic processing that sets the stage for future computer simulations.

To help to sort out competing maps of the macaque brain in relation to the analysis of homologies between the brains of macaque and monkey, we have developed several neuroinformatics tools to create an on-line knowledge management system, the NeuroHomology Database (NHDB), which is equipped with inference engines both to relate and translate information across equivalent cortical maps and to evaluate degrees of homology for brain regions of interest in different species.

1.1. Homology

The central concept of comparative biology is the concept of *homology*. It expresses the existence of typical and specific correspondences between parts of members of

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☆ This paper is dedicated to the memory of Patricia Goldman-Rakic (1937–2003) and Massimo Matelli (1951–2003).

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natural groups of living organisms (Nieuwenhuys, 1999). The term was first introduced by Owen in 1849, who defined a *homologue* as "the same organ in different animals under every variety of form and function" (Butler and Hodos, 1996). This definition was given before Darwin's theory of evolution, and the modern concept of homology was changed by evolutionary biology and genetics (Butler and Hodos, 1996). Accordingly, the concept of homology was defined in terms of 'continuity of information', inheritance of features from a common ancestry, or phyletic continuity.

The process of comparison of structures is not a direct one, but implies the identification of the relevant attributes and an inference process from a constellation of characteristic attributes (Striedter, 1999). The process of comparison at the level of the central nervous system begins with the identification of brain structures. The definition of a brain structure, as being different from its neighboring structures is problematic itself. Generally, a given part of the central nervous system is considered as a specific brain structure on the basis of its position relative to brain landmarks or previously identified brain nuclei as well as developmental history, cell architecture, pattern and density of myelin, specific staining to different histochemical and immunohistochemical markers and connections with other previously identified nuclei. A number of investigators also include the functionality of brain structures (physiological properties of cells in given experimental conditions) and topographical positions of brain nuclei as additional criteria for establishing homologies (Campbell & Hodos, 1970; Northcutt, 1999).

As we shall document below in our analysis of the evolution of brain mechanisms related to language, different investigators, focusing on different techniques, have come up with different parcellations of the brain, raising one major challenge to the search for homologies. In particular, it is worth noting that the basic system for numbering cortical regions is due to Brodmann (1909) and that he assigned the same numbers to regions of human and monkey cerebral cortex that he considered homologous. However, subsequent work has modified some of his suggestions and called others into question. For our work it will be particularly important to note that macaque area 45 (Walker, 1940) may not be homologous to Brodmann's human area 45 (Bailey & von Bonin, 1951; see Fig. 6). Moreover, quite different paths of evolution, responsive to the need of different organisms for similar functions, may yield organs with similar functions yet divergent evolutionary histories—these are called *homoplasic*, rather than *homologous*. Lacking a time-lapse movie of the evolution of species, and hampered by the fact that brains do not fossilize, we must rest the evolutionary criterion for homology on an inferential basis. Thus in much of what follows, we shall use criteria such as those listed in the previous paragraph, and take high similarity across these measures as prima facie evidence for a possible homology. We thus use the terms *degree of homology* and *degree of similarity*, so that rather than asserting that two structures are homologous as a binary all-or-none-concept, we shall weigh the evidence for homology, using a set of similarity criteria. Many homology studies have looked at the criteria of relative position, cytoarchitecture, and hodology (the sets of afferent and efferent connections). Other useful criteria for comparison are myeloarchitecture, chemoarchitecture, functionality, and continuity through intermediate species. Puelles and Medina (2002) are less comfortable than we about degrees of homology, and use developmental considerations to support their stricter separation of homology (sameness) and similarity. However, they use homology and sameness as synonyms, and this does not seem to us appropriate when two species have diverged significantly from their common ancestors—a single organ x in ancestor A might differentiate into two organs y and y' in modern species B and three organs z, z' and z'' in modern species C. For example, a region involved in hand movements in monkey might be homologous to regions involved in both hand movements and speech in humans. Thus there may be no absolute homology between these five modern organs since they are differentially modified from the common ancestor.

Those of us who seek to understand the brain and its evolution should realize that homology itself is not usefully treated as a binary concept except at the grossest level, such as identifying visual cortex across mammalian species. Even if genetic analysis were to establish that two brain regions were homologous in that they were related to a common ancestral form it would still be important to have access to a measure of similarity to constrain too facile an assumption that homology guarantees similarity across all criteria. Indeed, from the perspective of computational and comparative neuroscience, declared homologies may be the start, rather than the end, of our search for similarities that will guide our understanding of brain mechanisms across diverse species.

We now turn to two hypotheses on the neural basis of language evolution to frame our discussion of macaque homologues of human language-related areas, and the NHDB that we have developed to study these and a far broader range of neural homologies. Fig. 1 illustrates the problems to be faced in seeking homologies between the human and macaque brains. Fig. 1A shows a lateral view of the left hemisphere of the human brain showing various sulci as well as a number of areas (numbered according to Brodmann) relevant to language performance. Fig. 1B shows areas of the macaque brain considered by Aboitiz and García (1997) in establishing homologies with the human brain, while Fig. 1C shows the areas considered by Rizzolatti and Arbib (1998). The challenge to be addressed below is that not only are the labels different in Fig. 1B and C, but so too are the parcellations of cerebral cortex to which they are attached.

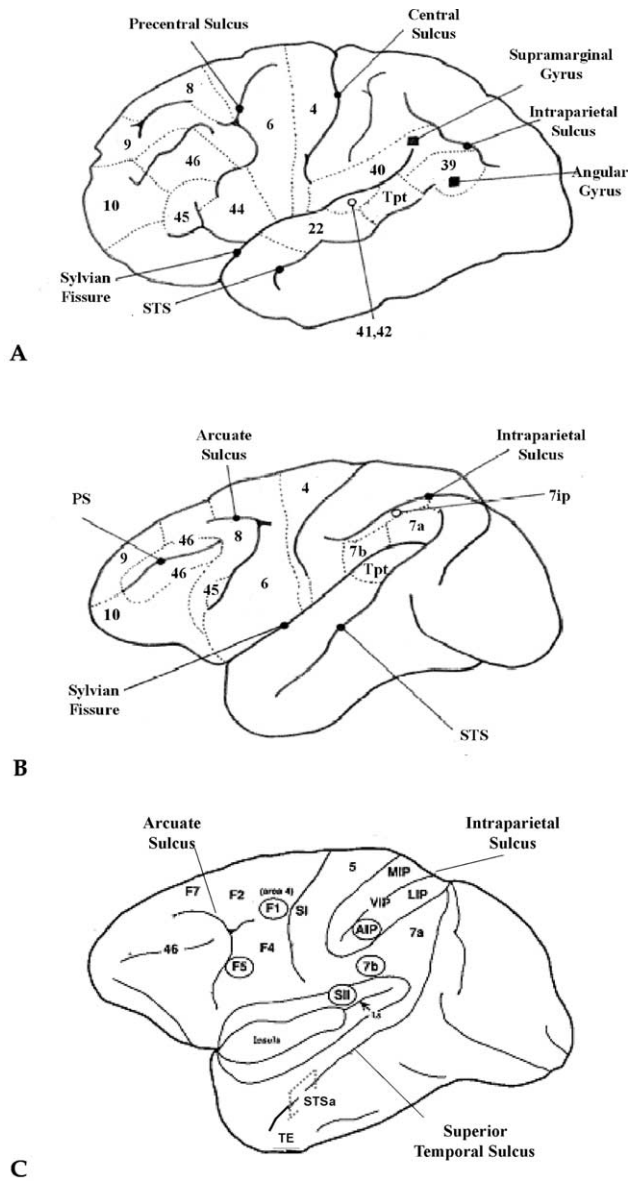

Fig. 1. (A, B) Architectonic areas considered by Aboitiz and García in comparing the human (A) and the macaque (B). Numbers correspond to Brodmann's classification. AG, angular gyrus; AS, arcuate sulcus; CS, central sulcus; IPS, intra-parietal sulcus; PCS, precentral sulcus; PS, principal sulcus; SF, sylvian fissure; SMG, supramarginal gyrus; STS, superior temporal sulcus. (C). A side view of the left hemisphere of the macaque brain. Area 7b is also known as area PF. ((A) and (B) adapted from Aboitiz and García, 1997; (C) adapted from Jeannerod et al., 1995.)

2. Evolving the language-ready brain

What is the evolutionary path leading to language in humans, and what are the relevant data on brain mechanisms? Since the fossil record offers no trace of brain structure beyond clues from ancient skulls on brain size and perhaps some fissures of the brain, the answers to these questions are varied and controversial (Wilkins & Wakefield, 1995). The present article outlines the development of a neuroinformatics framework for linking similar and putatively homologous structures in macaque and human to help answer this question. As background, this section summarizes two hypotheses for this grounding, that of Aboitiz and García (1997) and the MSH of Rizzolatti and Arbib (1998).

The generally accepted view of the human cortical areas involved in language gives special prominence to Broca's area and Wernicke's area (though many other areas are also implicated in language), both lateralized in the left hemisphere for most humans. However, it must be noted that there is no one-to-one correlation between Brodmann areas and the damage caused by strokes, tumors or surgery, and thus no universally agreed delineation of these areas.

Broca's area is located on the inferior frontal gyrus (pars triangularis and opercularis), and comprises BA (Brodmann area) 44 and BA 45. Some publications use the term Broca's area for BA 44, 45 and 47, others use it for BA 44 only. Amunts et al. (1999) conducted a 3D reconstruction of 10 human brains and found that the cytoarchitectonic borders between areas 44 and 45 did not consistently coincide with sulcal contours. (The volumes of area 44 differed across subjects by up to a factor of 10!) They found that area 44 but not area 45 was left-over-right asymmetrical in all brains. Five of five male brains and three of five female brains had significantly higher cell densities in left area compared to right area 44. These hemispheric and gender differences were not detected in area 45. They see these asymmetries as strengthening the case for area 44 as the anatomical correlate of the functional lateralization of speech production.

Wernicke's area is located in the posterior part of the superior temporal gyrus and in the floor of the Sylvian sulcus (Aboitiz & García, 1997). It corresponds to the posterior part of BA 22, or area Tpt (temporo-parietal) as defined by Galaburda and Sanides (1980). Lesion-based views of Wernicke's area may include not only the posterior part of BA 22 but also (in whole or in part) areas 42, 39, 40, and perhaps 37. Thus future research must not only seek a firmer basis for (degrees of) homology between cortical areas of macaque and human but also a firmer understanding of the functional contribution of each area.

Deacon (1997) makes symbolization central to his account of the co-evolution of language and the human brain. He stresses the componential homology which allows us to learn from relations between the brains of macaques and humans; more recently his writings stress the role of self-organization as the child's brain adapts to the cultural environment in which the child develops (Deacon, 2003). Jerison (1976, 1985) (see also Gould, 1975) has placed special emphasis on the relatively high placement of human brain weight against body weight in a plot of primates, but we seek to see what can be learned from analyzing the brain on more of a component-by-component basis. Where Deacon places most emphasis on the enlargement of frontal cortex we place more emphasis on the differential development of specific subsystems which support language-readiness. Interestingly, Semendeferi, Lu, Schenker and

Damasio (2002) argue that magnetic resonance imaging shows that human frontal cortices are not disproportionately large in comparison to those of the great apes. They thus suggest that the special cognitive abilities of humans may be due to differences in individual cortical areas and to a richer interconnectivity, rather than an increase in the overall relative size of the frontal lobe during human evolution. However, we shall later suggest that focusing of connectivity may also have been important as it would focus the types of structured associations that could be learned as the brain develops.

2.1. The Aboitiz–García hypothesis

Aboitiz and García (1997) propose the following sequence for the evolution of the capacity of the human brain to support language:

1. The capacity to give names to yield the lexicon which underlies the ability to refer to objects or events in the external world. They associate this with the elaboration of a precursor of Wernicke's area in the superior temporal lobe as a zone for cross-modal associations which include a phonological correlate.
2. Syntax arose to express regularities in the ways in which different elements are combined to form linguistic utterances. They associate this with the differentiation of an inferoparietal-frontal (Broca's) area with its connections to the incipient Wernicke's region developing as a phonological rehearsal device that eventually differentiated into the language areas. This phonological-rehearsal apparatus providing some basic syntactic rules at the levels of phonemes and morphemes. The coordinated operation of networks involving granular frontal cortex and the semantic system represented in the temporo-parietal lobes, together with the phonological-rehearsal loop just mentioned, generated higher levels of syntax and discourse.

We now review these hypotheses in somewhat more detail. Aboitiz and García (1997) accept Geschwind's (1964) theory that in the monkey cross-modal sensory associations need an intact limbic system to develop, while in the human non-limbic cortex, cross-modal cortico-cortical interactions facilitated establishment of associations between the sound of a vocalization and the image of an object. This, Geschwind argued, permitted the generation of a lexicon in which arbitrary sounds (vocalizations) represented objects identified through the visual or the tactile system. This still leaves open the question (to be addressed below) of how multimodal concepts in Wernicke's area obtained a linguistic dimension by being mapped into phonological sequences. This account has also been espoused by Wilkins and Wakefield (1995). However, the commentaries on this latter paper showed that the hypothesis is now controversial. If trained from an early age, chimpanzees and gorillas are capable of learning some aspects of sign language and can also learn to communicate with 'lexigrams' Indeed, the bonobo Kanzi can link human speech to signs. Moreover, Kohler et al. (2002) show that monkeys can use sounds to activate mirror neurons for manual actions (as defined below). However, there is still no evidence that apes can move beyond the capability of a two-year old human infant, never reaching the 'naming explosion' that occurs in humans in their third year. What is it about the human brain that supports it?

Vervet monkeys have different cries specifying distinct predators (Cheney & Seyfarth, 1990). The acoustic structure of each alarm call is in great part genetically preprogrammed but its specific meaning seems to be refined through learning (cf. Winter, Handley, Ploog, & Schott, 1973). Vervet monkey infants, for instance, react to eagles with warning calls but, in contrast to adults, react in the same way to pigeons and geese. Conversely, infants react to warning calls with alertness but do not show the orientation toward the sky typical for adults. Aboitiz and García (1997) thus concede that the neural substrate for the development for a lexicon exists in an incipient form in higher primates. But this concession weakens Geschwind's hypothesis, and forces us to be more specific about the changing functionality and the neural changes that made it possible. Moreover, a key element of MSH (see below) has been to explain why Broca's area is not the homologue of the anterior cingulate area which is the area of cerebral cortex primarily involved in monkey vocalization (see Jürgens, 1997, for a review).

Aboitiz and García (1997) hypothesize that multimodal concepts in Wernicke's area are mapped into phonological sequences as follows: the system of long temporo-parietal-prefrontal connections serves to integrate sensory and mnemonic information from the temporo-parietal lobes with the organization of behavior, both short- and long-term, by the frontal systems. They further stress that language processing is closely linked to working memory (i) in terms of the anatomical arrangement of the neural networks involved, and (ii) because it operates in the context of an efficient working memory system. One of their main suggestions is that selective pressure for the capacity to learn complex vocalizations through imitation and repeated practice was a key aspect in establishing a phonological working memory system that allowed temporary storage of phonological representations in order to rehearse them internally. Through the action of natural selection favoring good learners, this system eventually differentiated into some primordial language regions. Concomitantly, a prefrontal system in which information from other sensory modalities was integrated and coordinated with the representation of complex vocalizations was also being developed.

