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Feature Review

Dual Neural Network Model for the Evolution of Speech and Language

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Explaining the evolution of speech and language poses one of the biggest challenges in biology. We propose a dual network model that posits a volitional articulatory motor network (VAMN) originating in the prefrontal cortex (PFC; including Broca's area) that cognitively controls vocal output of a phylogenetically conserved primary vocal motor network (PVMN) situated in subcortical structures. By comparing the connections between these two systems in human and nonhuman primate brains, we identify crucial biological preadaptations in monkeys for the emergence of a language system in humans. This model of language evolution explains the exclusiveness of non-verbal communication sounds (e.g., cries) in infants with an immature PFC, as well as the observed emergence of non-linguistic vocalizations in adults after frontal lobe pathologies.

Trends

A dual-network model for the evolution of language is proposed that consists of two interacting brain networks.

A phylogenetically conserved PVMN produces genetically predetermined vocalizations in nonhuman primates and non-verbal vocalizations in humans.

During the course of primate evolution, an additional VAMN in the lateral frontal lobe (including Broca's area) emerges that cognitively controls vocal output.

In humans, the VAMN gains control over articulation by modulating the output of the PVMN.

The new VAMN also plays a vital role in establishing semantics and syntax, two hallmark characteristics of symbol systems in humans.

The Apparent Discrepancy

Few questions in biology are as difficult and controversial as the evolution of human **speech** and **language**, and the emergence of essential speech and language brain structures such as Broca's area in the lateral frontal lobe. This is because human language vastly outperforms any primate communication system in scope and flexibility [1–3], with seemingly no counterpart in the animal kingdom, even among hominids. The vocalizations of nonhuman primates are largely innate, stereotypic, and were thought to be almost exclusively uttered affectively (Box 1) [4,5]. Humans, on the other hand, learn speech sounds, use them flexibly in combinatorial symbol systems, and can volitionally control their utterances.

This apparent discrepancy between monkey vocalization and human language is also reflected in traditionally disparate research agendas. On the one hand, neurobiologists have meticulously deciphered the neural pathways causing nonverbal vocal output in monkeys. This body of work has identified different numbers of primarily subcortical pathways that allow nonhuman primates to produce innate vocalizations. However, cortical association areas that are of paramount importance to human language production, such as Broca's area in the inferior frontal lobe, have not been assumed to play a part in it. Cognitive neuroscientists, on the other hand, usually focus on the linguistic **articulation** network and strive to understand how Broca's area allows humans to structure **semantic** verbal expressions. How the language executive associated with Broca's area becomes coupled to the necessary vocal machinery in the brainstem and how it can emerge throughout evolution has largely been neglected. Occasionally, links between Broca's area and the primate vocal pathways have been suspected but remained speculative as a consequence of lacunae in neurobiological data [5–8].

This review tries to bridge this gap by integrating novel insights about vocalizations in monkeys as well as verbal and nonverbal output in humans. We review recent behavioral, anatomical, and

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Box 1. Monkey Vocalization

While human speech is above all a learned vocal pattern, the vocal motor system of non-human primates consists mainly of stereotyped and largely innate calls that are almost exclusively uttered affectively [2,5]. These assumptions are mainly bolstered by so-called 'Kaspar Hauser' experiments as well as by deafening and lesion studies. In these experiments, squirrel monkeys were raised without auditory feedback from conspecifics, by either hand-raising them or by muting the mother. These monkeys still produced the complete species-specific vocal repertoire and used it in the appropriate motivational and social contexts [177,178]. Deaf-born or deafened monkeys showed similar call patterns as their normal-hearing conspecifics, with only minor changes in call frequency and amplitude [178,179]. Finally, several studies in Old World and New World monkeys observed no differences in vocal pattern production after lesioning brain structures that are homologs to the brain regions that are crucial for speech production in humans [18,35–37].

However, several behavioral studies report that monkeys are able to **volitionally initiate vocal output** and instrumentalize their calls in a goal-directed (adaptive) way. Non-human primates are able to produce a vocalization or remain silent when submitted to operant conditioning tasks [65,76,84,180–183]. These studies support field studies showing that non-human primates vocalize in different ways when addressing different individuals [184], and produce or withhold alarm calls depending on the social context [185]. Therefore, calls might encode the vocalizing individual's information about the presence of a predator [185], the behavior of other individuals [186], or specific external events [187]. In a recent study we demonstrated that rhesus monkeys are able to selectively emit different call types in response to distinct visual cues [86]. Furthermore, several studies observed volitional changes of vocal parameters such as vocal duration, amplitude, and frequency within the natural constraints [33,84–86]. These results indicate that monkeys have rudimentary control over specific acoustic call parameters. In addition, recent work on highly-vocal marmoset monkeys has revealed dynamics in auditory perception of vocalizations [188], vocal flexibility [189], and some evidence of auditory comprehension learning [190,191]. Overall, these results indicate that monkeys are capable of some types of vocal learning, in other words they are able to cognitively control the onset of their vocal output and to modify their vocal patterns within the range of their natural repertoire.

Glossary

Articulation: complex movements of the cranial muscles (facial, lip, tongue, jaw) to alter a basic tone, which is produced by the vocal folds, into decodable sounds.
Grammar: rules that govern how words can be combined to form sentences.
Language: a generative symbol-system to generate infinite meanings (semantics) based on a finite set of rules (syntax) (and usually is used to communicate).
Limbic network: complex network of brain structures including ACC, hypothalamus, amygdala and several other structures that seem to be primarily responsible for emotion and that participate in memory formation and learning.
Motor/central pattern generator: a neuronal circuit that produces motor commands such as vocalizations. Pattern generators produce distinct outputs even in isolation from motor and sensory feedback.
Pyramidal tract: direct projections from neurons in the primary motor cortex to interneurons and motoneurons in the brainstem (corticobulbar tract) or the spinal cord (corticospinal tract).
Semantic: meaning of linguistic expressions.
Speech: human speech is the ability to cognitively control and produce a series of arbitrary complex articulatory movements.
Volitional vocal initiation: ability to vocalize in response to abstract, learned sensory stimuli in a goal-directed manner.

physiological findings suggesting that monkeys possess the rudiments to cognitively control their vocal output so as to develop a neurobiological scaffold for language evolution in primates. Cognitive or executive control – the ability to orchestrate thought and action in accordance with internal goals [9] – is an obligatory precursor for speech and language production. Over the course of primate evolution, executive control structures residing in the PFC gradually became coupled to ancient vocal pattern-generating and **limbic networks**. By comparing and contrasting the corticocortical and corticosubcortical connections relevant for human speech and language production with those present in nonhuman primates for vocalizations, we identify crucial biological preadaptations for the emergence of a full-blown language system. Based on these findings, we suggest a dual-network model of speech and language evolution that accounts for the observation that the humble beginnings of the structural and functional evolution of a cortical speech and language system can already be observed in nonhuman primates. This model integrates seemingly disparate neurobiological findings in human and nonhuman primates and attempts to provide a conceptual framework of how speech and language might have arisen during primate evolution.

