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Prefrontal cortex and the evolution of symbolic reference

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Symbol systems such as numbers and language are of paramount importance to human cognition. In number theory, numbers are symbolic signs embedded in a system of higher-order sign–sign relations. During ontogeny, numerical competence passes through different referential sign relations with increasing complexity, from an iconic to an indexical and finally symbolic stage. Animals such as nonhuman primates are constrained to indexical reference. However, because symbolic reference emerges from indexical reference, behavioral and neuronal representations of semantic sign-numerosity associations in animals can elucidate the precursors of symbol systems. A neurobiological explanation of how numerical signs take their meaning is proposed by suggesting that neurons in the granular prefrontal cortex, a novel brain structure evolved in primates, enable high-order associations and establish links between nonsymbolic numerosities and arbitrary signs.

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Introduction

In 1980, Epstein *et al.* [1] published a paper they entitled – one must assume provocatively – 'Symbolic communication between two pigeons'. The protagonists of the study were two pigeons whimsically named 'Jack' and 'Jill'. Housed in adjoining plexiglas cubicles, Jack and Jill were taught by operant conditioning to interact by depressing keys embossed with English letters or letters arranged to form words.

In a typical task sequence, Jack asks Jill for a color name by depressing the key labeled WHAT COLOR? Jill then checks the color of a hidden light and pecks on the key labeled with the color name. After that, Jack rewards Jill with food by pressing the THANK YOU key. Finally, Jack ends the communication by selecting the correct color as indicated by Jill and also gets a reward.

Does this now mean that pigeons 'can learn to engage in a sustained and natural conversation without human intervention, and that one pigeon can transmit information to another entirely through the use of symbols', an interpretation winkingly offered by Epstein *et al.* [1], just as for chimpanzees in a very similar experiment [2]? No, it does not. Because even though there are superficial similarities between animals' usage of labeled keys and symbolic sign systems in humans, there are also profound discrepancies [3••,4]. As exemplified below for the number system, a true symbol system encompasses much more then just isolated sign–object associations.

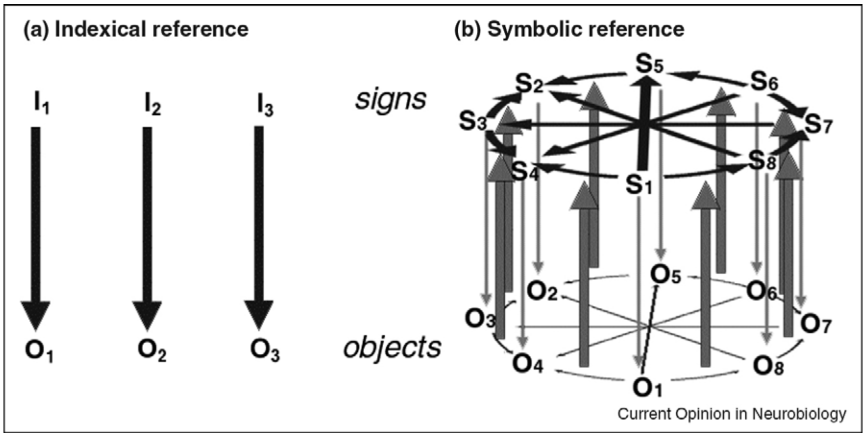
But even if it is beyond animals' capacity to understand true symbol systems, their more primitive semantic abilities are instructive in many respects. After all, some sort of meaningful associations have been established between arbitrary signs and objects. In the pigeon study [1], for example, the pecking key labeled RED refers to the color red. Arguably, this is a very simple and concrete association, but associations can also be established between signs and abstract categories, such as numerosity (set size) [5–9]. I will argue that abstract relations between signs are necessary, but by no means sufficient semantic associations that ultimately give rise to symbolic competence that is exclusively found in humans.

When studying sign systems, some important questions arise. First, what exactly is a sign, and how is a symbol defined? In this article, the term 'sign' will be used as an umbrella term for all possible associations between a signifier and a signified. As discussed later, a 'symbol' is the most complex and abstract form of a sign embedded in a system of sign–sign relations.