'Working Memory' (called 'active memory' by Fuster, 1995) holds information about, e.g. objects or events (whether recently perceived, recalled from LTM, or

inferred), for some period prior to executing some action for which this information may be relevant. Specific neurons have been observed that hold the encoding of some stimulus for the 'delay period' from the time the stimulus is observed to the time when the action is initiated (Fuster, 1995; Goldman-Rakic, 1987). We—like Aboitiz and García—will follow Goldman-Rakic (1995b) in appealing to multiple special-purpose working memory systems organized in parallel, viewing the prefrontal cortex as subdivided into a mosaic of areas for specialized working memory tasks. Working memory for the spatial location of objects involves connections between parietal area 7 and dorsolateral prefrontal BA 46 and BA 8; working memory for object characteristics depends on connections between area TE of the inferior temporal lobe and its connections with the inferior convexity of the prefrontal cortex, BA 45 and BA 12 (Wilson, Ó Scalaide, & Goldman-Rakic, 1993). Aboitiz and García (1997) then argue that linguistic working memory involves connections between inferoparietal areas BA39-40 and frontal areas BA44-47 (which roughly correspond to their phonological-rehearsal loop). Granular frontal areas (BA 9 and especially BA 46) relate with more general aspects of working memory in humans.

Aboitiz and García (1997) take pains to relate these human areas to the macaque brain (Fig. 1). (For the moment we just list *their* correspondences. Later sections will say more about these various brain regions and the posited homologies.) In the macaque the equivalent of Broca's area (BA 45) receives major projections from the inferior parietal and the inferior temporal lobes. Aboitiz and García propose that the inferoparietal areas from which some of these projections arise in the monkey (areas 7b and 7ip) are homologous to areas 40 (supramarginal gyrus) and perhaps 39 (angular gyrus) in the human. Aboitiz and García (1997) equate human Wernicke's area with Tpt and see it as feeding (directly or indirectly) areas 40, 39, etc. that project to Broca's area—but we might also read this as further support for the view that Wernicke's area may include (parts of) Brodmann areas 22, 42, 39, 40, and perhaps 37. Tpt also projects directly to prefrontal cortex (Broca's area in an extended version), thus participating in language working memory. Direct projections from Tpt to areas 44–45 (restricted Broca's area) are scarce if they exist in the macaque. These connections may have become strengthened in the human lineage, perhaps participating in the generation of some automatic linguistic sequences. Direct connections between inferotemporal area TE and Broca's region are then seen as a possible third pathway to transmit linguistically relevant object information, suggesting that the connectivity of the language regions may be more complicated than the currently accepted model of Broca's and Wernicke's areas directly connected via the arcuate fasciculus.

Based on data from brain lesions and connectional information, Aboitiz and García (1997) propose that beside areas 44/45 (and 47), frontal granular areas such as 9 and 46 (forming together an extended Broca's area) also participate in language processing, especially in aspects related to working memory tasks. They suggest that these frontal granular areas not only relate to the distribution of attention but also handle cognitive (semantic) information that is relevant for language processing. For example, when recalling the objects observed in a room, one might say "there is a lamp with a red shade (object/feature information) in the left bottom corner (visuospatial information)". Tasks such as this probably require the coordinated activity of the respective working memory circuits that are located in granular frontal cortex (cf. Rolls & Arbib, 2003, on the structured working memory required for visual scene perception).

Since frontal projections from area Tpt (≈ human Wernicke's region) do not terminate massively in areas 44–45 (≈ human Broca's area) in monkey, Aboitiz and García (1997) propose that in human evolution, area Tpt may have become increasingly connected with inferoparietal regions such as the supramarginal gyrus (area 40) thus feeding the latter with auditory information to be used in the phonological loop (Fig. 2). They then suggest that in the human the posterior superior temporal region represents a transitional zone in which concepts progressively acquire a phonological correlate while the supramarginal gyrus (area 40, and perhaps also the angular gyrus, area 39) in the parietal lobe stores this phonological representation for a brief time. Some neurons in human area 40 (and perhaps in area 39) may then project to Broca's region (areas 44 and 45), thus establishing a neuronal circuit for the phonological-rehearsal system of linguistic working memory. If they exist, direct projections from Tpt or neighboring areas to Broca's region may participate in language processing in at least two possible ways: (i) generating a shortcut between Wernicke's and Broca's regions for some automatic

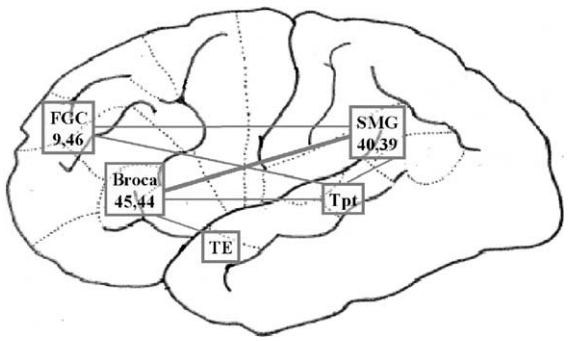

Fig. 2. Network of connectivity for language in the human brain proposed by Aboitiz and García (1997), emphasizing the connection, which may largely correspond to the arcuate fasciculus, between SMG (supramarginal gyrus) and Broca's area. Area TE, which projects to area 45, may also participate in language processing. Connections between Tpt and Broca's area, and between Tpt and SMG (direct or indirect) have not been substantially confirmed in the monkey but (especially the latter) are proposed by Aboitiz and García to have developed in the hominid line. FGC, frontal granular cortex.

routines, and (ii) participating in higher levels of language processing.

2.2. The Mirror System Hypothesis

As background for the MSH, we briefly review the neurobiology of the macaque to ground claims as to the brain of the common ancestor of macaques and humans of perhaps 20 million years ago, and hypotheses on how such brains changed to become language-ready. (See Jeannerod et al. (1995), Rizzolatti and Arbib (1998), and Rizzolatti, Fogassi, and Gallese (2002) for further details and references to the literature.)

Primate vocalization: Macaques exhibit a primate call system (a limited set of species-specific calls) and an orofacial (mouth and hand) gesture system (a limited set of gestures expressive of emotion and related social indicators). This communication system is *closed* in the sense that it is restricted to a specific repertoire. This is to be contrasted with the open nature of human languages which can form 'endlessly many' novel sentences from the current word stock and add new words to that stock. Strikingly, the cortical invocation for primate calls is in a region of cingulate cortex distinct from F5, which Rizzolatti and Arbib (1998) argue to be the macaque homologue of human Broca's area. One challenge met by MSH is to explain why it is F5, rather than the cingulate area involved in macaque vocalization, that is homologous to the human's frontal substrate for language. Note that the claim is not that Broca's area is genetically preprogrammed for language, but rather that the development of a human child in a language community normally adapts this brain region to play a crucial role in language performance.

Brain mechanisms for grasping: Parietal area AIP, the anterior region of the intra-parietal sulcus (Fig. 1C) and ventral premotor area F5 (Fig. 1C ≈ ventral 6 of Fig. 1B) anchor the cortical circuit in macaque which transforms visual information on intrinsic properties of an object into hand movements for grasping it. AIP processes visual information to implement perceptual schemas for extracting grasp parameters (affordances) relevant to the control of hand movements and is reciprocally connected with the so-called *canonical neurons* of F5. Discharge in most grasp-related F5 neurons correlates with an action rather than with the individual movements that form it so that one may relate F5 neurons to various *motor schemas* corresponding to the action associated with their discharge:

AIP (object affordances) ↔ F5 (abstract motor schemas)→

F1 (motor cortex instructions to lower motor areas and

motor neurons).

A mirror system for grasping in macaques: Among the F5 neurons related to grasping there is a subset, the *mirror neurons*, which are active not only when the monkey executes a specific hand action but also when it observes a human or other monkey carrying out a similar action. These neurons constitute the 'mirror system for grasping' in the monkey and we say that these neurons provide the neural code for matching execution and observation of hand movements. (By contrast, the canonical neurons are those grasp-related neurons that are not mirror neurons; i.e. they are active for execution but not observation.)

The populations of canonical and mirror neurons appear to be spatially segregated in F5 (Rizzolatti & Luppino, 2001). The region of F5 buried in the dorsal bank of the arcuate sulcus, F5ab, contains the canonical mirror neurons, while the convexity located caudal to the arcuate sulcus, F5c, includes the mirror neurons (Rizzolatti & Luppino, 2001; Rizzolatti et al., 2002). Both sectors receive a strong input from the secondary somatosensory area (SII; buried within the Sylvian fissure, Fig. 1C) and parietal area PF (shown as 7b in Fig. 1B and C). F5ab is the selective target of area AIP.

STSa, in the rostral part of STS, has neurons which discharge when the monkey observes such biological actions as walking, turning the head, bending the torso and moving the arms. Of most relevance to us is that a few of these neurons discharged when the monkey observed goal-directed hand movements, such as grasping objects (Perrett, Mistlin, Harries, & Chitty, 1990)—though STSa neurons do not seem to discharge during movement execution as distinct from observation. STSa and F5 may be indirectly connected via inferior parietal area PF (BA 7b) (Cavada & Goldman-Rakic, 1989a,b; Matelli, Camarda, Glickstein, & Rizzolatti, 1986; Petrides & Pandya, 1984; Seltzer & Pandya, 1994).

A mirror system for grasping in humans: The notion that a mirror system might exist in humans was tested by PET experiments which showed that grasp observation significantly activated the superior temporal sulcus (STS), the inferior parietal lobule, and the inferior frontal gyrus (area 45—part of Broca's area). F5 in macaque is generally considered (see the discussion of Fig. 6 below) to be the homologue of Broca's area in humans. Thus, the cortical areas active during action observation in humans and macaques correspond very well, indicating that there is a fundamental primate mechanism for recognition of manual actions: we argue that individuals recognize actions made by others because the neural pattern elicited in their premotor areas during action observation is similar to a part of that internally generated to produce a similar action. Note, however, that 'understanding' involves the cooperation of many brain systems, and cannot be reduced to just the activity in a subset of F5 neurons and that the monkey data here concern primarily hand movements. There are related data on neurons in F5 responsive to orofacial movements.

The Mirror System Hypothesis: What turns a movement into an action is that it is associated with a goal, so that initiation of the movement is accompanied by the creation

of an expectation that the goal will be met. We distinguish 'praxic action' in which the hands are used to interact physically with objects or other creatures, from 'communicative action' (both manual and vocal). Our assumption is that macaques use hand movements only for praxic actions. The mirror system allows other macaques to understand these actions and act on the basis of this understanding. Similarly, the macaque's oro-facial gestures register emotional state, and primate vocalizations can also communicate something of the current situation of the macaque. However, building on the idea that the mirror system in macaque is the homologue of Broca's area in humans, Rizzolatti and Arbib (1998) developed:

The *Mirror System Hypothesis*: Language evolved from a basic mechanism *not* originally related to communication: the *mirror system for grasping* with its capacity to generate *and* recognize a set of actions. More specifically, human Broca's area contains a mirror system for grasping which is homologous to the F5 mirror system of macaque, and this provides the evolutionary basis for *language parity*—i.e. an utterance means roughly the same for both speaker and hearer.

This provides a neurobiological 'missing link' for the hypothesis that communication based on manual gesture preceded speech in language evolution (e.g., Hewes, 1973; Kimura, 1993; Armstrong et al., 1995; Stokoe, 2001). Arbib (2002) has amplified the original account of Rizzolatti and Arbib to hypothesize seven stages in the evolution of language, with imitation grounding two of the stages. The first three stages are pre-hominid:

S1: Grasping;
S2: A mirror system for grasping shared with the common ancestor of human and monkey; and
S3: A simple imitation system for grasping shared with common ancestor of human and chimpanzee.

The next three stages then distinguish the hominid line from that of the great apes:

S4: A complex imitation system for grasping;
S5: *Protosign*, a manual-based communication system, breaking through the fixed repertoire of primate vocalizations to yield an open repertoire;
S6: *Proto-speech*, resulting from the ability of control mechanisms evolved for protosign coming to control the vocal apparatus with increasing flexibility.

The final stage is claimed to involve little if any biological evolution, but instead to result from cultural evolution (historical change) in *Homo sapiens*:

S7: *Language*, the change from action-object frames to verb-argument structures to syntax and semantics; the co-evolution of cognitive and linguistic complexity.

2.2.1. Computational modeling

To reinforce the above outlines of neurophysiological data on grasping mechanisms in the macaque brain and to exemplify the role of neural modeling in our conception of neuroinformatics, we introduce two models that link F5 to other regions of the macaque brain: the FARS model focuses on the canonical neurons of F5, while the MNS1 model emphasizes the learning capacities of mirror neurons. We then build on these models to offer a preliminary brain diagram for neurolinguistics that in some sense does for MSH what Fig. 2 does for the model of Aboitiz and García (1997).

The FARS model (Fagg & Arbib, 1998; Fig. 3A gives a partial view) provides a computational account of the system centered on the AIP → F5 pathway: AIP cells encode 'affordances' for grasping and send (neural codes for) these on to the canonical neurons of area F5, which selects one of these for action.

$$\mathrm{AIP} \rightarrow \mathrm{F5}_{\mathrm{canonical}} \tag{1}$$

IT (inferotemporal cortex) and PFC (prefrontal cortex) modulate F5's selection of an affordance. However, the dorsal stream via AIP does not know 'what' the object is, it can only see the object as a set of possible affordances. The ventral stream (from primary visual cortex to IT), by contrast, is able to recognize what the object is. This information is passed to prefrontal cortex which can then, on the basis of the current goals of the organism and the recognition of the nature of the object, bias F5 to choose the affordance appropriate to the task at hand. (Recent neuroanatomical data suggest that PFC may act on action selection at the level of parietal cortex rather than premotor cortex, See below.) Fig. 3A gives only a partial view of the FARS model, which also provides mechanisms for sequencing actions. It segregates the F5 circuitry which encodes unit actions from the circuitry encoding a sequence, possibly the part of the supplementary motor area called pre-SMA (Rizzolatti, Luppino, & Matelli, 1998). The administration of the sequence (inhibiting extraneous actions, while priming imminent actions) is then carried out by the basal ganglia.

Anatomically, FARS heavily relies on connections between prefrontal cortex and F5. However, there is evidence (reviewed by Rizzolatti & Luppino, 2001) that these connections are very limited whereas rich connections exist between prefrontal cortex and AIP. Furthermore AIP, unlike F5, receives direct input from IT (Webster, Bachevalier, & Ungerleider, 1994).