The PVMN for Innate Primate Vocalizations

All primates possess a PVMN that produces genetically predetermined vocalizations in nonhuman primates and non-verbal vocalizations in humans. This PVMN consists of two structurally and functionally distinct parts: a vocal pattern-generating system in the brainstem, and an upstream limbic vocal-initiating network driving the **pattern generator** based on affective states (Figure 1A,B) [4,5,10].

The core of the PVMN, the brainstem vocal pattern-generating system is highly conserved in all vertebrate taxa [11], and mainly consists of the interconnected areas periaqueductal grey (PAG), parabrachial nucleus (PB), and ventrolateral pontine reticular formation; the latter controls all phonatory motoneuron pools (nuclei of cranial nerves V, VII, XII; ambigual nucleus) which, in addition to controlling the musculature of the respiratory system, also innervate the muscles of the larynx, oral cavity, and tongue to produce the actual vocal sound (Figure 1A,B) [5,12–16].

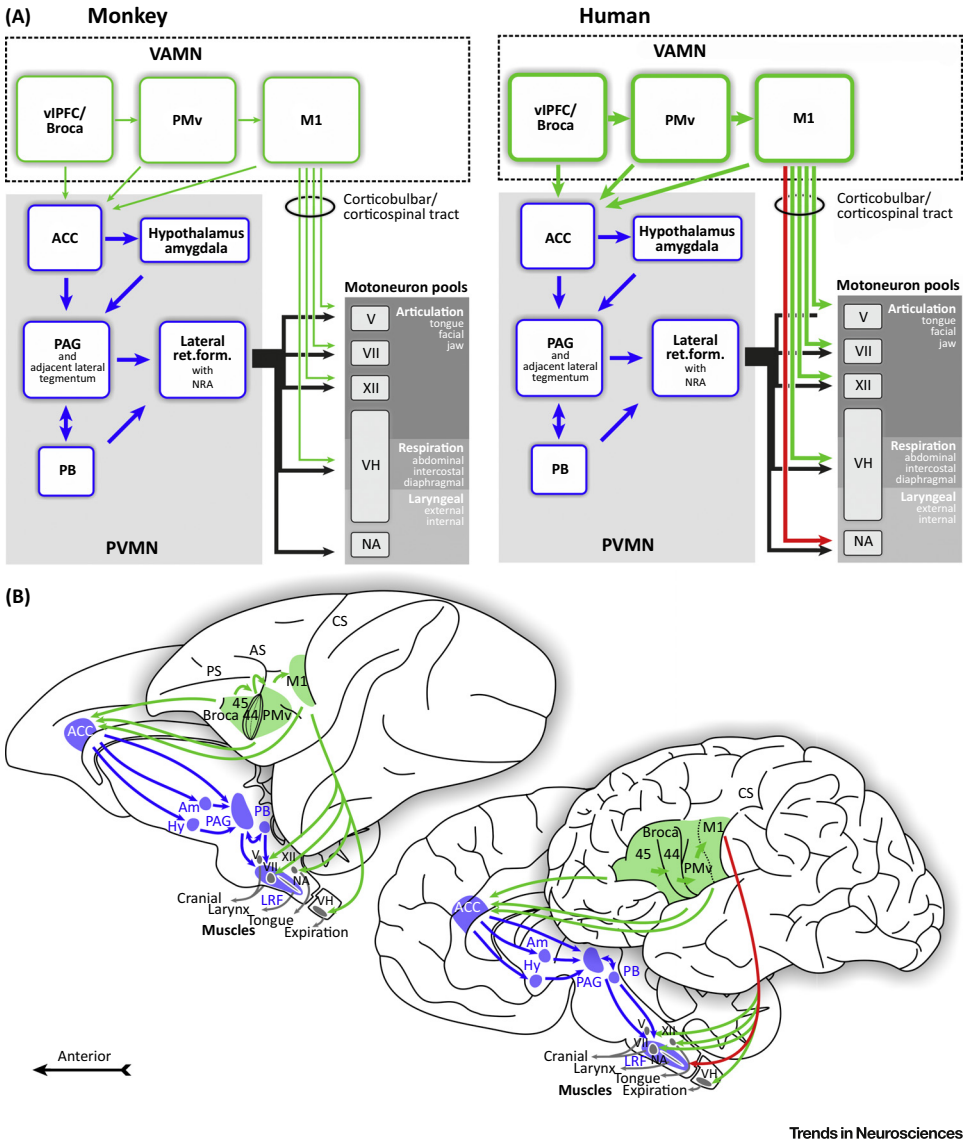


Figure 1. Dual-Network Model. (A) Simplified circuit diagram summarizing the most relevant structures for vocal production in monkeys and speech in humans. Arrows indicate anatomically verified and relevant direct connections. The VAMN (indicated in green) is capable of initiating and modulating vocal production in monkeys during cognitive control of vocal onset, or the modulation of vocal patterns within natural constraints. These connections are enhanced during speech evolution in the primate lineage. (B) Anatomical locations and connections of the structures comprising the dual-network in monkeys (left) and humans (right). Lateral (front) and medial (back) views of the endbrain hemispheres are shown. Regions and arrows shaded in blue indicate the structures of the PVMN. Regions and arrows shaded in green depict cortical areas involved in the VAMN. Red arrow indicates the direct connection between the larynx area of the primary motor cortex with the ambigual nucleus as a new development in the human lineage (adapted from [4,67,200]). Abbreviations: Am, amygdala; ACC, anterior cingulate cortex; AS, arcuate sulcus; CS, central sulcus; Hy, hypothalamus; LRF, lateral reticular formation; M1, ventral primary motor cortex; NA, ambigual nucleus; NRA, retroambigual nucleus; PAG, periaqueductal grey; PB, parabrachial nucleus; PMv, ventral premotor cortex; PS, principal sulcus; PVMN, primary vocal motor network; VH, respiratory motorneuron pools in the ventral horn of the spinal tract; V, motor trigeminal nucleus; VAMN, volitional articulatory motor network; VI,I facial nucleus; XII, hypoglossal nucleus.