Second, how do referential sign–object associations evolve both phylogenetically in the animal kingdom and ontogenetically in children? I will argue that symbolic reference is uniquely human and depends on the faculty of language. However, because symbol systems emerge out of and are grounded on lower-level references between signs, a better understanding of semantic sign–object associations will help to elucidate the foundations of the symbol grounding problem, the question of how a symbol is given a meaning.

Third, how do signs take their semantic content, their meaning? A neurobiological explanation will be proposed by suggesting that the granular prefrontal cortex, a structure

Figure 1



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Graphic illustration of the difference between indexical and symbolic reference. **(a)** In indexical reference, associative links between signs and objects are one-to-one and essentially independent of one another. (For numerical entities, such as numerosities, inherent relationships between numerical objects may already be present.) **(b)** Symbolic reference, on the other hand, is based upon a combinatorial system of sign–sign relationships (upper horizontal black arrows); the remaining transitively indexical links between objects and symbols (gray downward directed arrows) become secondary. Strategy shifts (thick upward pointing arrows) to rely on relationships between signs ('semantic space') to pick out objects indirectly via relationships between objects (lower horizontal arrow system). Adapted from [12,15].

thought to constitute a new development in primates, allows additional processing capabilities such as sign and symbol acquisition and manipulation.

These questions will be addressed in the context of the number domain, a system of symbols that is (somewhat) simpler and thus more easily accessible than natural language. Number theory shares key features (such as recursion and syntactic rules) with linguistic operations, and its investigation may thus have implications for the faculty of language.

Systems of signs: icons, indices, and symbols

The French linguist Ferdinand de Saussure [10] argued that the basis for meaning and reference is established by virtue of a one-to-one mapping of a signifier onto the signified. Broadly speaking, a sign (function) consists of two parts: a signifier (sign vehicle, token) which is used to denote something else, the signified (referent, interpretant). Sign vehicles can take the form of sounds, images or even actions, but such things at first have no intrinsic meaning and become signs only when they are associated with meaning. Thus, as long as it is interpreted as signifying or referring to something else, anything can be a sign.

Referential associations between a signifier and a signified can adopt different levels of complexity. Following a semiotic taxonomy introduced by the American philosopher Charles Sanders Peirce [11], Deacon [12] distinguishes three kinds of signs: *icons*, *indices* and *symbols*. These sign categories are ordered according to increasing complexity of the relation between the sign and the signified.

The simplest sign, an **icon**, is characterized by similarity between sign and object (reference based on similarity). For example, the sign (☎) is an icon for telephone, and (●●●) could be an icon for numerosity 3. In contrast, an **index** is characterized by spatial or temporal association between sign and object (reference based on contiguity or correlation) (Figure 1a). Mercury position in a thermometer is an index for temperature, tears are an index for sorrow. Animal communication typically is indexical, that is vervet monkey alarm calls indicate the presence of specific predator categories [13]. Moreover, conditioned sign–object associations established by reward contingencies are typically indexical. Indices permit stimulus generalization, but not yet logical generalizations. In the number domain, empirical properties such as the cardinality (numerosity) of sets or the position of elements in a sequence can be associated with arbitrary shapes or sounds to give rise to a numerical indexical sign. Sign understanding in any animal – be it in the domain of communication or number – does not go beyond indexical associations [3••,4].

Symbols, finally, are defined at first glance by some arbitrary but conventional link between signifier and signified, as in the case of human language (reference based on convention). But as exemplified by Deacon [12], arbitrariness is neither a necessary nor a diagnostic feature of symbolic representation. In contrast to indices, which refer to objects as individual signs, symbols are always part of a referential system (Figure 1b) so that they can be manipulated on the basis of compositional rules (i.e. syntax) [14]. Reference shifts from the token to the system [15]. Symbolic reference is crucially a link between sign–sign relations, not between individual sign–object relations [16].

Symbolic reference is the basis of human language and number theory, whereby relations are established between words or numbers, respectively. The relevant relations are linear in nature, such as the order of words in a sentence, as well as hierarchical, such as 'object of' or 'subject of'. In that respect, numbers are part of a symbol system comprising rules for combining the symbols into meaningful strings.