Rizzolatti and Luppino (2003) thus suggest that FARS be modified (Fig. 3B) so that information on object semantics and the goals of the individual influence AIP rather than F5 neurons. Thus, selection of an appropriate grip would occur in AIP by biasing those affordances that would lead to the grip appropriate to the individual's current intentions. In 'FARS modificato', AIP still describes several affordances initially, but only one of

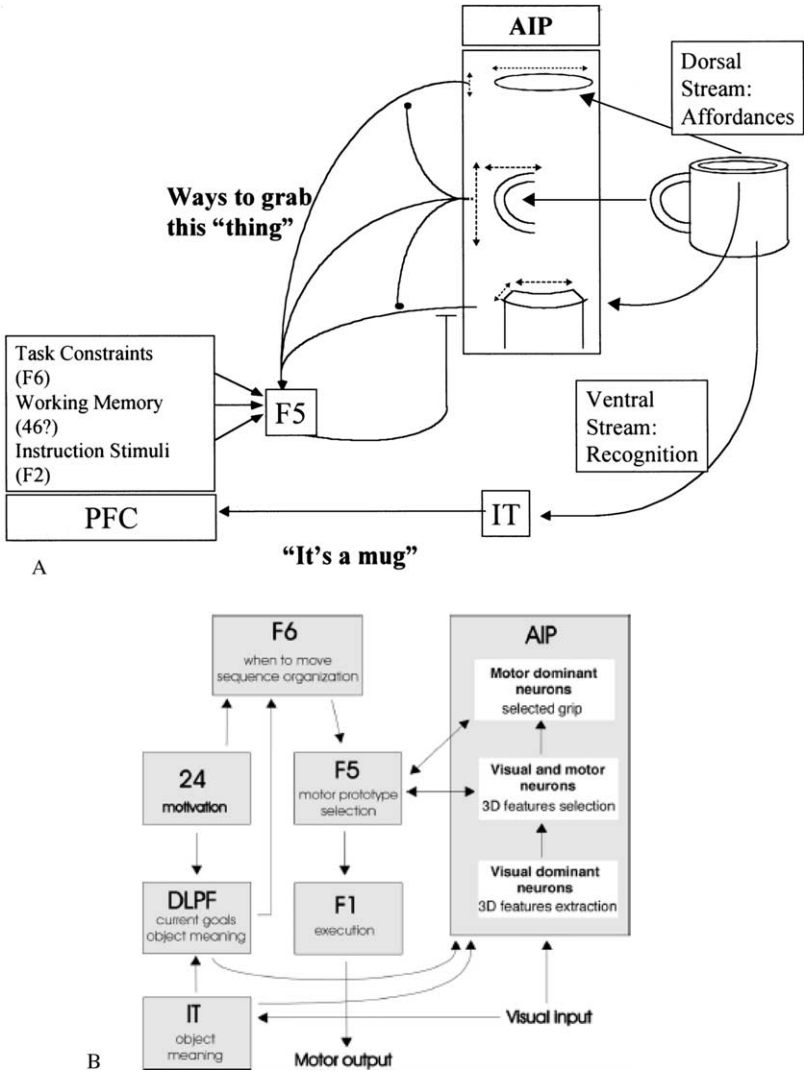

Fig. 3. **(A) Partial view of the FARS model**: This emphasizes the role of IT (inferotemporal cortex; it includes areas like the TE of Fig. 1C) and PFC (prefrontal cortex) in modulating F5's selection of an affordance. The idea is that AIP does not 'know' the identity of the object, but can only extract affordances (opportunities for grasping for the object consider as an unidentified solid); prefrontal cortex uses the IT identification of the object, in concert with task analysis and working memory, to help F5 select the appropriate action from 'the AIP menu'. (B) 'FARS modificato' (based on the anatomy reviewed by Luppino & Rizzolatti, 2001) suggests that FARS be modified to have PFC influence AIP rather than F5.

these is selected to influence F5. This affordance then activates the F5 neurons to command the appropriate grip once it receive a 'go signal' from F6. Although this version has not been implemented on the computer, it seems clear that the modified program would be able to produce many of the results found with the original model; the few variations would pose interesting challenges for neurophysiology.

We now turn to the macaque mirror system for grasping. Here, the task is to determine whether the shape of the hand and its trajectory are 'on track' to grasp an observed affordance of an object, and so we have to find other regions of the brain that provide appropriate visual processing. The most relevant brain region in the parietal cortex is PF (7b) which contains neurons responding to the sight of goal directed hand/arm actions (Fogassi et al., 1998). As we have seen, STSa is another region that seems to be very important in detecting biologically meaningful stimuli such as hand movements.

The MNS model (Oztop & Arbib, 2002) is organized around the idea that Eq. (1) is complemented by

$$\mathrm{PF} \rightarrow \mathrm{F5}_{\mathrm{mirror}} \tag{2}$$

As shown in Fig. 4 (see the caption for details), the MNS model shows how the interactions of the above brain regions provide mechanisms to evaluate the key criteria for activating a mirror neuron:

- The preshape that the monkey is seeing corresponds to the grasp that the mirror neuron encodes.

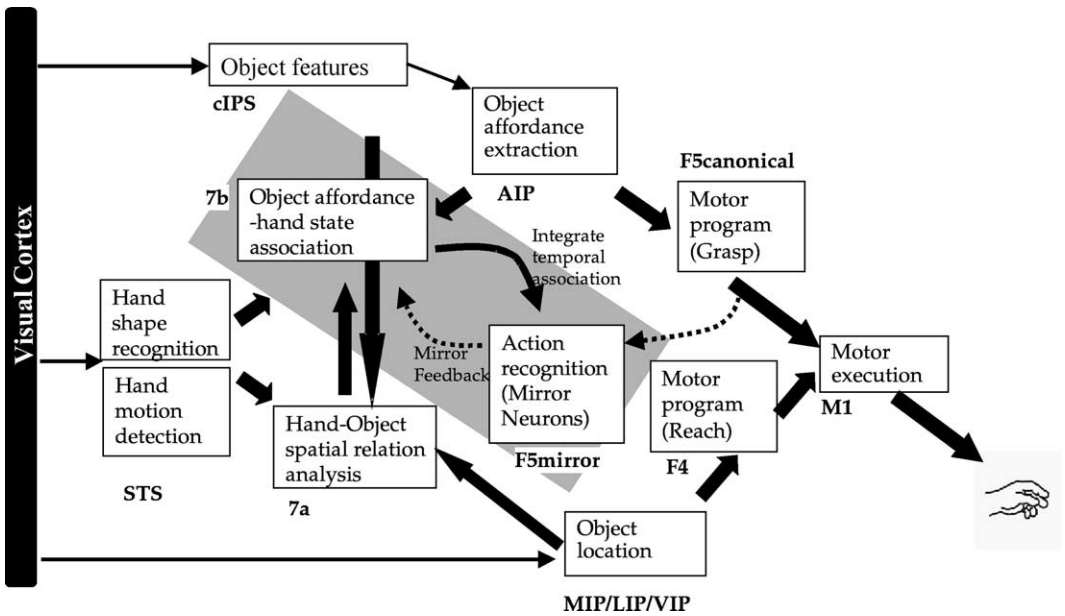

Fig. 4. The MNS (Mirror Neuron System) model. (i) Top diagonal: Object features are processed by AIP to extract grasp affordances, these are sent on to the canonical neurons of F5 that choose a particular grasp. (ii) Bottom right: Recognizing the location of the object provides parameters to the motor programming area F4 which computes the reach. The information about the reach and the grasp is taken by the motor cortex M1 to control the hand and the arm. (iii) Essential elements for the mirror system: Bottom left are two schemas, one to recognize the shape of the hand of the actor being observed by the monkey whose brain we are interested in, and the other to recognize how that hand is moving. Just to the right of these is the schema for hand-object spatial relation analysis. It takes information about object features, the motion of the hand and the location of the object to infer the relation between hand and object. Just above this is the schema for associating object affordances and hand state. Together with F5 canonical neurons, this last schema (in PF = 7b) provides the input to the F5 mirror neurons.

- The preshape that the observed hand is executing is appropriate to an affordance of the object that the monkey can see (or remember).
- The hand must be moving on a trajectory that will bring it to grasp the affordance.

Oztop and Arbib (2002) provide an explicit account of how the mirror system may learn to recognize the hand-object relations associated with grasps already in its repertoire; Oztop, Bradley and Arbib (2003) discuss how new grasps may be acquired without the help of the mirror system; while future work will build on this to probe the role of the mirror system in imitation. Such learning models, and the data they address, make clear that *mirror neurons are not restricted to recognition of an innate set of actions but can be recruited to recognize and encode an expanding repertoire of novel actions*.

2.3. A brief comparison and steps towards a synthesis

Let us briefly contrast the two evolutionary theories we have considered.

1. Note the striking difference in the parcellations of the macaque brain used by Aboitiz and García (Fig. 1B) and Rizzolatti and Arbib (Fig. 1C). As we shall see below, this poses challenges both for study of the macaque and for comparative analysis of macaque and human.
2. Aboitiz and García assume that the human brain evolved (in part) to support language. They offer an essentially *retrospective* theory. They look at the features of the human brain, seek the homologous areas of the macaque brain, note what has changed (some areas enlarge, some connections are strengthened) and then suggest how these changes could support a lexicon of spoken words and a syntax to bind them into sentences.
3. By contrast, Rizzolatti and Arbib offer more of a *prospective* theory. They start from an analysis of the monkey's capabilities, especially the fact that species-specific vocalizations have their cortical outpost in the anterior cingulate but that a different area, involved in hand movements, is homologous to Broca's area. The Arbib (2002) version assumes that the human brain evolved (in part) to support protosign and protospeech, with the richness of human languages being a 'post-biological accumulation of inventions', and offers hypotheses on how intermediate stages from the mirror system for grasping led via imitation and protosign to protospeech.
4. However, Rizzolatti and Arbib are relatively silent on the phonological loop and other working memory systems whose emphasis is an important feature of the Aboitiz and García theory.

To set the stage for the future development of a neurolinguistic model grounded in MSH, we briefly link

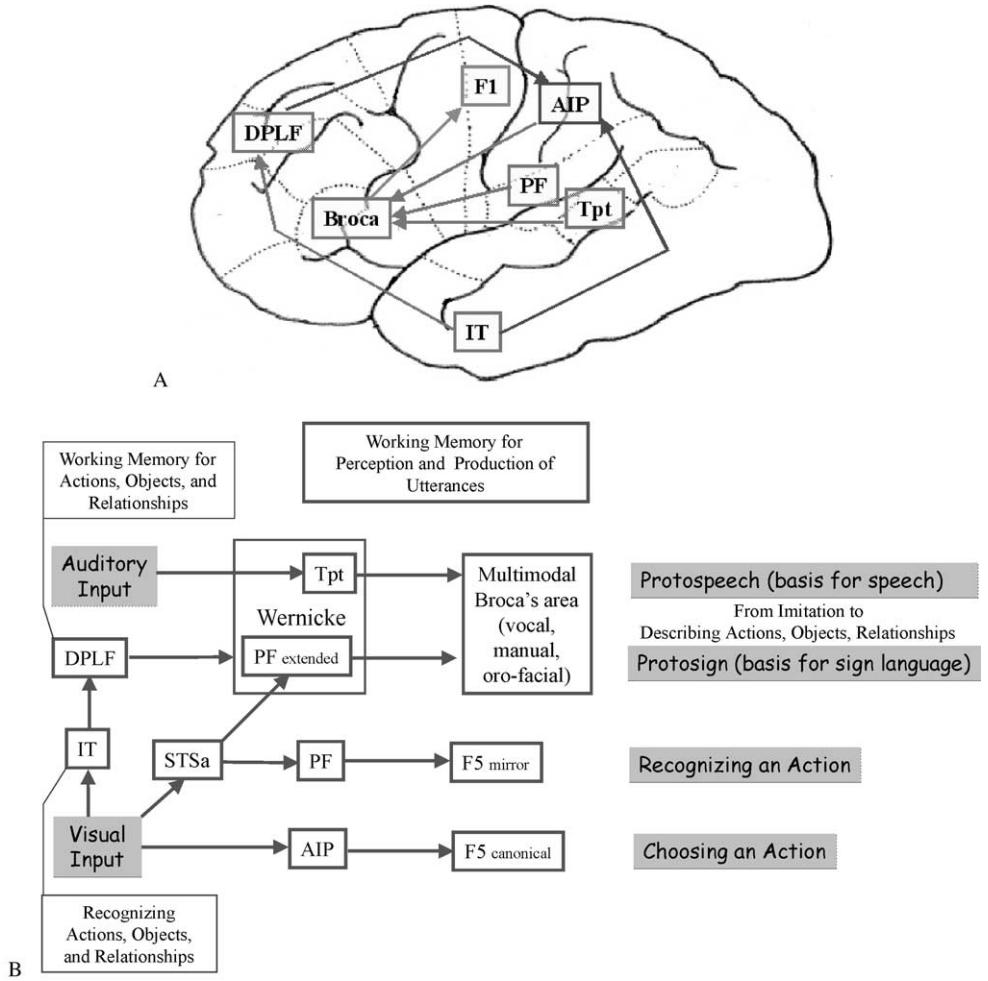

Fig. 5. (A) A recasting and extension (in part) of FARS Modificato (Fig. 3B) designed for maximal congruence with the Aboitiz–García schematic of Fig. 2. (B) A high-level view of the cumulative emergence of three fronto-parietal systems: choosing an action → recognizing an action → describing an action (in multiple modalities). This schematic builds on and modifies the schematic presented in Arbib (2001) to maximize its congruence with (A).

our view of AIP and F5 in macaque to data on human abilities, using insights gained from FARS Modificato and the Aboitiz–García focus on Tpt to derive the view of the language-related areas (and more) of the human brain shown in Fig. 5A. This allows us to expand upon a sketch from Arbib (2001) of how one might develop a neurolinguistic model on the basis of the MSH to derive the system shown in Fig. 5B.

Fig. 5B is a hybrid, mixing macaque and human regions and gives the impression that three fronto-parietal systems end in three distinct brain structures. In fact, current research has not really settled the question. In any case, the possibility that one monkey area may be homologous to different human regions implicated in one or more of praxic hand movements, protosign, protospeech, signed language and speech offers challenge to overly binary views of homology. Much needs to be done to delineate subareas of Broca's area that can be distinguished on this basis and their hodology—while noting that differences that are found (and the variations in the pattern of such differences from individual to individual) may reflect the self-organization of the brain as the child grows within a language community rather than any innate 'fate map' for these differences. DeRenzi et al. (1966) found that the majority of patients with apraxia of speech had oral apraxia and a high coexistence of oral and limb apraxia while Marquardt and Sussman (1984) found that all 12 of their 15 patients with Broca's aphasia had apraxia of speech while five had limb apraxia. Double dissociations occur in individual cases. Thus, either separate networks of neurons are engaged in the generation of speech and non-speech movement of the same muscles, or the same general network underlies speech and non-speech movements but these have separate control mechanisms which can be differentially damaged (Code, 1998).