The pivotal role of these brainstem structures has been deciphered based on electrophysiological recording, stimulation, and lesion studies in monkeys. In all of these brainstem areas, neurons show vocalization-related neuronal activity [13,15,17–19]. Electrical and chemical stimulation of the PAG reliably elicits distinct calls of the complete species-specific vocal repertoire in monkeys [20,21], whereas lesioning PAG results in mutism [22,23]. In contrast to the more general (or global) function of the PAG in producing calls, the PB is involved in the gating of vocal onset on

the basis of the momentary respiratory status [5] because electrical stimulation of the PB produces only simple vocalizations [20,24], and PB lesions uncoupled respiratory rhythms from laryngeal activity during vocalizations elicited via PAG stimulation [23].

This brainstem vocal pattern-generating system is controlled by a limbic vocal-initiating network that projects to the PAG and the entire PVMN to elicit vocalizations representing affective states. Its most important structures comprise a vocalization region in the anterior cingulate cortex (ACC) around the rostrum of the corpus callosum (including parts of areas 24, 25, and 32), the hypothalamus, other limbic diencephalic structures (such as the septum and the subcallosal gyrus), and the amygdala [23,25,26]. Electrical stimulation in all of these limbic structures including ACC elicits vocal utterances [20,27–29]. However, vocal latencies relative to stimulation onset were much longer (>1 s) compared to response latencies in PAG (<1 s) [20], suggesting that ACC and other limbic structures are coupled to, but are not part of, the pattern generator. In contrast to PAG stimulation, stimulation of most limbic structures could only elicit a subset of call types of the species-specific call repertoire. For example, vocalization with hedonistic quality can be elicited in the septum, while stimulation sites in the amygdala elicited more-aversive vocal utterances [20,30,31].

Bilateral ablations of the cingulate vocalization region have either no consistent effect on spontaneous vocal behavior [32–34], and lead to a decrease in spontaneous vocalization rate [35] or to calls weakened in amplitude and duration [36]. In all cases, however, animals were still able to spontaneously phonate after ACC lesions. In contrast to spontaneous calls, discriminatively conditioned vocal behavior was disrupted in monkeys with such bilateral lesions [35,36]. Ablations of other limbic structure such as amygdala and hypothalamus suppress distinct spontaneously uttered vocalizations, but do not abolish calls elicited by stimulating PAG [23,37].

These findings strongly suggest that the limbic vocal-initiating network is not involved in the production of vocal patterns themselves, but governs the affective (emotional or motivational) initiation of the vocal output.

The Role of the PVMN in Human Non-Verbal Vocalizations and Speech

It is important to realize that the phylogenetically conserved PVMN is still involved in vocalization in humans. One of its functions is to produce non-verbal vocal utterances such as crying, laughing, or moaning, all of which are innately predetermined and affective vocalizations considered to be directly homologous to monkey vocalizations [4,5]. Although brainstem lesions are often fatal, a clinical study revealed pathological laughter and crying due to a tumor beneath the brainstem that most likely deteriorated networks within the brainstem [38].

Several clinical studies also implicate the ACC in the initiation of non-verbal vocal utterances. In a type of frontal lobe epilepsy characterized by involuntary and stereotyped bursts of laughter ('gelastic seizures' [39]), the cingulate gyrus appears to be the most commonly disrupted site [40]. In agreement with this idea, electrical stimulation of the rostral ACC (and the hypothalamus) elicited uncontrollable, but natural-sounding laughter [39,41,42]. At the same time, ACC is important for speech. In humans, bilateral infarction of the ACC near the rostrum of the corpus callosum results in akinetic mutism [43,44], but with the potential for restoration of speech characterized by monotonous intonation, suggesting that the ACC is involved in the emotional intonation of human speech [37,45]. This idea is supported by recent imaging studies showing ACC activation during anger-expression of human speech [46]. Another important function of the PVMN is vocal output during speech production. Midbrain areas such as the PAG play a significant role in vocal production in humans, and its lesions can cause akinetic mutism [47,48]. In a case report, lesions in the PAG resulted in mutism, in other words it caused not only the absence of all non-verbal vocal utterances, but also the absence of speech [49]. Interestingly,

this patient was still able to produce the articulatory movements that are accompanied by a specific speech pattern, but the tonal component was no longer elicited [49]. However, PAG is active during the expression of non-verbal vocal utterances such as laughter in humans [50]. Moreover, a PET study showed that PAG is functionally coupled to a wide array of regions during voiced speech, but not during whispered speech [51].

Collectively, patient studies indicate that the PVMN is responsible for eliciting non-verbal affective vocalization but, in addition, plays a major role in speech production at the expense of affective vocalizations. Because the PVMN cannot subserve both affective preprogrammed vocalizations and volitional speech articulation at the same time, the evolution of speech and language may have required the taking-over and dissolution of the majority of preprogrammed vocalization patterns [52]. Potentially recapitulating such an evolutionary scenario during ontogeny, both laughter and crying constitute extremely important forms of communication in human infancy, bridging the gap between a prelinguistic stage to the later stage of speech and language acquisition. The advent of speech and language in Hominini therefore predicts the emergence of a new neocortical cognitive control network that occupies the ancient brainstem vocalization circuits through a VAMN. The neurobiological foundations for this radical reorganization are visible in nonhuman primates.

Volitional Articulatory Motor Network

Humans possess an additional VAMN consisting of cortical structures crucial for human speech control, and which is already present, although being anatomically and functionally underdeveloped, in the monkey brain. The VAMN comprises the inferior frontal gyrus (IFG), the caudally bordering ventral premotor cortex (area 6, PMv), and ventrolateral primary motor cortex (area 4, M1) including the facial and laryngeal motor cortex (Figure 1A,B). The central executive of this network is Broca's area, located in the IFG of the granular ventrolateral PFC (vlPFC). The granular PFC was added newly to the anterior pole of the frontal lobe during the evolution of primates [53,54].