Evolution of numerical sign–object associations

If animals, as proposed in this article, are generally not capable of symbolic reference, why be concerned with their understanding of indexical references and its underlying neuronal machinery? The reason is that 'ultimately, symbolic reference grows out of and is dependent on patterns of indexical reference. Consequently, conditions and requirements of indexical reference will constrain symbolic references as well.' [17]. Thus, the neuronal mechanisms of indexical numerical reference in nonhuman primates are relevant for the development of a symbolic number concept in our own species.

Research over the last decades has provided evidence for nonsymbolic representations of numerical quantity in a variety of animals (for reviews see [18,19]). Nonverbal numerical representations are inherently iconic, because the size of an empirical set is represented by the size of an analog magnitude (accumulated quantity). The performance of animals at least equaled the performance of human infants tested with no training, or adult humans lacking number words [20,21]. These nonverbal abilities suggest considerable continuity in numerical quantity representations in the course of evolution.

However, striking discontinuities emerge once numerical signs are introduced. After extensive training, animals master indexical associations of shapes and quantities [5–9], but such representations do not progress on to the level of symbols. For instance, a chimpanzee familiarized with numerical signs needed extensive training for every newly introduced sign, and the introduction of a new numerical sign was always accompanied by poorer identification of the maximum numerical sign learned in the previous stage [5].

Animals may also perform approximate arithmetic operations, but this does not account for a symbolic number concept. The simplest process that can be regarded as one-by-one addition is the enumeration of items presented sequentially over time, an operation mastered, for instance, by rhesus monkeys [22,46]. Even more, monkeys can also approximately add the numerical values of two sets of objects [23]. Animals thus seem to have an intuitive understanding of approximate addition. Pigeons [24], monkeys [25] and a single ape [6] have been shown to access this capability even when being tested with signs they have been trained to association with numerosities. The chimpanzee Sheba, for example, which had been trained to associate numerosities with the shapes of Arabic numerals, mastered simple addition problems based on Arabic numerals up to the sum 4 (such as 1 + 1 or 1 + 3) without additional training [6]. For an animal, this is for sure a most sophisticated and astonishing behavior, but it is far from a symbolic understanding of numbers. As indicated above, nonsymbolic addition of numerosities, from one-by-one addition to a numerical combination of sets of objects, seems to be a default numerical operation in animals (and probably also humans). The chimpanzee Sheba most likely just did that and combined numerosities by making a detour via sign-numerosity relationships. Even though the addition problems were kept really simple (by also including operations like 1 + 0 or 2 + 0) and thus the combinatorial possibilities were severely restricted, the chimpanzee's performance was still noisy. Such noisy representations are a hallmark of analog magnitude representations and operations on them.

Approximate addition (or subtraction) operations are surely impressive and they constitute high-level cognitive skills, but they do not require any symbolic understanding. Even if animals can apply an additive rule to novel pairs of numerosities (in transfer tests), it would just be a form of stimulus generalization indicating a conceptual understanding of approximate addition that can perfectly be accomplished based on iconic or indexical numerical representations. Nonsymbolic addition and subtraction are probably the most important precursor for symbolic calculation, but no more.

Children, however, rapidly transcend this stage, and numerical competence in humans passes from an iconic to an indexical and finally symbolic stage. Evidence for iconic stages can be found both in human history and in children's acquisition of numbers [26]. Traces of numerical icons – in which elements of one set are represented by elements of another set – are frequent in ancient numeral systems (e.g. Roman I, II, III, or Mayan •, ••, •••, ••••) and date back about 30 000 years when notches in carved bones were used to indicate quantity [27]. Similarly, children initially produce one counting word for each element of a set (they repeatedly go through the sequence *one-two-three-four*), but they do not use the last word in the counting sequence (the word *four*) to represent the cardinality of the entire set [28]. Here, the counting words are used as spoken icons, just as in finger counting.

At the next stage of development, links between signs and cardinalities are established, thus forming indexical reference. Associations between counting words and sets of a particular size reflect indexical links. For example, Russian ‘sorok’, forty, goes back to Old Nordic ‘sekr’, the word for furs that were traded in bundles of forty [29]. These are the kinds of signs animals such as nonhuman primates can be trained to use [5–9].