An important topic outside the focus of this paper is that of analyzing the data on human functional neuroanatomy afforded by brain imaging. Instead we refer the reader to Arbib, Billard, Iacoboni, and Oztop (2000) which contributes to the quest to relate human brain imaging data (e.g. from PET, Positron Emission Tomography, and fMRI, functional Magnetic Resonance Imaging) to the underlying

neural networks. Models tied to human brain imaging data often focus on a few 'boxes' based on brain regions associated with significantly (though rather little, in percentage terms) enhanced blood flow, rather than analyzing the cooperative computation of multiple brain regions. As Arbib et al. (2000) show, one can link brain imaging to neurophysiological data by using Synthetic PET imaging (Arbib, Bischoff, Fagg, & Grafton, 1995; see also Tagamets & Horwitz, 1998; Tagamets & Horwitz, 2003). This method uses computational models of biological neural circuitry based on animal data to predict and analyze the results of human PET studies. This technique makes use of the hypothesis that rCBF (regional cerebral blood flow) is correlated with the integrated synaptic activity in a localized brain region. Arbib et al. (2000) exemplify this general research program with two case studies, one on visuo-motor processing for control of grasping (applying Synthetic PET to the FARS model discussed in this paper) and the other to imitation of motor skills (paying particular attention to data on the mirror system in monkey, which is central to stages S3 and S4 of the extended MSH).

Here we leave the explicit discussion of hypotheses on the evolution of the language ready brain and focus the rest of this article on the comparison of two currently extant species—macaque and human.

3. Macaque homologues of human cortical areas involved in language

The relative positions of Broca's area on the inferior part of the frontal cortex and Wernicke's area on the superior part of the temporal lobe suggest that candidates for homologous structures of these language-related areas may be located in corresponding locations in the macaque cortex. Accordingly, the homologous structures of the human Broca's area may be found on the inferior part of the macaque agranular frontal cortex, in the vicinity of the arcuate sulcus (considered to be the macaque homologue of the human precentral and prefrontal sulci), and the macaque homologues of Wernicke's area may be located at the junction between the temporal and parietal cortices. If the nomenclature proposed by Brodmann is applied to the macaque cortex, one should find corresponding structures of the human areas 44 and 45. Both of these human areas are considered to have their counterparts in the macaque cortex, even though there is no consensus over their exact locations and extensions. The macaque homologue of Wernicke's area appears to include the macaque area Tpt, located on the posterior part of the superior temporal gyrus.

3.1. A first pass on Broca's area

To initiate our discussion of these homologies, we start with the analysis by Matelli (in Rizzolatti & Arbib, 1998) arguing that areas 44 and 45 in the left hemisphere of

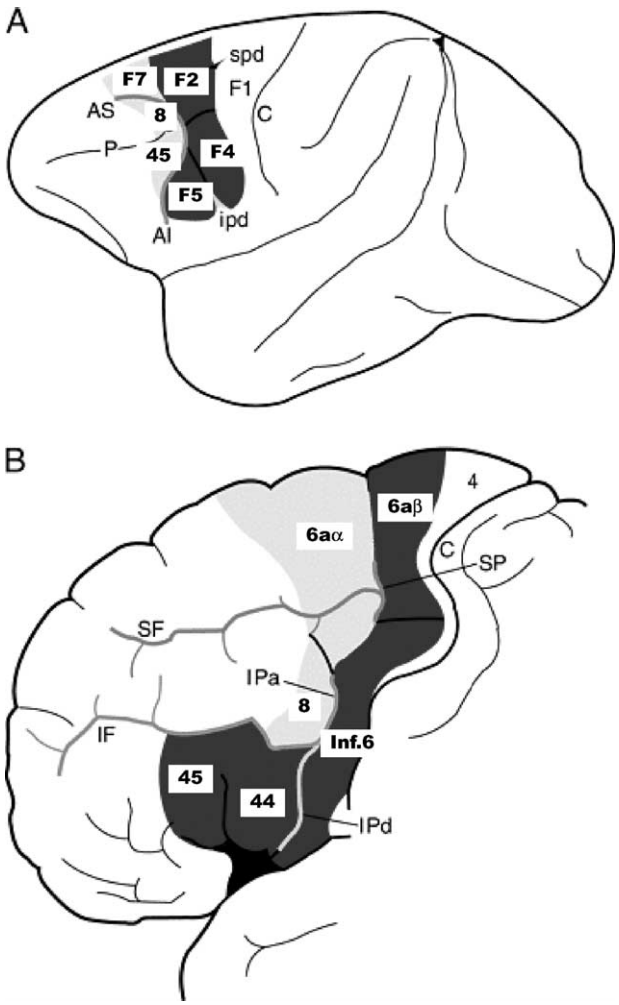

Fig. 6. Cytoarchitectonic map of the caudal part of the macaque frontal lobe and possible homologies with human frontal cortex analysis (adapted from Rizzolatti & Arbib, 1998). (A) Areas F7, 8 and 45 are areas mostly related to orienting behavior, while areas F2, F4, and F5 are areas mostly related to interactions with the external world. (B) Parcellation of portions of the human frontal cortex. The homologies based on cytoarchitectonics and electrical stimulation presented here are (F7,8,45) ≈ (6aα,8), (F2,F4) ≈ (6 aβ,Inf.6), and F5 ≈ (44,45). Sulcal equivalences based on data on the anatomical and functional organization of the premotor cortices in the two species are described in the text.

the human brain are homologous with area F5 in the macaque (Fig. 6). Fig. 6A shows the parcellation of prearcuate cortex (Walker, 1940) and agranular frontal cortex (Matelli, Luppino, & Rizzolatti, 1985) of the macaque. Areas F7, 8 and 45 are areas mostly related to orienting behavior, while areas F2, F4, and F5 are areas mostly related to interactions with the external world (see Bruce, 1988; Matelli & Luppino, 1992; Suzuki & Azuma, 1983; Vogt & Vogt, 1926). Fig. 6B shows the parcellation of portions of the human frontal cortex using the terminology of Foerster (1936) and Vogt and Vogt (1926) (see also Bruce, 1988). The homologies (F7,8,45) ≈ (6aα,8), (F2,F4) ≈ (6aβ,Inf.6), and F5 ≈ (44,45) are hypothesized on the basis of cytoarchitectonics and electrical stimulation

(see Preuss, Stepniewska, & Kaas, 1996) plus sulcal embryology (Ono, Kubik, & Abernathey, 1990).

The distribution of the sulci play the key role in this analysis. The human superior frontal sulcus (SF) and superior precentral sulcus (SP) are viewed as homologous to the superior limb of the macaque arcuate sulcus (AS); while the inferior frontal sulcus (IF) and the ascending branch of the inferior precentral sulcus (IPa) of human brain are viewed as homologous to the inferior limb of the macaque arcuate sulcus (AI). Finally, the descending branch of the inferior precentral sulcus (IPd) is viewed as homologous to the inferior precentral dimple (ipd) of the macaque brain. Rizzolatti and Arbib (1998) offer the following reasons for these homologies. The precentral sulcus develops from two separate primordia. Both of them have, during development, a horizontal branch representing the primordia of SF and IF, respectively. Moreover, the precentral sulcus in the adult brain is typically formed by two separate segments. Thus, they suggest that the human homologue of the macaque arcuate sulcus is formed by SF plus SP together with IF plus IPa. The descending branch of inferior precentral sulcus (IPd) corresponds, in this view, to the inferior precentral dimple of the macaque. In humans it abuts IF. The proposed sulcal equivalence fits well the available data on the anatomical and functional organization of the premotor cortices in the two species. The equivalence between human IPd and macaque ipd is well supported by the fact that in both macaques and humans this sulcus marks the border between F4/inferior area 6 and F5/area 44.

Arguments for homology based on correspondences of sulci and gyri between humans and macaque are not without problems: For example, the intermediate or middle frontal sulcus (Ono et al., 1990) is present in more than 80% of the hemispheres of the human brain, but is not included in Fig. 6. The consideration of this sulcus, however, may perhaps bias the whole argumentation. Furthermore, although Ono et al. (1990) reported this the precentral sulcus consists of two segments for 48 and 64% of the left and right hemispheres they studied, respectively, this sulcus can also consist of three or four segments in the remaining 52 and 36% of the hemispheres. It is beyond the scope of this paper to consider the analysis of sulci further, but this problem does highlight the great variability in anatomy of individual human brains, a variability matched by the uncertain effects of damage to any given area of the human brain. In short, homologies based on 'typical' brains provide only a first approximation to the analysis of the individual human brain shaped by genetic and experiential particularities.

Moreover, different studies of the brain of any one species use different techniques to define brain regions, and this problem is compounded when it comes to seeking homologies between different species. Indeed, human BA 44 is characterized cytoarchitectonically as dysgranular, while F5 of the macaque seems to be an agranular area. In addition, BA 44 of the human is characterized by an interhemispheric asymmetry at the microstructural level (Galaburda, 1984; Amunts et al., 1999), which has been interpreted as the anatomical correlate of language dominance. Thus the analysis of Fig. 6 is by no means the last word on homologies for Broca's area. Indeed, we later present evidence in support of the view that F5 is homologous to area 44 alone, rather than to the combination of areas 44 and 45. A major aim of the remainder of this paper, then, is to provide tools which aid the placement of evidence for similarities provided by different studies into a unified framework.

3.2. The problem of parcellation of ventral agranular cortex in the macaque

We will discuss the similarities of Wernicke's and Broca's areas with several macaque cortical areas. We first analyze evidence based on the relative position and cytoarchitecture of brain areas and then discuss the hodological similarities (i.e. the similarities of neuroanatomical connections with other brain regions) of the various cortical areas. But first we must observe that that the parcellation of part of macaque prefrontal cortex given in Fig. 6A is just one of many schemes. The comparison of the major parcellation maps of the agranular premotor cortices and of area 45 in the macaques show that the positions and extents of areas 44 and 45 may differ from author to author. Moreover, several cortical maps do not use the numerical nomenclature proposed by Brodmann, but use their own notation. The methods employed to identify and describe cortical structures can be specific to each of the authors of the considered maps, but differences in identification and description may appear even though the same criteria have been used. Therefore, in order to unify the results of experiments performed in different cortical maps, one has to relate the equivalent schemes either on the basis of the statements made by the authors concerning nomenclature, or to use inference algorithms for topologically relating areas defined in different parcellation schemes.

The classical view of these areas, the macaque agranular frontal cortex, divides them into Brodmann's area 4 and area 6 (Brodmann, 1909). This subdivision was based on the fact that Betz cells, pyramidal cells characteristic of layer V of the primary motor cortex (area 4), are rare in area 6 (Matelli, Luppino, & Rizzolatti, 1991). Initially, area 6 was considered by Brodmann to be a single structure, but subsequent studies subdivided it. Table 1 summarizes the major parcellation schemes for the ventral agranular cortex in the macaque and Fig. 7 depicts several maps that have been proposed by different authors (with Fig. 7a cercopithecus rather than macaque, and Fig. 7f a variation on Fig. 6A). Unfortunately, different techniques were employed in defining these parcellations, and the results are sometimes contradictory.

Table 1
Ventral area 6: equivalent parcellation schemes

Parcellation scheme	Component areas	Criteria
Brodmann (1909) (B)	6	Cytoarchitecture
Petrides and Pandya (2002) (P)	6	Cytoarchitecture
	44	
	45b	
von Bonin and Bailey (1947) (vB47)	FBA	Cytoarchitecture combined with myeloarchitecture
	FCBm	
Von Bonin and Bailey (1949) (vB49)	6	Cytoarchitecture combined with myeloarchitecture
	44	
Vogt and Vogt (1919) (V)	6a: 6aα,6aβ	Cytoarchitecture combined with myeloarchitecture
	6b: 6bα,6bβ	
	4c	
Barbas and Pandya (1987) (BP)	6Va	Cytoarchitecture combined with myeloarchitecture
	6Vb	
	4C	
Preuss and Goldman-Rakic (1991a,b) (GR)	6Va	Cytoarchitecture combined with myeloarchitecture
	6Vb	
	PrCO	
Lewis and Van Essen (2000a,b) (vE)	6Va: 6Val, 6Vam	Cytoarchitecture combined with myeloarchitecture, and with chemoarchitecture (SMI-32 immunoreactivity)
	6Vb	
	4c	
	PrCO	
Matelli et al. (1985) (M)	F4	Cytoarchitecture combined with chemoarchitecture (cytochrome oxidase staining)
	F5	
Petrides, Paxinos, Huang, Morris, and Pandya (1999) and Paxinos, Huang, and Toga (2000) (PP)	6VC (F4)	Cytoarchitecture combined with chemoarchitecture (several markers)
	6VR (F5)	
	44	
	45b	

3.3. Functional aspects

We have seen that neurophysiological studies of the macaque ventral agranular cortex allowed us to distinguish *mirror neurons* in F5 (these discharge not only when the macaque grasped or manipulated objects in a specific way, but also when the macaque observed the experimenter make a similar gesture) from *canonical neurons* in F5 (which are active only when the macaque itself performs the relevant actions). Canonical neurons receive object-related input from AIP and lie in the region of F5 buried in the dorsal bank of the arcuate sulcus, F5ab. Mirror F5 neurons lie in the convexity located caudal to the arcuate sulcus, F5c, and receive input from the PF region of parietal cortex encoding observations of arm and hand movements (Rizzolatti & Luppino, 2001; Rizzolatti et al., 2002). We shall see below that the minimal extent of Brodmann's area 44 as considered by us for macaque appears to at least overlap F5c and therefore may contain the mirror neurons. It is also possible that the macaque homologue of area 44, as considered in this paper includes the F5 canonical neurons, since these two populations of neurons are not totally segregated (Rizzolatti & Luppino, 2001).

Recent neurophysiological evidence suggests that the mirror neurons may be further dissociated. Kohler et al. (2002) report that some of the mirror neurons of F5 respond to auditory stimuli, and are called audio-visual mirror neurons. Presumably the existence of such neurons can be explained by the auditory inputs received from the auditory cortices, including Tpt, which we will discuss below. Area 45 also appears to contain auditory-responsive neurons (Romanski & Goldman-Rakic, 2002) but, unlike the audio-visual mirror neurons of area 44, these cells may be involved in non-spatial acoustic processing.

3.4. Area 44 in the macaque

As can be seen from Table 1, the agranular precentral cortex of the macaque was differently parcellated by various researchers, each taking into account various combinations of neuroanatomical criteria. This raises two questions to be addressed in this paper: (i) what part of the ventral agranular cortex should be designated area 44? and (ii) a more generic issue, what are the relations between the different parcellation schemes?