Broca's area classically comprises cytoarchitectonic areas 44 (pars opercularis) and 45 (pars triangularis) in the left hemispheres, complemented by some authors by area 47 (pars orbitalis) [55]. Broca's pioneering work on brains of aphasics [56] revealed that areas 44 and 45 on the left side of the brain are instrumental for the production, or articulation, of speech and language. Studies on the cytoarchitectonics of macaque brains identified homologs of area 45 on the posterior convexity of the vlPFC, and of area 44 in the fundus of the inferior limb of the arcuate sulcus, a landmark that separates the PFC from the PMv (Figure 1B) [57,58]. No direct connections exist between the vlPFC and the primary motor cortex, but there are extensive projections to adjacent PMv that, in turn, send projections to primary motor cortex and the spinal cord. Specifically, area 44 is connected with the anterior PMv at the convexity of the inferior arcuate sulcus. The anterior PMv integrates sensorimotor signals of the posterior parietal cortex with cognitive information originating from vlPFC, pre-SMA, and cingulate area 24, the latter being in turn connected with the vlPFC [59]. Information in anterior PMv is then broadcast to the adjacent areas of the PMv and finally to ventrolateral M1, which also integrates laryngeal sensorimotor information [60] for the generation and control of face/mouth movements [61]. Neurons in both the PMv and M1 have direct access to the spinal cord, and thus can influence the generation and control of speech-related movements [62].

While the motor cortex of non-primate mammals is connected with the phonatory motor nuclei via interneurons in the reticular formation, only primates show direct connections via the corticobulbar and corticospinal tracts, respectively [63]. These connections give both New World and Old World monkeys the capability to volitionally control their articulatory muscles to respond with licking at a feeding tube in an operant conditioning task [64], and to

mimic articulatory vocal movements in a detection task [65], respectively. In humans only, additional direct connections of the motor cortex with the ambigual nucleus seem to exist [66] (Figure 1A,B), and humans also possess direct projections into the anterior horn of the thoracic and upper lumbar cord (reviewed in [5]). The motor cortex therefore plays a crucial role within the VAMN in humans [67]. Lesions in the human ventral motor cortex, which controls cranial and laryngeal muscles via the corticobulbar tract, lead to severe speech impairments, while the production of innate non-verbal vocal utterances such as laughing and crying remains intact [68].

Despite the crucial role of Broca's area in human speech and language production, neither electrical stimulation nor lesions in homologous areas of monkeys have significant effects on spontaneous vocalizations [5]. For example, bilateral destruction of the 'cortical face area', including the premotor, motor, and sensory representation of the jaw muscles, lips, tongue, velum, and larynx, does not affect the acoustic structure of vocalizations in either squirrel or macaque monkeys [18,32,69]. Similarly, ablation of lateral frontal areas in macaques does not affect vocalizations [35,36]. Moreover, electrical stimulation in the motor cortex of monkeys does not elicit vocal output [70,71], and vocal utterances cannot reproducibly be elicited by stimulating the premotor and motor cortex of anesthetized chimpanzees [72–74]. These findings were taken as evidence that the lateral frontal lobe areas do not play any role in monkey vocalizations. If true, this would constitute an apparent discontinuity between the human speech system and the monkey vocalization network.

Recent experiments in nonhuman primates, however, showed that the monkey homolog of Broca's area, as well as the premotor and/or primary motor cortices, are all involved in the initiation of volitional calls that have been uttered in response to visual or auditory stimuli, respectively [65,75–77]. Vocalization-related activity that specifically predicts the preparation of instructed vocalizations in response to the detection of arbitrary visual stimuli was recorded in monkey vlPFC (areas 44 and 45) [76] and PMv [65,76] (Figure 2). Moreover, the activity of many call-related neurons before vocal output correlated with call parameters of instructed vocalizations. Furthermore, neuronal responses during conditioned vocalizations were higher than during spontaneous vocalizations, suggesting a specific involvement of the monkey homolog of Broca's area during volitional monkey vocalizations (Figure 2). At first sight, these results seem to be contradictory to earlier studies showing that bilateral ablation of ventrolateral aspects of the frontal lobe have no significant impact on discriminatively conditioned vocal behavior [36]. However, the exact positions of areas 44 and 45 were anatomically not verified until recently [57,78]. Therefore, the most likely explanation for this discrepancy is that experimental lesions in the previous studies have not included the full extent or even the bulk of the monkey vlPFC, PMv, and M1. In all lesioned monkeys, ablations left areas 6vr, 44, 45, and M1 at least partially intact in one hemisphere (see Figure 1 in [36]).

Based on recent results and neuroanatomical projections, the vlPFC might take control over the vocal motor network via ACC or alternatively via the premotor cortex that has direct input to motor cortex [79,80]. Because electrical microstimulation in area 44 and the PMv elicited orofacial and laryngeal responses (Figure 3) [65,79,81–83], the pathway leading from vlPFC via PMv to M1 to the corticobulbar and corticospinal tract to control phonatory motor neurons seems more likely.

An influence via the VAMN could explain the rudimentary capability of monkeys to change vocal parameters such as vocal duration, amplitude, and frequency during cognitive vocal behavior [84–86]. Amplitude and frequency modulations can be generated by increasing the expiratory air flow passing the vocal folds in the larynx. This modulation might be solely controlled via direct