To arrive at a symbolic number concept (or linguistic concept), the transition of indices into a symbolic linguistic system is required, a stage at which only humans arrive during childhood. Once children learn to count verbally (i.e. symbolically) between the ages of 2 and 4, they generalize the counting procedure to larger numbers with no evident upper bound and with no specific training [30,31]. Children acquiring a set of elementary arithmetic facts and calculation procedures can perform arithmetic operations on all the numbers they can count. At that point, numbers became part of a symbol system. Finally, they extend number knowledge beyond the limits of their counting procedures, using arithmetic operations to represent fractions, zero, and negative numbers. These and many other developments distinguish numerical skills in human children from the most highly trained animals. It marks a profound discontinuity between human and nonhuman minds [3••,4].

A neurobiological proposal of symbolic reference

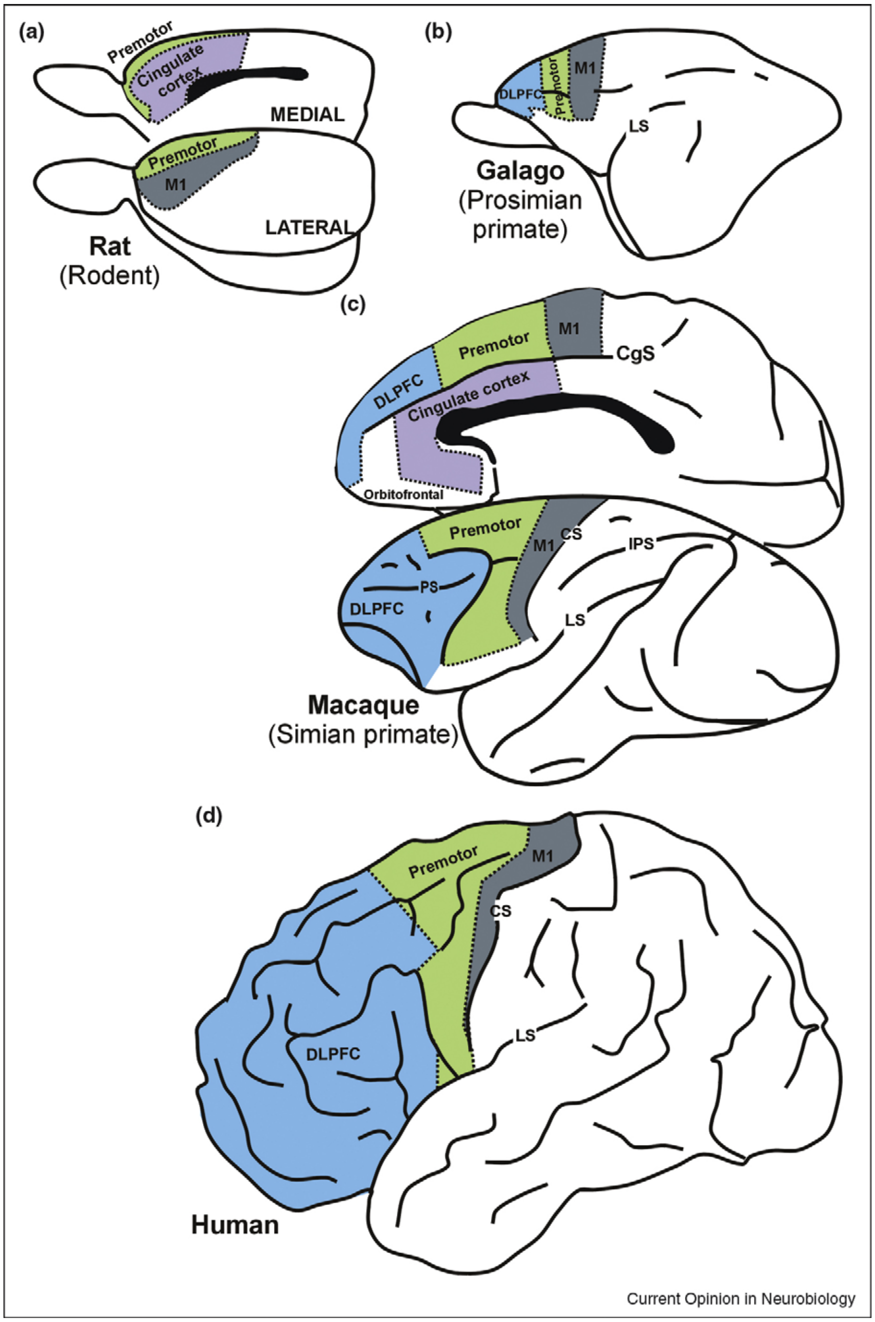
Where and how could symbolic numerical reference evolve – both phylogenetically and ontogenetically – in the primate brain? A brain structure is required that has access to information from all sensory modalities, shows coding flexibility by learning, and, most importantly, can analyze high-order associative relationships. Lesion studies in humans suggest that the lateral frontal cortex is a key structure for establishing semantic associations. Damage to the human lateral frontal cortex results in severe impairment of conditional associative tasks that require learning of arbitrary associations between a set of stimuli and a set of responses [32,33]. Patients with prefrontal lesions typically fail in conditional association tasks such as card-sorting games that require them to change sorting criteria. Networks within the lateral frontal cortex may thus fulfill the requirements necessary 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 lateral prefrontal cortex in humans.