The term area 44 was used in the parcellation schemes vB49 and P (these abbreviations refer to the parcellations of the left column of Table 1) but Petrides and Pandya restrict area 44 to the caudal part of the bank of the inferior arcuate sulcus, while von Bonin and Bailey view area 44 as including a part of the ventral agranular cortex, caudal to the arcuate sulcus. Area 44 (vB49) (i.e. area 44 of the vB49 parcellation) appears to be identical with FCBm (vB47) on the basis of the homology of FCBm in humans defined by Von Economo and Koskinas (1925) (Petrides & Pandya, 1994). Moreover, according to Matelli et al. (1986) (Rizzolatti et al., 2002) area 44 (vB49) appears to be identical with F5 (M). This implies that all the structural, chemoarchitectonical, hodological and functional aspects of area 44 (vB49), FCBm and F5 can be unified in a single description of this part of the ventral precentral cortex in the macaque. However, the other parcellation schemes listed in Table 1 are more difficult to relate one to another.

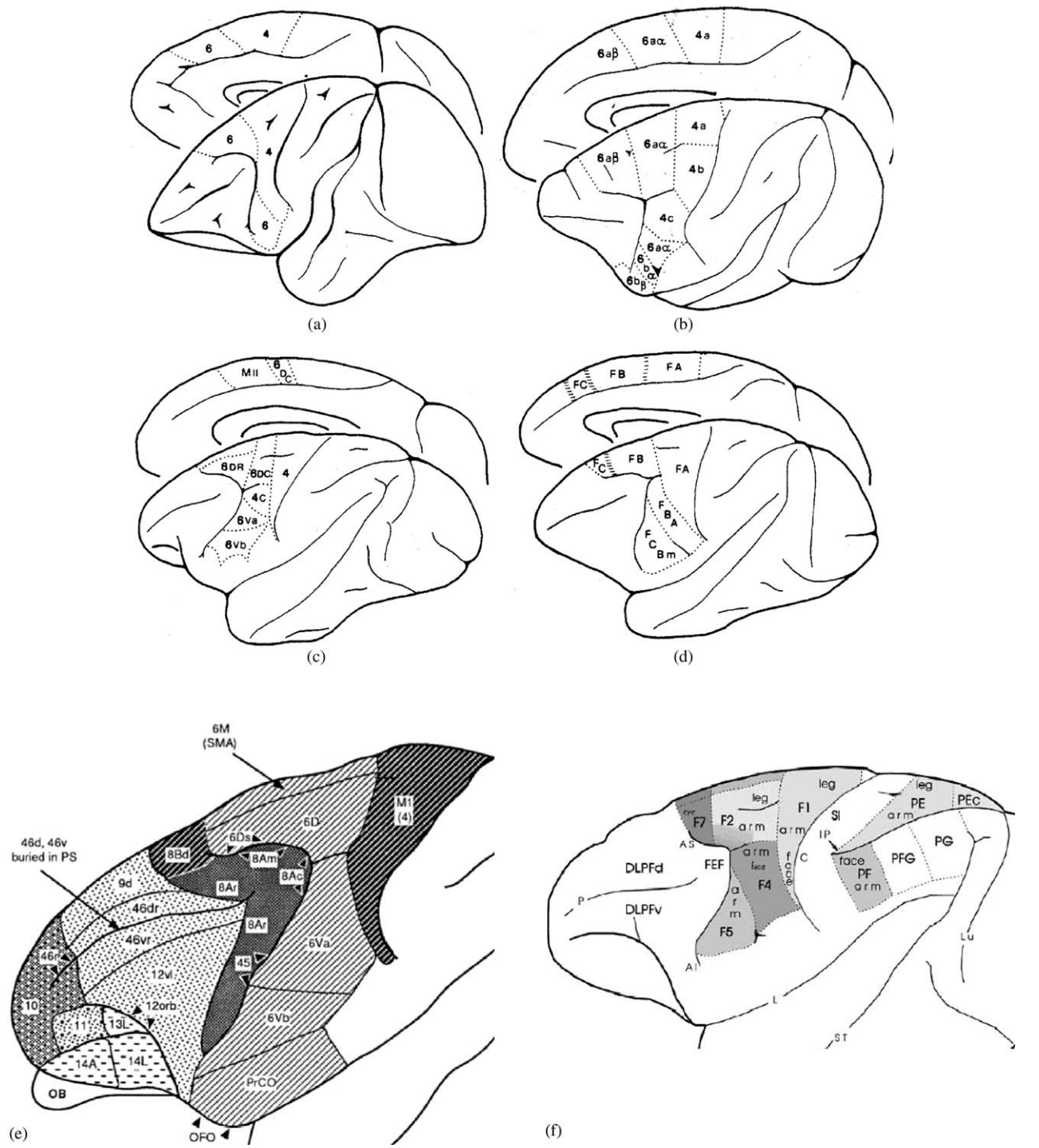

Fig. 7. Six different parcellation schemes of the agranular frontal cortex in the macaque, (a) the parcellation scheme provided by Brodmann (1909) for Cercopithecus, (b) the parcellation scheme of Vogt and Vogt (1919), (c) the map provided by Barbas and Pandya (1987), (d) the map of the macaque cortex of von Bonin and Bailey (1947), (e) the cortical map of Preuss and Goldman-Rakic (1991a) and (f) the parcellation map of Matelli (1985). [Adapted from Barbas and Pandya (1987), Matelli et al. (1991), Preuss and Goldman-Rakic (1991a), Rizzolatti et al. (2002), and Vogt and Vogt (1919).]

3.5. Area 45 in the macaque

The first description of area 45 in the macaque was provided by Walker (1940) as a structure distinguished by having the rostrally bordering area 8a (not shown in our figures) and by being confined to the anterior part of the lower ramus of the arcuate sulcus. Cytoarchitectonically, area 45 is distinguished from 8a by the presence of large pyramidal cells in the third and fifth layers (Walker, 1940). Area 45 in the macaque was also recognized by Preuss and Goldman-Rakic (1991a) as being part of the inferior ramus of the arcuate sulcus and extending for a short distance onto

the cortical surface, inferior to area 8Ar (Fig. 7e) and frontal to area 6Va. The cytoarchitectonical description of area 45 by Preuss and Goldman-Rakic is similar to that provided by Walker. Petrides and Pandya (1994, 2002) identify area 45 in the ventral-most part of the rostral bank of the inferior limb of the arcuate sulcus, extending onto the prefrontal lateral surface up to the infraprincipalis dimple (This is a very small patch of cortex below the Principal sulcus, around a small sulcus which is not labeled in Petrides & Pandya. Area 9/46 starts above that small sulcus). Based on cytoarchitectonic differences, Petrides and Pandya further subdivide area 45 into 45a and 45b. Comparing the parcellation scheme proposed by Preuss and Goldman-Rakic with that of Petrides and Pandya, one can observe that there is an overlap between area 45 defined in both maps, but area 45 as defined by Preuss and Goldman-Rakic may be more restricted than that of Petrides and Pandya—area 45 of Petrides and Pandya may overlap with area 12vl of Preuss and Goldman-Rakic. Both structures appear to have a well-developed layer IV, but detailed comparison between these two structures was not possible, since Petrides and Pandya offer a detailed cytoarchitectonic description of area 45, but do not provide a myeloarchitectonic profile of this cortical structure, while Preuss and Goldman-Rakic analyze area 12v (Fig. 7e) myeloarchitectonically, but do not give a detailed cytoarchitectonic description of this area (Petrides & Pandya, 1994, 2002; Preuss & Goldman-Rakic, 1991a). Functionally, the cortex located on the rostral part of the inferior ramus of the arcuate sulcus overlaps with the frontal eye fields (FEF) since microstimulations of the neurons elicit small saccades (Bruce, Goldberg, Bushnell, & Stanton, 1985; Cadoret, Bouchard, & Petrides, 2000; Schall, Morel, King, & Bullier, 1995; Stanton, Deng, Goldberg, & McMullen, 1989). However, not all of this part of the arcuate sulcus can be included in FEF. Stimulations of neurons buried in the depth of the rostral bank of the arcuate sulcus evoke jaw contractions and other neurons have receptive fields located on the tongue (Cadoret et al., 2000). Therefore, area 45 may contain two functionally distinct areas: FEF located more dorsally and non-FEF located deeper and more ventrally in the sulcus.

3.6. Back to Broca's area

Broca's area in humans includes Brodmann areas 44 and 45. One might hope to relate human areas 44 and 45 to the corresponding structures in the cortex of macaques but we have seen that different neuroanatomists have different views on whether and how to use areas 44 and 45 to parcellate macaque cortex. Clearly, shared notation does not automatically ensure homology between human and macaque cortical areas!

As discussed above, if the arcuate sulcus in macaque is considered to be the homologue of the human precentral sulcus, one may find homologous cortical structures in the vicinity of the inferior part of the sulcus. Area 44 in humans has large neurons in layer IV (Pandya & Yeterian, 1996). Layer II is densely packed, layer III contains small and medium pyramidal cells, especially in the upper part, and layer V is divided in two sublayers, VIa and VIb, with medium sized pyramidal cells present in VIa (Petrides & Pandya, 1994). von Bonin (1949) provided a description of area 44 in the macaque which generally resembles the structure of the human area 44 and is identical with area FCBm and F5 as defined by Matelli et al. (1985). Pandya and Yeterian identify an area with similar architectonic features as human area 44 in the caudal bank of the lower ramus of the arcuate sulcus, which appears to be identical with that part of F5 which is contained in the caudal bank of the inferior arcuate sulcus. Therefore, the minimal extent of the macaque homologue of the human area 44, according to position relative to the arcuate sulcus and cytoarchitectonics criteria is a subpart of the agranular premotor cortex, area FCBm, or F5 (M).

We now briefly summarize further data supporting the homology between F5 and area 44. In both F5 and human 44 there is a representation of hand and mouth actions. Perhaps the strongest motor activation of area 44 was obtained in a task in which participants have to continuously change finger grip (Binkofski et al., 1999). However, the somatotopy of macaque area F5 is markedly different from that in F1. Matelli et al. (1986) found that while there are virtually no connections between hand and mouth areas in F1, the two representations are heavily connected in F5. Turning to humans, fMRI experiments (e.g. Buccino et al., 2001) show activations during action observation located in the dorsal sector of area 44, extending into area 6. Why should these activations include both dorsal 44 and ventral area 6? Giacomo Rizzolatti (personal communication) suggests that when there are actions including arm movements, area 6 (not just area 44) is activated. F5 is strictly connected with F1 where individual finger movements are specifically coded. The independent control of fingers is even more developed in human M1 than in monkey F1. It is thus likely that actions where individual control of fingers is the fundamental motor aspect are represented in 44/F5, while more global actions (perhaps even some hand actions) are represented in area 6.

Area 45 in humans is granular, with clusters of large pyramidal cells in the lower part of layer III and a well developed layer IV. The description of area 45 provided by Walker (1940) suggests that the possible homologue in the macaque cortex is located ventrally to area 8A and in the anterior part of the inferior limb of the arcuate sulcus. The macaque area 45 is characterized by large pyramidal cells in layers III and V (Walker, 1940). As discussed above, Petrides and Pandya (2002) partially agree with the description provided by Walker, locating area 45 on the rostral part of the inferior arcuate sulcus, but include in it the frontal bank of the inferior part of the arcuate sulcus, as well as the part of the inferior prefrontal convexity between the arcuate sulcus and infraprincipalis dimple (Pandya & Yeterian, 1996; Petrides & Pandya, 1994, 2002).

Comparing the map provided by Walker with that of Petrides and Pandya, then the cortex which may be common to both maps is the subarea 45b (PP). Since the cytoarchitectonic features of areas 45b and 45 of Walker are very similar, we include here the rostral bank of the inferior arcuate sulcus in the minimal extension of area 45, as defined by Walker. Moreover, the cutting procedures employed by Walker (1940) may not provide the optimal angle to investigate the cytoarchitecture of the banks of the arcuate sulcus, while Petrides and Pandya (2002), in order to study the cytoarchitecture of the anterior and posterior banks of the sulcus, performed perpendicular cuts to the direction of the lower limb of the sulcus. The localization and extension of the minimal macaque homologue of human area 45, which shares the relative position and cytoarchitecture similarity criteria, is in accord with the parcellation schemes proposed by Preuss and Goldman-Rakic (1991a), and by Lewis and Van Essen (2000 a,b). Thus, the human area 45 may have the macaque counterpart area 45b (P) which has the cytoarchitectonical characteristics of the human area 45: large neurons in the deeper part of layer III, a well developed layer IV and medium-size neurons in layer V. This area is ventral to that part of the rostral bank of the arcuate sulcus which is included in the macaque FEF, and contains an orofacial representation (Cadoret et al., 2000).

3.7. Wernicke's area homologues

We saw that Wernicke's area, in the most limited definition, corresponds to the posterior part of BA 22, or area Tpt (temporo-parietal) as defined by Galaburda and Sanides (1980), whereas lesion-based views of Wernicke's area may include not only the posterior part of BA 22 but also (in whole or in part) areas 42, 39, 40, and perhaps 37. In this section, we focus on the narrow definition, and start by characterizing the macaque area Tpt. This is part of the lateral belt line of auditory-related areas in the superior temporal gyrus (Preuss & Goldman-Rakic, 1991b). It is distinguished from the adjacent auditory structure by its cytoarchitectonics profile which resembles more that of the neighboring posterior parietal cortex than those of temporal cortices (Galaburda & Pandya, 1983). Area Tpt was identified not only in macaque, but also in Galago (Preuss & Goldman-Rakic, 1991b), leading to the hypothesis that Tpt might be a more ancient structure than Broca's area (Aboitiz & García, 1997). Area Tpt appears to be the macaque homologue of Brodmann area 22 (BA 22), based on criteria of relative position and cytoarchitecture (Galaburda & Sanides, 1980; Preuss & Goldman-Rakic, 1991b). Both BA 22 in humans and Tpt in the macaque are located in the posterior part of the superior temporal gyrus. Both structures present a layer IV which is not as strong as in the anteriorly located auditory structures and fuses with layer V, a sublayer IIIc, a layer V which is split, and a densely populated layer VI (Galaburda & Pandya, 1983; Galaburda & Sanides, 1980). The differences between Wernicke's area and the macaque Tpt are in their relative sizes, the human area 22 being more extended than Tpt (Aboitiz & García, 1997), and highly asymmetric towards the left hemisphere (Aboitiz & García, 1997).

3.8. The hodology criterion

So far we have stressed cytoarchitecture and relative location in the brain in seeking to relate brain regions across species. Another important source for comparison is *hodology*—the analysis of afferent and efferent structures of brain regions. Hodology has a particular importance in establishing homologies between brain structures from different species since it may provide indications of the functionalities of the structures being compared.

Since in the macaque there is no corresponding fiber tract for the human arcuate fasciculus, even though the fibers originating from the superior temporal gyrus toward the frontal and prefrontal cortices resemble it (Seltzer and Pandya, 1988), in order to evaluate the similarity criteria of afferent and efferent connection, one has to assess the similarities of the connections between Tpt and areas 44 and 45 in the macaque.