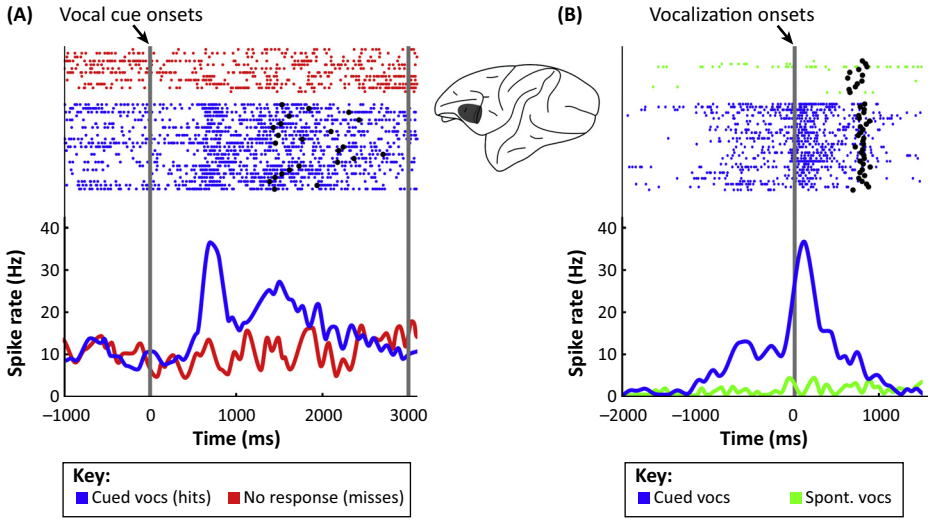


Figure 2. Activity Related to the Preparation of Vocalizations of Single Neurons in the Monkey Homolog of Human Broca's Area. (Inset) Lateral view of a macaque brain indicating the position of the ventrolateral prefrontal cortex (vlPFC). (A) Example neuron recorded in the monkey homolog of human Broca's area showing a significant increase in neuronal activity during trials with cued vocalizations (hits) in comparison to no response trials (misses). (B) Example neuron recorded in the monkey homolog of human Broca's area showing significantly higher activity before vocal onset of volitional coo calls (cued vocs) compared to spontaneous coo calls (spont. vocs). (A,B) Upper panels show raster plots, black dots indicate vocal onset during hit trials in (A) and mark call offsets in (B); lower panels represent the corresponding spike-density histograms averaged and smoothed for illustration. The vertical grey lines indicate the onset and offset of the go-signal in (A) and vocal onset in (B) (adapted from [76]).

pyramidal projections from the motor cortex to the respiratory motoneuron pools within the ventral horn of the spinal tract [87]. Distinct changes in call frequency – independently of call amplitude – might be modulated by indirect projections of the laryngeal motor cortex to the ambigual nucleus via corticofugal projections to the reticular formation of the lower brainstem [81,88,89]. For changes in call duration, modulation of the PVMN is necessary.

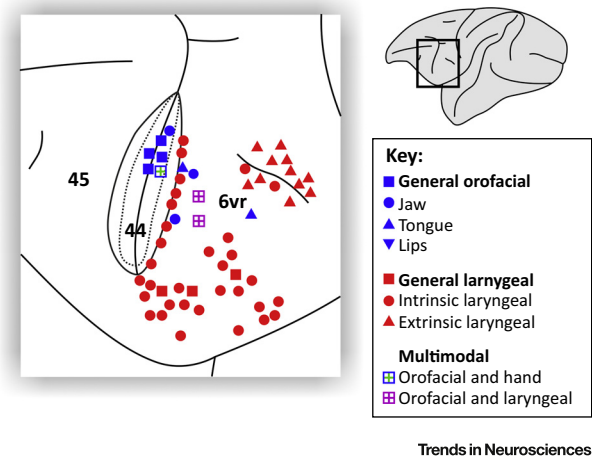


Figure 3. Representation of Electrical Stimulation Sites in Monkey Areas 6vr and 44 Which Elicited Orofacial [General (i.e., Not Defined in Greater Detail), Jaw, Tongue, or Lip Movements], Laryngeal [General (i.e., Not Defined in Greater Detail), Intrinsic Laryngeal or Extrinsic Laryngeal] or Multimodal Responses (Orofacial and Hand Movements or Orofacial and Laryngeal Movements at the Same Penetration Site). The inferior arcuate sulcus is unfolded to show the location of area 44 within the sulcus. Stimulation sites taken from [65,79,82,83].

Brain imaging evidence suggests that the mechanism of how the lateral frontal lobe gains control over articulation is not a direct excitation of the phonatory motor neurons in the brainstem, but is instead a disinhibition of articulatory muscle activity briefly before vocal output [90]. This line of argumentation would predict that non-verbal, emotional vocalizations might emerge once the modulatory (and/or inhibitory) influence of the voluntary articulation network vanishes [91]. Indeed, non-verbal vocal utterances remain intact despite devastating impairments in speech and language production (Broca's aphasia) after damage to the posterior IFG [56,68,92,93]. Moreover, patients with a clinical diagnosis of primary progressive aphasia develop abnormal laughter-like vocalizations that increasingly replace speech in the context of progressive speech-output impairment leading to mutism, until ultimately laughter-like vocalizations are the only extended utterance produced by these patients [94]. Interestingly, some non-verbal vocal utterances occur more often during the conversation of aphasic than of nonaphasic adults [95], suggesting a competitive modulatory influence of the VAMN over the PVMN.

In agreement with such a modulatory, possibly inhibitory, effect of the VAMN is the classic finding that electrical stimulation of the Broca's area leads to speech arrest rather than to speech production [96–98]. Direct cortical recordings revealed that Broca's area is predominantly activated before the utterance of a speech signal, but is silent during the corresponding articulation [99], again indicating that Broca's area is indirectly involved in coordinating speech initiation rather than in producing speech output directly [93,100]. These findings are supported by recent findings in awake neurosurgical patients in which the activity of distinct cortical speech sites was focally decreased via cooling [101]. Cooling of Broca's area predominantly altered speech timing, again indicating an involvement of Broca's area in speech coordination rather than in direct speech production. By contrast, focal lowering of temperature in speech motor cortex led to modulation of articulation, confirming the direct role of the speech motor cortex in articulatory motor control. The recent cognitive control signals found in the monkey lateral frontal lobe, in combination with the modulatory function of the VAMN and the emergence of non-linguistic vocalizations after its damage in humans, suggest that the humble beginnings of speech control can already be witnessed in nonhuman primates. From there, they seemed to have evolved into a full-blown language-production system in humans after expansion of PFC circuitry (Box 2).