The dorsolateral prefrontal cortex (DLPFC; sometimes subdivided into dorsolateral/ventrolateral areas by the principal sulcus in the macaque brain) is of great interest from an evolutionary point of view (Figure 2). Functionally, DLPFC is known to play an important role in the highest levels of cognitive functioning supporting flexible goal-directed behavior. Anatomically, the DLPFC seems to constitute new tissue added to the anterior pole of the frontal lobe during the evolution of primates [34••]. (See [34,35] and [36] for a detailed discussion of why anatomical (input from the mediodorsal nucleus of the thalamus), pharmacological (reception of dopamine projections) and neuropsychological (spatial working memory deficits after lesions) arguments favoring a DLPFC in rats fall short.) Only primate DLPFC has a layer 4 made of densely packed, small cells; such regions are often called ‘granular’ prefrontal cortex (including areas with a subtle, ‘dysgranular’ layer 4). Among the newly developed ‘granular’ neural tissue and circuitry of the DLPFC are frontal Brodmann areas 44, 45 and 47 (inferior frontal cortex) as well as area 46 and frontal pole cortex area 10 [37]. In contrast, other parts of the frontal cortex (motor, premotor, some medial and orbital regions) lack internal layer 4 of the six-layered isocortex; these evolutionary older areas are shared with other mammals such as rodents [35]. In addition, primates are distinguished among mammals by the presence of strong connections linking higher-order frontal, posterior parietal (PPC) and temporal association cortices. The DLPFC and the PPC, for instance, are both mutually interconnected, but also via a common thalamic structure, the dorsal pulvinar, which appears to be unique in primates [34••].

Neuronal correlates of simple sign–object relations, such as learned associations between two purely sensory stimuli without intrinsic meaning, have been found in the DLPFC. Neurons in the DLPFC have been shown to signal the association between pairs of pictures [38,39] or between colors and sounds [40]. Furthermore, this frontal lobe structure is important for active retrieval and top–down control of associative representations [41••]. The prime concern in numerical competence, however, is the question of where and how single cells learn to associate the inherent meaning of numerosity, a quantity category, with a shape, or sign vehicle.

This issue was addressed by a recent single-cell study in macaque monkeys, showing that individual neurons in the DLPFC indeed signal the meaning of signs. Diester and Nieder [42••] recorded the activity of prefrontal and posterior parietal neurons in rhesus monkeys trained to associate the shapes of Arabic numerals with the numerosity of dot patterns ranging form 1 to 4. Thus, the monkeys learned that the numerical value of one dot corresponded to the shape of numeral ‘1’, the numerical value of two dots was assigned to the shape of numeral ‘2’, and so on. The discrimination performances of the monkeys associating dot numerosities with numeral shapes showed all characteristics typical of analog magnitude judgments, such as the numerical distance and size effect. Even when matching numeral shapes with numeral shapes, the monkeys relied on the numerical values associated with the shapes [9]. This indicates that these signs were indeed judged according to their assigned analog magnitudes, even though a simple shape matching strategy could have been easier for