Several connectivity studies indicated the lack of connections from Tpt to the ventral part of the inferior arcuate sulcus (Aboitiz and García, 1997). Instead, the areas around the ventral part of the inferior arcuate sulcus receive input from the secondary auditory area ProA (Aboitiz and García, 1997). The tract tracing experiments performed by Petrides and Pandya (1988) showed that areas located around the inferior ramus of the arcuate sulcus receives connections from the auditory cortices Ts2 and Ts3, while the output of Tpt was mainly directed towards the dorsal parts of areas 6 and 8. However, several tract tracing experiments indicate the presence of connections from Tpt to the macaque homologues of Broca's area (Deacon, 1992; Petrides & Pandya, 2002). The retrograde tracing experiments performed by Deacon (1992) show that the ventrocaudal part of Tpt (i.e. that region of Tpt which is buried inside the STS) sends projections to the caudal part of the inferior ramus of the arcuate sulcus, which corresponds to area 44. Petrides and Pandya (2002) injected retrograde tracers in area 45. The patterns of labeled projections showed strong inputs from the auditory cortices and from the association areas from the superior temporal gyrus, including Tpt. The differences in results of the cited neuroanatomical experiments may be explained by differences in the tract tracing techniques employed. Retrograde fluorescent tracers are more sensitive than the radioactive amino acids and small injections of retrograde tracers may reveal specific patterns of connections of different subparts of the investigated areas. Other inputs which are of interest for this paper originated from the inferior parietal lobule areas PG and POa (Petrides & Pandya, 2002). The above mentioned tract tracing experiments show that at least those parts of Tpt which are neighboring or are inside the superior

temporal gyrus send projections to areas 45 and 44 as defined by Petrides and Pandya.

An additional set of connections that terminate in the inferior part of the arcuate sulcus and in those structures which are considered the homologues of Broca's area originate from areas of the inferior parietal lobule. Area 45 (GR) which corresponds to 45A (PP) receives connections from both inferior parietal areas 7a and 7b (Cavada & Goldman-Rakic, 1989a). Areas 7b as defined by Preuss and Goldman-Rakic (1991b) corresponds to areas PF and PFG (Petrides & Pandya, 2002; Rizzolatti & Luppino, 2001), and area 7a overlaps with area PG (Cavada & Goldman-Rakic, 1989a,b; Preuss & Goldman-Rakic, 1991b), while area POa partially corresponds to LIP, situated on the lateral bank of the intra-parietal sulcus (Seltzer and Pandya, 1986; Lewis & Van Essen, 2000a). Regarding the parietal inputs of macaque area 44, area F5 (M) receives connections from the anterior intra-parietal area (AIP), PF, PFG and PG (Luppino, Murata, Govoni, & Matelli, 1999; Luppino & Rizzolatti, 2000; Matelli et al., 1986; Rizzolatti & Luppino, 2001).

Since the minimal extent of the macaque homologue of human area 44 may be on the rostral sector of F5 (M), one should investigate the pattern of parietal projections which terminate in this part of F5. Recall that the region of F5 buried in the dorsal bank of the arcuate sulcus, F5ab, contains the canonical neurons, while the convexity located caudal to the arcuate sulcus, F5c, includes the mirror neurons. Retrograde tracers injected in the rostral part of F5 revealed projections from AIP to the caudal bank of the arcuate sulcus. In the parcellation scheme proposed by Lewis and Van Essen (2000a,b), 6Val and 6Vam are two agranular frontal areas that may correspond to area 44. Area 6Val appears to be caudal to the inferior part of the arcuate sulcus, while 6Vam is buried in the sulcus (Lewis & Van Essen, 2000a). 6Val receives major connections from AIP, while the major posterior parietal inputs of 6VAm originate from 7a and the dorsal sector of LIP (Lewis & Van Essen, 2000b). As noted earlier, one may dissociate the cortex bordering the sulcus from its caudal bank: AIP appears to project towards the cortex caudal to the sulcus and possibly towards the cortex buried in the sulcus, while connections from areas 7a and LIP may be characteristic for the bank of the arcuate sulcus. Since LIP is related to eye movements, one may speculate that LIP takes part in object localization to direct the reach that carries the grasp, with the shape of the grasp itself being attuned more to affordance input from AIP.

Analysis of the patterns of connections of macaque areas 44 and 45 show that the homologous structures of Broca's area receive connections from the auditory cortices, as well as from Tpt. The fiber tracts which originate from the auditory and association areas located in the superior temporal gyrus (especially its posterior part) and targeting different frontal and prefrontal cortices, appear to be organized and follow a course *somewhat* similar to the human arcuate fasciculus (Seltzer and Pandya, 1988). However, unlike those of the arcuate fasciculus, the fiber tracts originating from the superior temporal gyrus terminate on several prefrontal and frontal cortices, located rostral and dorsal to the macaque areas 44 and 45. Therefore, one may infer that in the macaque a rudiment of the arcuate fasciculus may exist. However, both its sources and termination sites appear to be more diversified than in human. This, together with the presence of major inputs from the posterior parietal areas suggest that, phylogenetically, the human arcuate fasciculus arose as a more specialized structure from a rather diffuse group of fibers connecting superior temporal gyrus with prefrontal and frontal areas in the macaques, possibly replacing or incorporating the posterior parietal inputs.

3.9. Summary of homologies

In this section we summarize the above discussion on similarities between the human language-related cortices and several macaque areas that are homology candidates.

While there is a wide consensus that the macaque homologue of human BA 22 (Wernicke's area in the strict sense) is Tpt, the process of identification of homologues of Broca's area is more complicated. Ontogenetic and topological criteria identify the possible homologues of the human areas 44 and 45 in the vicinity of the inferior part of the arcuate sulcus, namely the ventral agranular cortices F5. Moreover, functional similarities between the human and macaque structures of interest indicate that F5 may be the homologous structures of Broca's area. However, the structural analysis of macaque and human cortices indicate that the macaque homologues may be areas 44 and 45, located on either side of the inferior ramus of the arcuate sulcus. We consider in this paper the minimal extents of the macaque areas 44 and 45 to be those parts of the frontal and prefrontal cortices which most resemble the architectonics of Broca's area structurally, and there is a general consensus over their relative positions and cytoarchitecture. The minimal extent of the macaque area 45 is located in the rostral bank of the inferior arcuate sulcus, as defined by Petrides and Pandya and the minimal macaque area 44 is identical to F5. The analysis of hodology of these cortical areas shows that a macaque fiber tract corresponding to the arcuate fasciculus may exist, but it is not as conspicuous as the human tract, and both the sources and targets of projections are more diversified. Moreover, the connections between the inferior parietal lobule areas and areas 44 and 45 appear to be important in the macaque, while there is no information between any corresponding connections in human brains. Given this evidence, we hypothesize that the macaque homologues of Broca's area are areas 44 and 45 as considered in this paper. We also hypothesize that the macaque areas 44 and 45 are convergence points of the action recognition information conveyed by the connections with posterior parietal cortices with auditory information

from the superior temporal gyrus. In this sense, the results of Kohler et al. (2002) and Romanski and Gold-Rakic (2002) may indicate a functional dissociation of areas 44 and 45, area 44 being involved in processing spatially related auditory information in the context of action recognition process, while a possible role of area 45 may be in the non-spatial processing of auditory inputs.

We are, however, aware that more structural, neurophysiological and functional studies have to be performed both in humans and macaques, as well as great apes, in order to give a better account of the homologous structures of the human language-related structures across different primate species.

4. The NeuroHomology Database (NHDB)

Section 3 completes our introduction to an evolutionary account of the readiness of the human brain for language grounded in the theories of Aboitiz and García (1997) and Rizzolatti and Arbib (1998) and informed by the search for homologies between different cortical areas in macaque and human. Along the way, we have noted how computational modeling of large-scale neural networks and systems has informed our theorizing, helping situate our work with respect to the *Neuroinformatics* theme of this Special Issue of *Neural Networks*. In Section 4, we continue our contribution to *Neuroinformatics* by presenting the *NHDB*, the neuroinformatics framework we have constructed for the storing of data on brain regions and their connectivity in different species, for comparing results across different parcellations, and for extracting data from the database to assess the degrees of similarity and homology between brain regions of different species. Moreover, the NHDB provides inference engines for evaluation of the reliability of the connectivity information in the literature, and for translation of connectivity matrices in equivalent maps.

Before describing NHDB, a brief status report is necessary. Much of the data reviewed in this paper has already been entered into NHDB, but the present system is not yet powerful enough to serve as an 'automated assistant' for all the homology inferences summarized above. Nonetheless, we hope the reader will appreciate the synergy between the two efforts reported here: (i) the investigation of neurohomologies between macaque (and, in future, other primates and other species) to ground analysis of new models of the evolution of the language-ready brain, and (ii) the development of systems for the management of data on brain regions, their components and connections, including inference engines to support comparison and integration of data across different parcellation schemes and different species.

As seen through the user interface, the NHDB system contains three interconnected modules, *Brain Structures*, *Connections* and *Similarities*, which can be accessed independently. We have designed the web interface in independent parts to allow queries from a larger category of users. A user who wants to find if there is any homology between two structures, X and Y, from different species, can also inspect the definitions of X and Y found in different sources, as well as the pattern of connectivity of these two structures. They can also apply inference tools to evaluate the degree of similarity between two brain regions, to the extent that the necessary data have been entered into the database. Additionally, users can create their own profiles and manage the information for personal use.

NHDB has at present two online versions. NHDB-I contains a knowledge-base that allows the insertion of neurobiological data from the cellular to the structural level and has two inference engines for evaluation of connectivity information and of similarities between brain structures from different species. NHDB-I is designed in Microsoft Access and uses the WebMerger CGI parser engine as a web interface. It can be accessed online at the URL:

http://brancusi.usc.edu/scripts/webmerger.exe?/database/homologies-main.html

both to search for neurobiological information and for insertion of new data. However, NHDB-I does not address the problem of translation of the neurobiological data between different parcellation schemes, nor does it contain a scheme for encoding essential data at the cellular level of the nervous system. To remedy this, the second version of the system, NHDB-II, has a partially different structure that allows encoding of cellular data, and contains two inference engines designed for translation of connectivity data in different parcellation schemes. NHDB-II is designed in Informix 4.0 and uses the Illustra parser engine as a web interface. It can be accessed online at the URL:

http://java.usc.edu/neurohomologies/apb/webdriver?MIval = homologies-main.html

Each version of the NHDB system contains links to the other. NHDB-I contained as of mid-2002 about 500 reports of brain structures, more than 1000 reports of neuroanatomical connections and about 100 established similarities or homologies between brain structures from rats, macaques and humans. NHDB-II contains about 100 reports of brain structures and 200 reports of neuroanatomical connections. We plan to transfer all the information currently in NHDB-I to NHDB-II, but since NHDB-I has a series of modules that have not been replicated yet in NHDB-II, we currently regard these knowledge management systems as two separate entities with partially overlapping functionalities.

Several features of NHDB have been extended and refined in a new online KMS, the Brain Architecture Management System (BAMS; http://brancusi.usc.edu/bkms). BAMS allows complex searches of brain regions and projections and includes inference engines

for analyzing connections patterns and qualitative spatial relations between brain regions (Bota, Dong, & Swanson, 2003).

It is our hope that the previous sections will attract the attention of neuroanatomists and that the present section will interest them in the NHDB—and that as a result they will turn to the cited technical papers (Bota, 2001; Bota & Arbib, 2003) for further information, access the websites, raise further technical questions and *mirabile dictu* contribute new data and data analysis.

The object-relationship schema (OR) of NHDB is presented in Fig. 8. The OR is centered on the object *Brain Structure*, uniquely defined by three attributes: name, species where it was identified, and atlas used for identification. Each of the objects and relations shown in Fig. 8 is usually captured in more than a single table. Variables that are allowed to be inserted in the knowledge-base of the NHDB can be numerical, Boolean or text.

The relations of the attributes cell types (cytology), chemoarchitecture, myeloarchitecture and functionality with the Brain Structures are of the type $m : n$ (i.e. there may be more than one relatum on each side of the relation).

The chemoarchitecture refers to that set of chemicals which is specific to an object in Brain Structure. Since the cytology of a brain structure constitutes one of the most important criteria for describing it, we have designed a specific database structure to capture the characteristics of neural cells, as revealed by Golgi staining. The database schema designed to capture the features of neural cell types is general enough to allow the insertion of data pertaining to any class or subclass of neurons. Thus, we have included those morphological characteristics which can be used to define a generic neural cell as it is described in the literature. The full discussion of the knowledge-base schema for cytology can be found in Bota (2001).

The attribute 'Functions' of an object in 'Brain Structures' refers to neurophysiological responses of its cellular components, or behavioral correlates of the brain nucleus. The functionality of a brain structure is given the fields 'stimulus' and 'response'. By stimulus we refer to any type of employed perturbation (e.g. from neurophysiological stimulation of single neurons, to lesions, to temporary inactivation of brain structures by using local cooling techniques, to the action of specific drugs), and by response we refer to any type of change of activity recorded from the individual cells, or behavioral alterations due to lesions of brain structures.

'Annotations' can be attached to the inserted reference(s) that describe brain structures or any of the associated attributes, as well as statements associated to reports of brain nuclei and inserted online by users. Multiple annotations may be associated with any unique brain structure. The relationships between 'Brain Structures' and 'Collator', and 'References', respectively, are of the type $m : n$. A collator can insert information about many brain nuclei and data referring to a single brain structure can be inserted by different collators. The same is true for references: the information about a brain structure can be found in different references and a report can contain data referring to many structures.

We define four types of relationships inside NHDB: Hierarchy, Spatial Relations, Connections and Similarities:

The *hierarchy path* for each brain structure is the chain of brain parts—each containing the one that follows it, with no intervening structure, and which terminates with the region of interest. This is established on the basis of the reference that describes it, or inferred from a commonly used frame of reference (Bota & Arbib, 2001). The relationship 'Hierarchy' is of type $1 : n$ with the object Brain Structure since any nucleus has a unique hierarchy, but any brain structure can participate in many hierarchies for nuclei recorded in the system that are parts of the stated nucleus.

The relationship 'Spatial Relations' refers to the topological and directional relations between different brain structures as found, or inferred from, the literature,

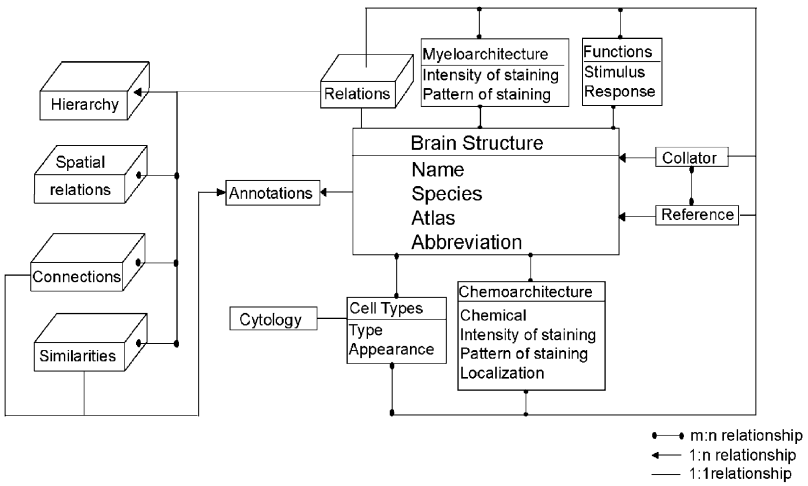

Fig. 8. The object-relationship schema (OR) of the NHDB systems.

or established from unrelated information by running the topological inference engine.