The PFC Receives and Classifies Communicative Signals

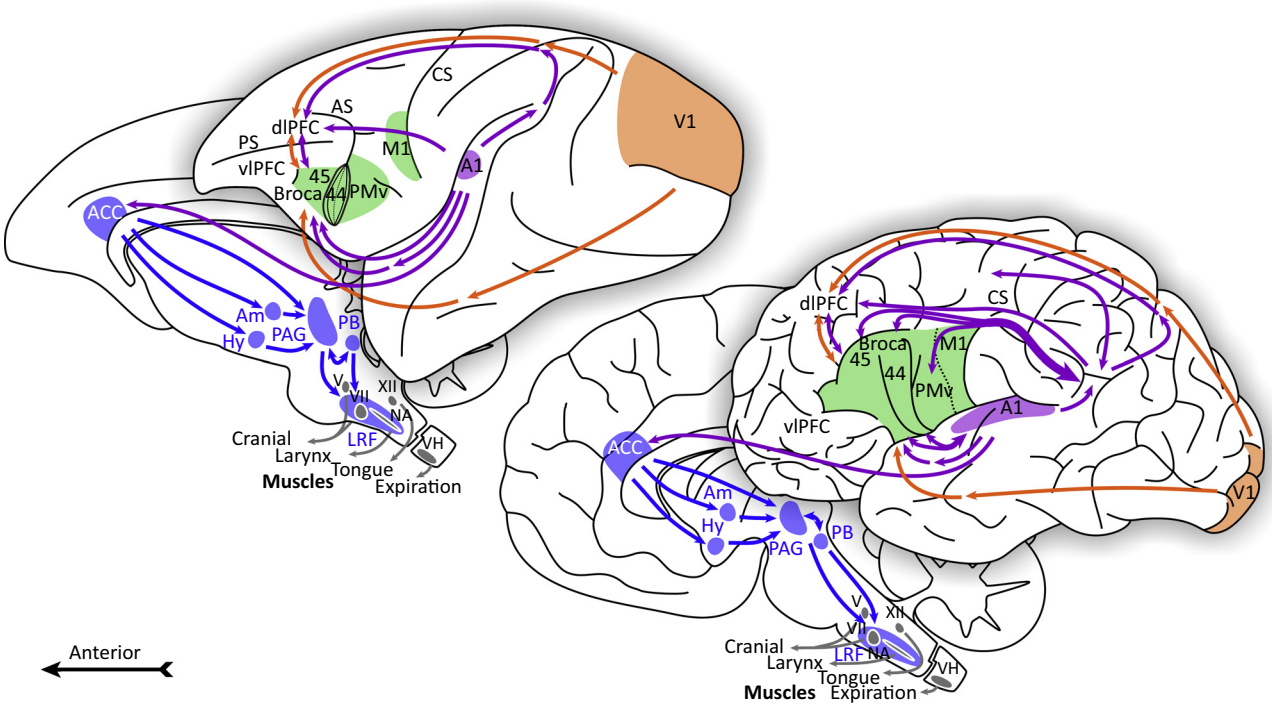
For a cortical network to control vocal output during reciprocal communication acts, sensory input from a sender is required. The vlPFC as the core of the VAMN receives highly processed information from higher-order sensory areas of all modalities (Figure 4). Neurons in the vlPFC categorize and maintain communicative signals in working memory to guide goal-directed output.

Auditory information reaches the lateral PFC via two largely anatomically and functionally segregated cortical streams: the anteroventral and the posterodorsal stream originating from the primary auditory cortex of the temporal lobe [102]. In the posterodorsal stream, the posterior auditory belt and parabelt areas project directly to the dorsolateral PFC (dlPFC; areas 8, 46, and 9) [102,103] (Figure 4). In addition, the posterior belt, parabelt, and superior temporal regions project indirectly to the posterior parietal association cortex before projecting to the dlPFC and principal sulcus (BA 46). This stream is thought to primarily encode auditory space [102] and quantity [104]. In the anteroventral stream, on the other hand, both the anterior belt and anterior parabelt regions project directly and reciprocally to vlPFC (areas 12/47, 45, 44, and 12 orbital) [103,105]. In addition to this direct projection, there is also an indirect projection to the PFC via the temporal association cortices. The anterior belt and parabelt regions are connected with the rostral (TS1, TS2) superior temporal gyrus (STG) that contains a 'voice region' in which neurons respond preferentially to monkey calls [106–108]. The STG in turn projects to relatively restricted

Box 2. The Neoteny Hypothesis of Cognitive Vocal Control for Language

How might the expansion of the VAMN have emerged in human primates over the course of evolution? One of the most powerful mechanisms evolution can use to remodel organs with very few genetic changes are delays in the timing of developmental stages [192]. A recent longitudinal behavioral study with monkeys trained to vocalize on command in response to a visual cue in a self-initiated trial suggests that retention of juvenile features, termed neoteny, might have been a key developmental event. Monkeys that laboriously master cued vocalizations during their juvenile phase gradually show more and more difficulties in producing such volitional calls with age, until they entirely discontinue controlled vocal behavior during adulthood [193]. This emerging disability was confined to volitional vocal production because the monkeys continued to vocalize spontaneously and continued to use hand movements as instructed responses during cognitive tasks in adulthood.

Because the decline in volitional call behavior correlated with the transition of the monkeys from juvenile phases to adulthood, these findings argue for a maturation process that might specifically affect the PFC. By prolonging development, greater neural plasticity early in ontogeny can be exploited to foster high-level cognition including speech and language [194,195]. In other words, linguistic capabilities may have been enabled because of an expansion of the juvenile period during the development of humans. This is supported by the finding that the PFC which contains Broca's language area experiences extraordinary long phases of developmental reorganization of neuronal circuits [196]. Genes related to the development of the PFC show excessive neotenic expression in humans relative to chimpanzees and rhesus macaques [197]. As a consequence, excessive synaptic connections and dendritic spines are initially overproduced to about twice the adult number before being pruned during puberty to reach the adult level at the onset of adolescence [196,198,199]. This pruning process might decouple the juvenile connection between the PFC and the PVMN during adolescence in monkeys. This points to non-activity-related developmental reorganization in the brain of maturing monkeys, rendering adult monkeys unable to bring vocalizations under cognitive control. This hypothesis suggests that expansion of the juvenile period during ontogeny may be one of the key events in the evolution of speech and language.