'*Connections*' refers to the knowledge-base that contains details about the neuroanatomical connections as found or inferred from the literature, and to the inference engines for evaluation of connections strengths and for translation of connectivity information in different atlases.

Finally, the relationship 'Similarities' refers to the knowledge base and the inference engine for evaluating the degree of similarity between brain structures from different species by taking into account eight different criteria. The descriptions of the inference engines and of the implemented algorithms can be found in Bota (2001 Bota & Arbib, 2000; Bota & Arbib, 2002, 2003).

4.1. Spatial relations between cortical structures in different maps

The qualitative topological and directional relations between different brain structures found in the literature may be augmented by running the topological inference engine. We have adapted the spatial inference algorithm of Egenhofer and Franzosa (1991) to processing topological relations between cortical structures. For them, the eight possible *topological relations* between a pair of 2D objects

$$U = \{\mathrm{d}, \mathrm{m}, \mathrm{o}, \mathrm{cv}, \mathrm{cvBy}, \mathrm{co}, \mathrm{isCo}, \mathrm{i}\},$$

are defined by: disjoint (d), meet (m), overlap (o), covers (cv), is covered (cvBy), contains (co), is contained or inside (isCo), and identical (i). The result of composition of topological relations need not yield an unequivocal answer (Egenhofer & Franzosa, 1991). Thus, if two objects A and B are in a topological relation t_1 and B and C in t_2, then the result of the topological composition between t_1 and t_2 can be a set of up to eight possible topological relations. To reduce the number of possible topological outcomes, additional qualitative information should be used.

The *directional relations* between two 2D objects can be given in terms of cardinal directions—Papadias (1994) and Sharma (1996) used

$$D_{\mathrm{n}} = \{\mathrm{N}, \mathrm{NE}, \mathrm{E}, \mathrm{SE}, \mathrm{S}, \mathrm{SW}, \mathrm{W}, \mathrm{NW}, \mathrm{Same}\}$$

The eight cardinal directions are used whenever the two related objects are either in a 'disjoint' or 'meet' topological relation. The directional relation 'Same' is applied whenever the related objects have a common interior. In order to apply qualitative spatial reasoning to infer spatial relations between cortical structures, we have replaced the geographical cardinal directions with the relative directions used in neuroanatomy. The interested user can find the full description of the spatial algorithm in Bota (2001) and Bota and Arbib (2003).

The knowledge-base for Spatial Relations stores topological and directional relations between brain structures as found, or inferred from, the associated references, as well as new directional relations resulted from the running of the spatial inference engine. Thus, the spatial relations between two cortical structures are inferred only once, when the query for establishing those is run for the first time. The result of the inference engine is recorded in the knowledge base of Spatial Relations and is retrieved whenever identical queries are run by users.

4.2. Translating neural connections across different parcellation schemes: the problem of multiple areas

As exemplified in Fig. 7, the parcellation schemes have been provided by different researchers can yield rather different cortical maps even for the same species. This leads to problems in the exact identification and assignment of different functions to specific brain structures. The reasons for different cortical maps are summarized as follows:

1. Different structural, chemoarchitectonical, hodological, and functional criteria are used by different researchers.
2. Even when the same criteria are used by two investigators, different maps may be proposed since some features may be recognized by one, but not by the other.
3. Naming and identification of a cortical structure in a species may be performed on the basis of putative homologies with structures in other species and we have seen that such homologies may be controversial.

We have inserted 23 topological and directional relations between 13 cortical structures from five atlases into the knowledge base of the NHDB. By running the spatial inference engine, we inferred 55 new topological relations between the structures considered. Bota (2001) has shown how the spatial reasoning system of NHDB can exploit such relationships to provide unambiguous results that have been independently confirmed in the literature, even in the case of limited direct information.

Users can perform online translations in the NHDB of the connectivity matrices of structures of interest by running the inference engine for translation of connectivity information in different neuroanatomical atlases. The algorithm for translation of connectivity matrices in different cortical maps is described in detail in (Bota, 2001). For example, we have used NHDB to reconstruct eight out of the nine connections of areas AIP, LIP and VIP with the premotor areas F4, F5 and F7 reported by Luppino and Rizzolatti (2000) by applying the NHDB system to translate connectivity reports collated from Andersen, Asanuma, Essick, and Siegel (1990), Cavada and Goldman-Rakic (1989a,b), Lewis and van Essen (2000b), and Preuss and Rakic (1991b). This demonstrates the power of NHDB in integrating reports on cortical connectivity even when the data are based on different parcellations.

An important feature of NHDB is its inference engine for evaluating the similarities between two brain structures from different species. We take into account eight different

Table 2
Summary of homologies

Human	Macaque	Similarity criteria	A&G	MSH
Area 44 (part of Broca's area)	F5	Relative position cytoarchitecture functionality	+(−)	+
Area 45 (part of Broca's area)	45b	Cytoarchitecture	+	−
Tpt (Wernicke's area, BA22)	Tpt	Relative position cytoarchitecture	+	+
?	7a		−	+
?	AIP		−	+
?	LIP		−	+

Column 1 human; column 2 our canonical parcellation of macaque; column 3 criteria used to ground the homology; column 4 + or − for agreement with A&G; Column 5 + or − for agreement with MSH.

criteria: relative position, cell types (cytology), chemoarchitecture, afferent and efferent connections, myeloarchitecture, functionality and superficial appearance. Each of the criteria is associated with specific attributes which are recorded in NHDB and we associate an *index of similarity* to each of those. The *overall degree of similarity* is then a function of the indexes of similarity defined for each of the homology criteria. A full discussion of the rationale for considering each of the criteria and the detailed formulas used by the inference engine can be found in Bota (2001) and Bota and Arbib (2003).

An intriguing aspect of the evaluation of the overall degree of similarity is related to the problem of recursion which is specific to the similarity criteria of relative position and hodology. The problem of recursion refers in this context to how similar are those structures which are related either spatially, or through fiber tracts, to the compared structures. The evaluation of the index of similarity for relative position and hodology depends on the overall degrees of similarity of those pairs of structures which are the common neighbors, or afferent or efferent nuclei, if there is information recorded in NHDB. Otherwise, the computation of the index of similarity associated with each of these homology criteria will depend on a bias parameter which represents an a priori evaluation of how similar are the related structures. An indirect source for the bias parameters is given by the phyologenetic trees constructed by using different set of characters. The phylogenetic tree we used to calculate the bias is a composite of those provided by Purvis (1995), Carroll (1997), Johnson et al. (1994), and Kirsch and Johnson (1983) (see Bota, 2001; Bota & Arbib, 2003 for details).

The information in the *Similarities* part of the NHDB system can be inspected online in two ways: browsing all the similarities in the knowledge-base at a given moment or searching the system for similarities by abbreviations of brain structures and species. The information which is retrieved when browsing similarities includes the abbreviations for the compared brain nuclei, the associated species, the common features, the reference and the collator, as well as the calculated overall degree of similarity. As for the other modules of the NHDB, users can access details of the associated references and of the collator, and insert personal annotations for each of the retrieved entries. Moreover, users may customize the similarities inference engine by changing the maximal number of common characters for homology criteria based on hodology, relative position, cell types and chemoarchitecture, and the values of indices of similarity for appearance, myeloarchitecture and functionality criteria. Users can also change the confidence levels of the tract tracing techniques which were used to reveal common patterns of afferent and efferent connections (Table 2).

5. Discussion

The paper sets forth a clear program of research in neurolinguistics, computational neuroscience and the further development of the NHDB. Basically, the results of human brain imaging will be best understood when they can be grounded in analysis of detailed circuitry. Such grounding can be of two kinds: (i) Relatively direct, where a human system may be posited to be 'directly homologous' (a high degree of homology) with a corresponding system in the macaque or other species (as in certain working memory systems for Aboitiz and García; and the mirror system for grasping for Rizzolatti and Arbib); and (ii) relatively indirect when a human system is 'somewhat related' (a low degree of homology) to some system in the macaque or, indeed, some system elsewhere in the human brain (consider parallels between different loops linking basal ganglia and cerebral cortex). In the former case, computational models of the neural networks of the human system can be based rather directly on models of the homologous macaque system; in the latter case, partial homologies can be used to define a search space of models which can then be tested by synthetic brain imaging. In each case, we need neuroinformatics to develop in a fashion which more tightly integrates modeling with databases (Bischoff-Grethe, Spoelstra, & Arbib, 2001) to allow the more effective integration of data from neuroanatomy, neurophysiology, brain imaging, and all the other modalities we have seen as helpful in providing criteria for the establishment of degrees of homology. The resultant cross-species framework will

allow progress in understanding the neural mechanisms of language (and diverse other cognitive processes) that would be impossible with too narrow a focus on the data of human brain imaging alone. This paper is just the beginning.

References

Aboitiz, F., & García, V. R. (1997). The evolutionary origin of the language areas in the human brain. A neuroanatomical perspective. *Brain Research Reviews*, *25*, 381–396.

Amunts, K., Schleicher, A., Burgel, U., Mohlberg, H., Uylings, H. B. M., & Zilles, K. (1999). Broca's region revisited: cytoarchitecture and intersubject variability. *Journal of Comparative Neurology*, *412*, 319–341.

Andersen, R. A., Asanuma, C., Essick, G., & Siegel, R. M. (1990). Corticocortical connections of anatomically and physiologically defined subdivisions within the inferior parietal lobule. *Journal of Comparative Neurology*, *296*(1), 65–113.

Arbib, M. A. (2001). The mirror system hypothesis for the language-ready brain. In C. Angelo, & P. Domenico (Eds.), *Computational approaches to the evolution of language and communication* (pp. 229–254). Berlin: Springer, Chap. 11.

Arbib, M. A. (2002). The mirror system, imitation, and the evolution of language. In N. Chrystopher, & D. Kerstin (Eds.), *Imitation in animals and artifacts* (pp. 229–280). Cambridge, MA: The MIT Press.

Arbib, M. A., Billard, A., Iacoboni, M., & Oztop, E. (2000). Synthetic brain imaging: grasping, mirror neurons and imitation. *Neural Networks*, *13*, 975–997.

Arbib, M. A., Bischoff, A., Fagg, A., & Grafton, S. (1995). Synthetic PET: analyzing large-scale properties of neural networks. *Human Brain Mapping*, *2*, 225–233.

Arbib, M. A., & Grethe, J. S. (Eds.), (2001). *Computing the brain: A guide to neuroinformatics*. San Diego: Academic Press.

Armstrong, D., Stokoe, W., & Wilcox, S. (1995). *Gesture and the Nature of Language*. Cambridge University Press, Cambridge, Massachusetts.

Bailey, P., & von Bonin, G. (1951). *The isocortex of the man*. Urbana, IL: University of Illinois Press.

Binkofski, F., et al. (1999). A fronto-parietal circuit for object manipulation in man: evidence from an fMRI study. *European Journal of Neuroscience*, *11*, 3276–3286.

Bischoff-Grethe, A., Spoelstra, J., & Arbib, M. A. (2001). Brain models on the web and the need for summary data. In M. A. Arbib, & J. Grethe (Eds.), *Computing the brain: A guide to neuroinformatics* (pp. 287–296). New York: Academic Press.

von Bonin, G. (1949). Architecture of the precentral motor cortex and some adjacent areas. In P. C. Bucy (Ed.), *The precentral cortex* (pp. 83–110). Urbana, IL: The University of Illinois Press.

von Bonin, G., & Bailey, P. (1947). *The neocortex of Macaca mulatta*. Urbana, IL: University of Illinois Press.

Bota, M., (2001). *Neural homologies: principles, databases and modeling*. PhD Thesis, University of Southern California.

Bota, M., & Arbib, M. A. (2001). The NeuroHomology Database. In M. A. Arbib, & J. Grethe (Eds.), *Computing the brain: A guide to neuroinformatics* (pp. 337–351). New York: Academic Press.

Bota, M., & Arbib, M. A. (2002). The NeuroHomology Database: an online KMS for handling and evaluation of the neurobiological information. In R. Kotter (Ed.), *Neuroscience databases: A practical guide* (pp. 203–220). Dordrecht: Kluwer.

Bota, M., & Arbib, M. A. (2003). Integrating databases and expert systems for the analysis of brain structures: connections, similarities and homologies. *Neuroinformatics*, in press.

Bota, M., Dong, H.-W., & Swanson, L. W. (2003). From gene networks to brain networks. *Nature Neuroscience*, *6*, 795–799.

Brodmann, K. (1909). *Vergleichende lokalisationlehre der grosshinrindein ihren prinzipien dargestellt auf grund des zellenbaues*. Leipizg: Barth.

Bruce, C. J. (1988). Single neuron activity in the monkey's prefrontal cortex. In P. Rakic, & W. Singer (Eds.), *Neurobiology of neocortex* (pp. 297–329). Chichester, NY: Wiley.

Bruce, C. J., Goldberg, M. E., Bushnell, M. C., & Stanton, G. B. (1985). Primate frontal eye fields. II. Physiological and anatomical correlates of electrically evoked eye movements. *Journal of Neurophysiology*, *54*(3), 714–734.

Buccino, G., et al. (2001). Action observation activates premotor and parietal areas in a somatotopic manner: an fMRI study. *European Journal of Neuroscience*, *13*, 400–404.

Butler, A. B., & Hodos, W. (1996). *Comparative vertebrate neuroanatomy: evolution and adaptation*. New York: Wiley-Liss, 7–13.

Cadoret, G., Bouchard, M., & Petrides, M. (2000). Orofacial representation in the rostral bank of the inferior ramus of the arcuate sulcus of the monkey. *Society of Neuroscience Abstracts*, *26*, 680 (Abstract no. 253.13).

Campbell, C. B., & Hodos, W. (1970). The concept of homology and the evolution of the nervous system. *Brain Behav Evol.*, *3*(5), 353–367.

Carroll, R. L. (1997). *Patterns and processes of vertebrate evolution.* Cambridge University Press.

Cavada, C., & Goldman-Rakic, P. S. (1989). Posterior parietal cortex in rhesus macaque. I. Parcellation of areas based on distinctive limbic and sensory corticocortical connections. *Journal of Comparative Neurology*, *287*(4), 393–421.

Cavada, C., & Goldman-Rakic, P. S. (1989). Posterior parietal cortex in rhesus macaque. II. Evidence for segregated corticocortical networks linking sensory and limbic areas with the frontal lobe. *Journal of Comparative Neurology*, *287*(4), 422–445.