Trends in Neurosciences

Figure 4. Anatomical Locations and Connections of Sensory Structures That Provide Input to the Vocalization/Speech Systems in Monkeys and Humans. Regions and arrows shaded in blue indicate the structures of the PVMN. Regions shaded in green depict cortical areas comprising the VAMN. Regions and arrows shaded in purple show the interaction with auditory structures. Regions and arrows shaded in orange indicate the connections from the visual system (adapted from [4,67,102,200]). Abbreviations: A1, primary auditory cortex; ACC, anterior cingulate cortex; Am, amygdala; AS, arcuate sulcus; CS, central sulcus; dlPFC, dorsolateral prefrontal cortex; Hy, hypothalamus; LRF, lateral reticular formation; M1, ventral primary motor cortex; NA, ambigual nucleus; PAG, periaqueductal grey; PB, parabrachial nucleus; PMv, ventral premotor cortex; PS, principal sulcus; PVMN, primary vocal motor network; V1, primary visual cortex; VH, respiratory motorneuron pools in the ventral horn of the spinal tract; vlPFC, ventrolateral prefrontal cortex; V, motor trigeminal nucleus; VAMN, volitional articulatory motor network; VII, facial nucleus; XII, hypoglossal nucleus.

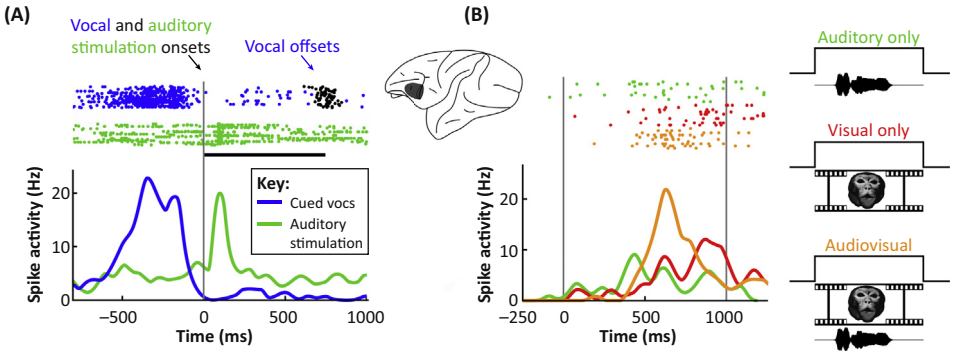


Figure 5. Audio–Vocal and Multisensory Activity in Single Neurons of the Monkey Ventrolateral Prefrontal Cortex (vlPFC). (Inset) Lateral view of a macaque brain indicating the position of the vlPFC. (A) Example neuron recorded in the monkey homolog of human Broca's area showing a phasic response during auditory stimulation and increased neuronal activity before volitional calls (cued vocs) (from [111]). (B) Example neuron showing nonlinear activity in response to auditory (vocalization), visual (silent movie), and audiovisual stimuli (congruent face-vocalization movie) demonstrating a significant interaction between auditory and visual stimuli, and exhibiting multisensory enhancement (adapted from [126]), Upper panels show raster plots (A,B); black dots indicate vocal onset during hit trials in (A), and lower panels represent the corresponding spike-density histograms averaged and smoothed for illustration. The vertical grey lines indicate the onset of the go-signal in (A), and the onset and offset of the vocalization, the silent movie, and the face-vocalization movies (B).

clusters of the vlPFC. The anteroventral stream is thought to encode auditory identity. Patches of single neurons in vlPFC respond robustly to complex sounds such as species-specific vocalizations or human vocalizations [109–111] (Figure 5A), and to some categories of vocalization calls [112]. In addition, dense auditory projections also exist from the rostral STG to the medial PFC, specifically to areas 32 and 25 of the ACC [113].

These separate projection streams in the auditory cortex are reminiscent of the temporal 'what' and dorsal 'where' visual pathways [114], or 'perception–action' pathways, respectively [115]. In the temporal visual pathway, higher-order representations of objects are found in the termination zone of the inferior temporal cortex where neurons encode specific object categories such as faces [116,117]. The downstream projections from IT cortex give rise to patches of face-selective neurons in the lPFC [118,119].

The largely segregated visual and auditory pathways converge in the vlPFC to give rise to neurons that represent higher-order multisensory and categorical representations of communicative signals. In line with evidence that vlPFC neurons represent perceptual and abstract categories [120,121], neuronal responses in this region correlate with monkeys' choices in an auditory same–different task [122] and during categorization of human speech sounds [123]. Supporting the integration of modal communication channels, neurons in vlPFC also respond to particular face–voice combinations [124–126] (Figure 5B). In addition, recent recording and inactivation studies in monkeys showed that the vlPFC is particularly important for processing behaviorally-relevant stimuli during auditory and audiovisual working memory [127,128]. Such multisensory PFC activity might enable human and nonhuman primates to recognize the correspondence between vocalizations and the facial postures associated with them [126–129].

Basic auditory tasks also activate the human vlPFC [130–132]. More-dorsal PFC regions (area 46/9) are utilized when verbal working memory is required, whereas vlPFC regions (47/12; 45) are recruited during active retrieval of verbal and nonverbal auditory information [133,134]. During the selective retrieval of information from auditory memory, the vlPFC interacts both with

the auditory temporal region (object information) and the inferior parietal lobule (spatial information) [134]. The broad involvement of the vlPFC in both verbal and nonverbal auditory tasks suggests that this area may be an interface in the auditory–vocal cycle. Collectively, these data suggest that vlPFC is specialized for processing and integrating social communication information in monkeys [135], in the same way as the human IFG is specialized for processing and integrating speech and gestures [136,137].

PFC Precursors of Semantics in Primate Referential Systems

The VAMN is much more than merely a high-order motor network. It also plays a vital role in establishing semantics and syntax, two hallmark characteristics of the two symbol systems – language and number theory. In symbolic reference, relations are established between spoken/written words or numbers, respectively, on the basis of compositional rules (i.e., syntax) [138,139]. However, simpler and both phylogenetically and ontogenetically earlier referential associations are 'indices' – signs that are characterized by spatial or temporal association between sign and object (reference based on contiguity or correlation) [140]. Animal communication typically is indexical, for example vervet monkey alarm calls indicate the presence of specific predator categories that have to be learned by juvenile monkeys [141]. Moreover, conditioned sign–object associations established in animals by reward contingencies are typically indexical, and can be investigated as a precursor for human symbolic reference [142].

Neurons in the vlPFC establish semantic associations: after training monkeys to associate the number of items in a set with arbitrary visual signs, many of the same lPFC neurons represent the abstract numerical meaning associated with such signs [143]. Similarly, fMRI studies show that the PFC is much more active in children learning semantic associations compared to proficient adults [144,145]. Damage to the human lateral frontal cortex results in severe impairment in tasks that require learning of arbitrary associations [146]. Networks within the lateral frontal cortex may thus fulfill the requirements for high-order associations between signs, ultimately giving rise to the cultural invention of linguistic and number symbols. Symbolic reference may thus emerge as a function of a largely expanded lPFC in humans [140].

Semantic associations require interactions of the PFC with the medial temporal lobe, which traditionally has been linked to declarative long-term memories [147]. Recordings in behaving monkeys show that, during learning and retrieval of long-term associations, the temporal lobe interacts with the PFC to store memories or reactivate information about past experiences [148,149]. With its link to the medial temporal lobe structures, the PFC is ideally suited to cognitively control memories, permitting an organism to establish sign reference and to strategically plan communicative acts in a flexible and goal-directed way.

PFC Precursors of Grammar in Primate Referential Systems

To establish a fully fledged symbol/language system, meaningful associations (semantics) are not sufficient. Sign sequences must be hierarchically structured according to action plans or rules guiding the structuring of signs – 'syntax'. Syntax refers to the rules governing structure in natural language sentences or mathematical systems. Syntax establishes relations between signs that determine the meaning of an expression. Therefore, syntax and semantics are inextricably linked in symbolic systems.

Simple syntactical rules can be mastered by monkeys [150]. As a putative correlate for simple syntactical processing, single neurons in the primate lPFC encode sequence plans [151], the start and end states of behavioral sequences [152], and changing abstract rules [153,154]. Moreover, precursors of a code for abstract temporal structures of sounds and hand movements have been revealed by single-unit and fMRI studies in monkey PFC [155,156]. In humans, fMRI data suggest that Broca's area processes the start- and end-points of higher-order motor

segments and controls the nesting of functional segments, thereby forming the hierarchical structure of action plans [157]. By contrast, other speech-related areas, such as the SMA complex and the insula, are more specifically involved in the precise timing of ongoing motor acts underlying the execution of motor sequences needed for articulation [157–159].

Although neuronal circuits representing abstract sequences and rules are present in the monkey vlPFC, a grasp of high-level recursive tree structures seems to be unique to human language and mathematics [160–162]. Complex syntactical representations may have impinged on inferior frontal cortex networks [163]: while simple, non-recursive **grammar** (finite-state grammar) activates the phylogenetically-older frontal operculum (i.e., premotor cortex), the computation of recursive hierarchical sequences (phrase/structure grammar) that is characteristic of human language additionally recruits the phylogenetically-younger Broca's area (areas 44 and 45). Human fMRI studies suggest purely syntax-related activation in Broca's area, either in BA 45 and 47 [164], in BA 45 [165], or in BA 44 [166]. Using meta-analytic connectivity-based parcellation, Clos *et al.* [167] identified five functionally distinct clusters within left area 44 (associated with action processing, sequencing, linguistic working memory, meaning, and task-switching/cognitive control). While these functions are highly relevant in the context of language production and comprehension, they will obviously also be recruited by other domains including action and social cognition, therefore pointing to putative pre-adaptive functions in nonhuman primates.

Outstanding Questions

How does activation or inactivation of distinct areas of the monkey homolog of the human Broca's area deteriorate volitional vocal output?

Do preSMA, SMA, and the insula play a significant role in cognitive control of vocal output in non-human primates?

How is the VAMN interconnected, and how is it linked to the PVMN, during development from prelinguistic infants to linguistic children?

What role do auditory feedback mechanisms play in shaping vocal patterns in non-human primates? How does the PFC participate in potential vocal learning mechanisms?

Conclusions and Future Directions

In this review we suggest that the incipient linking of the prefrontal central executive of the brain with the vocalization system is a key neurobiological event and pre-adaptation for the evolution of speech and language. Crucial evidence for this hypothesis stems from comparative investigations of the cytoarchitecture of the human and the monkey vlPFC. These studies demonstrated that the basic architectonic plans are similar in these two primate brains, despite considerable development of the vlPFC areas in the human brain [57,78,168]. In addition to anatomical similarities, recent neurophysiological experiments in nonhuman primates provide the necessary functional evidence. Studies in behaving macaque monkeys showed that neuronal activity in vlPFC is correlated with volitional call initiation [76]. Although these correlative measures have led to novel insights concerning the role of inferior frontal lobe structures in controlling vocal output, the causal efficacy of vocalization-related activity needs to be addressed in the future. This could be achieved by probing the direct impact of experimental neural perturbations (stimulation or inhibition) on vocal behavior [169]. If physiologically characterized vocalization-related neurons are causally involved in eliciting cued vocalizations, lower vocalization thresholds (i.e., higher vocalization rates) can be expected while electrically stimulating such neurons [170], whereas their transient chemical inactivation (i.e., by increasing synaptic inhibition) is predicted to temporarily impair volitional call initiation. Such coarse hypotheses are of course subject to adjustments and refinements with increasing knowledge about the cortical vocal network.

As indicated by the (simplified) connections in our model, the vlPFC is the central executive of the VAMN. At the same time, however, it likely interacts with other areas of a larger frontal lobe network to encode cognitively controlled vocalizations. Medial frontal lobe areas, such as the anterior cingulate cortex (ACC) and the pre-supplementary motor area (pre-SMA), might play additional roles not only in affective vocal output but also in controlling volitional vocalizations [5,29,171,172]. Data from the ACC and pre-SMA, among other areas, will be necessary to complete the emerging picture of a frontal vocal network.

A third important aspect is to clarify the level of specialization of frontal lobe circuitry in initiating goal-directed vocalizations. Instead of encoding any volitional motor act, neurons of the VAMN are expected to show some specificity towards controlling vocal output. To decipher the

vocalization-specific aspects of the VAMN, neurophysiological investigations in monkeys trained to perform volitional acts using not only the vocal apparatus but also other effector organs (e.g., hand movements) would be appropriate. This would allow the dedicated role of the VAMN *vis-à-vis* other volitional behaviors to be investigated. However, that neurons might respond exclusively to volitional vocal output does not appear to be realistic. After all, the primate vlPFC operates at the apex of the cortical hierarchy and is involved in a variety of executive functions in different domains [9,173–175]. Despite its reputation as classical language area, even Broca's area in humans is part of a larger cognitive control network and plays important roles in structuring a variety of hierarchically organized behaviors [157,176]. Neurophysiological studies in nonhuman primates will remain indispensable for identifying prefrontal cognitive control functions as well as specific aspects of human speech and language functions.

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