Cheney, L., & Seyfarth, R. M. (1990). *How monkeys see the world*. Chicago: University of Chicago Press.

Code, C. (1998). Models, theories and heuristics in apraxia of speech. *Clinical Linguistics and Phonetics*, *12*, 47–65.

Deacon, T. W. (1992). Cortical connections of the inferior arcuate sulcus cortex in the macaque brain. *Brain Res.*, *573*(1), 8–26.

Deacon, T. W. (1997). *The symbolic species: The co-evolution of language and the brain*. New York: W.W. Norton.

Deacon, T. W. (2003). The hierarchic logic of emergence: untangling the interdependence of evolution and self-organization. In B. Weber, & D. Depew (Eds.), *Evolution and learning: The baldwin effect reconsidered*. Cambridge, MA: The MIT Press, Chap. 14.

DeRenzi, E., Pieczuro, A., & Vignolo, L. A. (1966). Oral apraxia and aphasia. *Cortex*, *2*, 50–73.

Von Economo, C., & Koskinas, G. N. (1925). *Die Cytoarchitektonik der Hirnrinde des erwachsenen Menschen*. Berlin: Springer Verlag.

Egenhofer, M., & Franzosa, R. (1991). Point-set topological spatial relations. *International Journal of Geographical Information Systems*, *5*(2), 161–174.

Fagg, A. H., & Arbib, M. A. (1998). Modeling parietal-premotor interactions in primate control of grasping. *Neural Networks*, *11*, 1277–1303.

Foerster, O. (1936). *Brain*, *59*, 135–159.

Fogassi, L., Gallese, V., Fadiga, L., & Rizzolatti, G. (1998). Neurons responding to the sight of goal directed hand/arm actions in the parietal area PF (7b) of the macaque monkey. Soc. Neurosci. Abstr. 24, 257.

Fuster, J. M. (1995). *Memory in the cerebral cortex*. Cambridge: MIT Press.

Galaburda, A. M. (1984). Anatomical asymmetries. In N. Geschwind, & A. M. Galaburda (Eds.), *Cerebral dominance: the biological foundations*. Cambridge, MA: Harvard University Press.

Galaburda, A. M., & Pandya, D. N. (1983). The intrinsic architectonic and connectional organization of the superior temporal region of the rhesus monkey. *Journal of Comparative Neurology*, *221*(2), 169–184.

Galaburda, A. M., & Sanides, F. (1980). Cytoarchitectonic organization of the human auditory cortex. *Journal of Comparative Neurology*, *190*(3), 597–610.

Geschwind, N. (1964). The development of the brain and the evolution of language. *Monograph Series in Language and Linquistics*, *1*, 155–169.

Goldman-Rakic, P. S. (1987). Circuitry of the prefrontal cortex and the region of behavior by representational knowledge. In F. Blum, & V. Mountcastle (Eds.), *Handbook of physiology* (pp. 373–417). Bethesda, MD: American Physiological Society.

Goldman-Rakic, P. S. (1995b). Architecture of the prefrontal cortex and the central executive. *Annals of New York Academy of Science*, *769*, 71–83.

Gould, S. J. (1975). Allometry in primates, with emphasis on scaling and the evolution of the brain. *Contributions in Primatology*, *5*, 244–292.

Hewes, G. (1973). Primate communication and the gestural origin of language. *Current Anthropology*, *14*, 5–24.

Jeannerod, M., Arbib, M. A., Rizzolatti, G., & Sakata, H. (1995). Grasping objects: the cortical mechanisms of visuomotor transformation. *Trends Neurosci.*, *18*, 314–320.

Jeannerod, M., Decety, J., & Michel, F. (1994). Impairment of grasping movements following a bilateral posterior parietal lesion. *Neuropsychologia*, *32*(4), 369–380.

Jerison, H. J. (1976). The paleoneurology of language. *Annals of New York Academy of Science*, *280*, 370–382.

Jerison, H. J. (1985). Animal intelligence as encephalization. *Philosophical Transactions of the Royal Society of London. Series B: Biological Science*, *308*(1135), 21–35.

Johnson, J. I., Kirsch, J. A., Reep, R. L., & Switzer, R. C. 3rd (1994). Phylogeny through brain traits: more characters for the analysis of mammalian evolution. *Brain, Behavior and Evolution*, *43*(6), 319–347.

Jürgens, U. (1997). *Primate communication: signaling, vocalization* (2nd ed). *Encyclopedia of neuroscience*, Amsterdam: Elsevier.

Kimura, D. (1993) *Neuromotor Mechanisms in Human Communication* (Oxford Pshychology Series No. 20). Oxford University Press/ Clarendon Press, Oxford, New York.

Kirsch, J. A., & Johnson, J. I. (1983). Phylogeny through brain traits: trees generated by neural characters. *Brain, Behavior and Evolution*, *22*(2–3), 60–69.

Kohler, E., Keysers, C., Umilta, M. A., Fogassi, L., Gallese, V., & Rizzolatti, G. (2002). Hearing sounds, understanding actions: action representation in mirror neurons. *Science*, *297*, 846–848.

Lewis, J. W., & Van Essen, D. C. (2000a). Corticocortical connections of visual, sensorimotor, and multimodal processing areas in the parietal lobe of the macaque. *Journal of Comparative Neurology*, *428*(1), 112–137.

Lewis, J. W., & Van Essen, D. C. (2000b). Mapping of architectonic subdivisions in the macaque, with emphasis on parieto-occipital cortex. *Journal of Comparative Neurology*, *428*(1), 79–111.

Luppino, G., Murata, A., Govoni, P., & Matelli, M. (1999). Largely segregated parietofrontal connections linking rostral intraparietal cortex (areas AIP and VIP) and the ventral premotor cortex (areas F5 and F4). *Experimental Brain Research*, *128*(1–2), 181–187.

Luppino, G., & Rizzolatti, G. (2000). The organization of the frontal motor cortex. *News Physiological Sciences*, 219–224.

Luppino, G., & Rizzolatti, G. (2001). The cortical motor system. *Neuron*, *31*(6), 889–901.

Marquardt, T. P., & Sussman, H. (1984). The elusive lesion—apraxia of speech link in Broca's aphasia. In J. C. Rosenbek, M. R. McNeil, & A. E. Aronson (Eds.), *Apraxia of speech: Physiology, acoustics, linguistics, management*. San Diego: College-Hill Press.

Matelli, M., Camarda, R., Glickstein, M., & Rizzolatti, G. (1986). Afferent and efferent projections of the inferior area 6 in the macaque. *Journal of Comparative Neurology*, *251*(3), 281–298.

Matelli, M., & Luppino, G. (1992). *Experimental Brain Research Supplement*, *22*, 85–102.

Matelli, M., Luppino, G., & Rizzolatti, G. (1985). Patterns of cytochrome oxidase activity in the frontal agranular cortex of the macaque. *Behavioural Brain Research*, *18*, 125–137.

Matelli, M., Luppino, G., & Rizzolatti, G. (1991). Architecture of superior and mesial area 6 and the adjacent cingulate cortex in the macaque. *Journal of Comparative Neurology*, *311*(4), 445–462.

Nieuwenhuys, R. (1999). The morphological pattern of the vertebrate brain. *European Journal of Neuroscience*, *37*(2/3), 81–84.

Northcutt, R. G. (1999). Field homology: a meaningless concept. *European Journal of Morphology*, *37*(2-3), 95–99.

Ono, M., Kubik, S., & Abernathey, C. D. (1990). *Atlas of the cerebral sulci*. Stuttgart: Thieme Medical Publishers.

Oztop, E., & Arbib, M. A. (2002). Schema design and implementation of the grasp-related mirror neuron system. *Biological Cybernetics*, *87*(2), 116–140.

Oztop, E., Bradley, N., Arbib, M. A (2003). *Learning to grasp. I. The infant learning to grasp model (ILGM)* (in press).

Pandya, D. N., & Yeterian, E. H. (1996). Comparison of prefrontal architecture and connections. *Philosophical Transactions of the Royal Society of London. Series B: Biological Science*, *351*(1346), 1423–1432.

Paxinos, G., Huang, X.-F., & Toga, A. W. (2000). *The rhesus monkey brain in stereotaxic coordinates*. San Diego: Academic Press.

Perrett, D. I., Mistlin, A. J., Harries, M. H., & Chitty, A. J. (1990). Understanding the visual appearance and consequence of hand actions. In M. A. Goodale (Ed.), *Vision and action: The control of grasping* (pp. 163–342). Norwood, NJ: Ablex.

Petrides, M., & Pandya, D. N. (1984). Projections to the frontal cortex from the posterior parietal region in the rhesus macaque. *Journal of Comparative Neurology*, *228*(1), 105–116.

Petrides, M., & Pandya, D. N. (1988). Association fiber pathways to the frontal cortex from the superior temporal region in the rhesus monkey. *J Comp Neurol.*, *273*(1), 52–66.

Petrides, M., & Pandya, D. N. (1994). In F. Boller, & J. Graham (Eds.), *Comparative architectonic analysis of the human and macaque frontal cortex* (*Vol. 9*) (pp. 17–58). *Handbook of neuropsychology*, Amsterdam: Elsevier.

Petrides, M., & Pandya, D. N. (2002). Comparative cytoarchitectonic analysis of the human and the macaque ventrolateral prefrontal cortex and corticocortical connection patterns in the macaque. *European Journal of Neuroscience*, *16*(2), 291–310.

Petrides, M., Paxinos, G., Huang, X.-F., Morris, R., & Pandya, D. M. (1999). A delineation of the monkey cortex on the basis of the distribution of the neurofilament protein. In G. Paxinos, et al. (Eds.), *The rhesus monkey brain in stereotaxic coordinates*. San Diego: Academic Press.

Preuss, T. M., & Goldman-Rakic, P. S. (1991a). Architectonics of the parietal and temporal association cortex in the strepsirhine primate Galago compared to the anthropoid primate Macaca. *Journal of Comparative Neurology*, *310*(4), 475–506.

Preuss, T. M., & Goldman-Rakic, P. S. (1991b). Myelo- and cytoarchitecture of the granular frontal cortex and surrounding regions in the strepsirhine primate Galago and the anthropoid primate Macaca. *Journal of Comparative Neurology*, *310*(4), 429–474.

Preuss, T. M., Stepniewska, I., & Kaas, J. H. (1996). *Journal of Comparative Neurology*, *371*, 649–676.

Puelles, L., & Medina, L. (2002). Field homology as a way to reconcile genetic and developmental variability with adult homology. *Brain Research Bulletin*, *57*(3/4), 243–255.

Purvis, A. (1995). A composite estimate of primate phylogeny. *Philosophical Transactions of the Royal Society London. Series B: Biological Sciences*, *348*(1326), 405–421.

Rizzolatti, G., & Arbib, M. A. (1998). Language within our grasp. *Trends in Neurosciences*, *21*(5), 188–194.

Rizzolatti, G., Fogassi, L., & Gallese, V. (2002). Motor and cognitive functions of the ventral premotor cortex. *Current Opinion Neurobiology*, *12*(2), 149–154.

Rizzolatti, G., & Luppino, G. (2001). The cortical motor system. *Neuron*, *31*, 889–901.

Rizzolatti, G., & Luppino, G. (2003). Grasping movements: visuomotor transformations. In M. A. Arbib (Ed.), *The handbook of brain theory and neural networks* (2nd ed) (pp. 501–504). Cambridge, MA: The MIT Press.

Rizzolatti, G., Luppino, G., & Matelli, M. (1998). The organization of the cortical motor system: new concepts. *Electroencephalograph Clinical Neurophysiology*, *106*(4), 283–296.

Rolls, E. T., & Arbib, M. A. (2003). Visual scene perception. In M. A. Arbib (Ed.), *The handbook of brain theory and neural networks* (2nd ed) (pp. 1210–1215). Cambridge, MA: The MIT Press.

Romanski, L. M., & Goldman-Rakic, P. S. (2002). An auditory domain in primate prefrontal cortex. *Nature Neuroscience*, *5*(1), 15–16.

Schall, J. D., Morel, A., King, D. J., & Bullier, J. (1995). Topography of visual cortex connections with frontal eye field in macaque: convergence and segregation of processing streams. *Journal of Neuroscience*, *15*(6), 4464–4487.

Semendeferi, K., Lu, A., Schenker, N., & Damasio, H. (2002). Humans and great apes share a large frontal cortex. *Nature Neuroscience*, *5*, 272–276.

Sharma, J (1996). *Integrated spatial reasoning in geographic information systems: combining topology and direction*. PhD Thesis, University of Main.

Stanton, G. B., Deng, S. Y., Goldberg, M. E., & McMullen, N. T. (1989). Cytoarchitectural characteristic of the frontal eye fields in macaque monkeys. *Journal of Comparative Neurology*, *282*(3), 415–427.

Stokoe, W. C. (2001). *Language in hand: Why sign came before speech*. Washington, DC: Gallaudet University Press.

Striedter, G. F. (1999). Homology in the nervous system: of characters, embryology and levels of analysis. *Novartis Foundation Symposium*, *222*, 158–170.

Suzuki, H., & Azuma, M. (1983). Topographic studies on visual neurons in the dorsolateral prefrontal cortex of the monkey. *Experimental Brain Research*, *53*, 47–58.

Tagamets, M. A., & Horwitz, B. (1998). Integrating electrophysiological and anatomical data to create a large-scale model that simulates a delayed match-to-sample human brain imaging study. *Cerebral Cortex*, *8*, 310–320.

Tagamets, M. -A., & Horwitz, B., (2003). Synthetic Functional Brain Mapping, in *The Handbook of Brain Theory and Neural Networks*, (M. A. Arbib, Ed.), Second Edition, Cambridge, MA: A Bradford Book/The MIT Press, pp. 1146–1151.

Vogt, C., & Vogt, O. (1919). Allgemeinere ergebnisse unserer hirnforschung. *Journal of Psychological Neurology*, *25*, 279.

Vogt, C., & Vogt, O. (1926). *Naturwissenschaften*, *14*, 1190–1194.

Walker, A. E. (1940). *Journal of Comparative Neurology*, *262*, 256–270.

Webster, M. J., Bachevalier, J., & Ungerleider, L. G. (1994). Connections of inferior temporal areas TEO and TE with parietal and frontal-cortex in macaque monkeys. *Cerebral Cortex*, *4*(5), 470–483.

Wilkins, W. K., & Wakefield, J. (1995). Brain evolution and neurolinguistic preconditions. *Behavioral and Brain Sciences*, *18*, 161–226.

Wilson, F. A. W., Ó Scalaide, S. P., & Goldman-Rakic, P. S. (1993). Dissociation of object and spatial processing domains in primate prefrontal cortex. *Science*, *260*, 1955–1958.

Winter, P., Handley, P., Ploog, D., & Schott, D. (1973). Ontogeny of squirrel monkey calls under normal conditions and under acoustic isolation. *Behaviour*, *47*, 230–239.