Figure 2

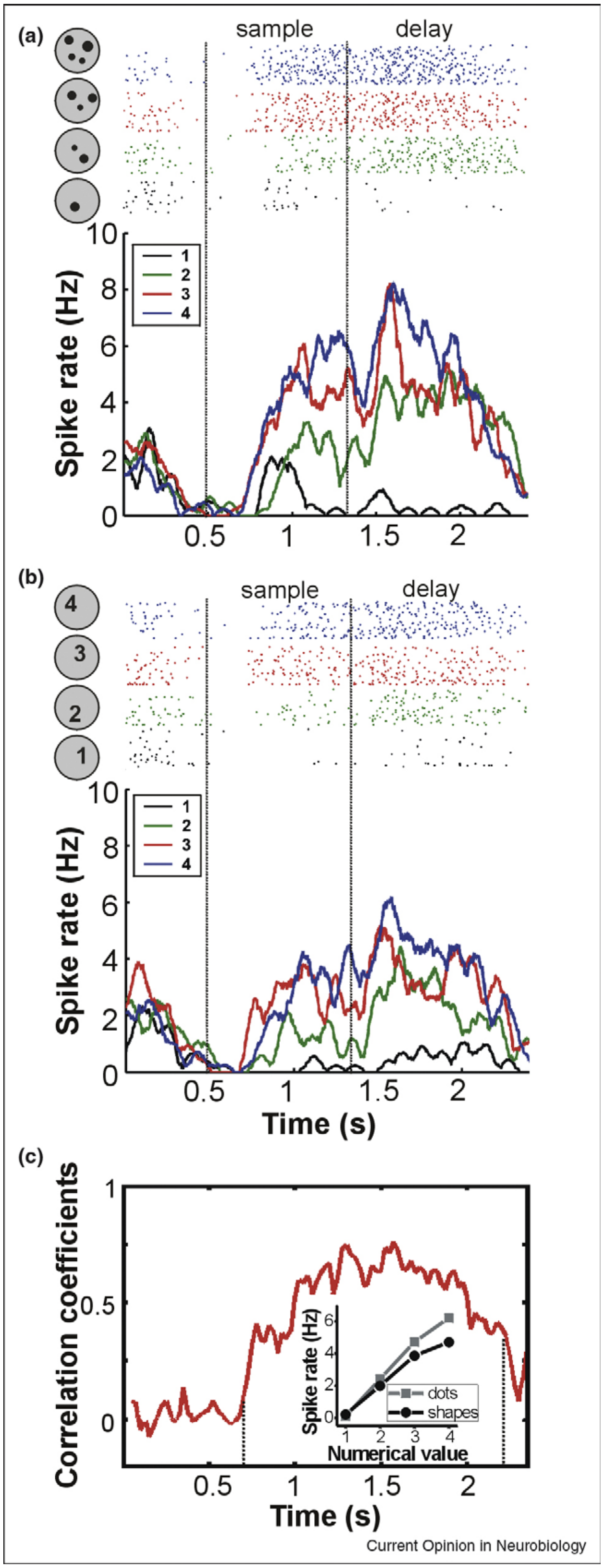


Evolution of the 'granular' dorsolateral prefrontal cortex in primates. The primate frontal lobe is subdivided into the primary motor area (M1), various premotor regions and the prefrontal cortex at the frontal pole. The prefrontal cortex (PFC), in turn, comprises a medial region (mainly anterior cingulate cortex), an orbital region, and a dorsolateral region (DLPFC; sometimes split into dorsolateral/ventrolateral areas as determined by the (course of the) principal sulcus). The DLPFC has only recently evolved during the course of primate evolution and is missing in other mammals such as rats **(a)**. The DLPFC progressively expands from prosimian **(b)** to simian primates **(c)** and reaches its largest extension in humans **(d)**. LS – lateral sulcus; IPS – Intraparietal sulcus; CS – central sulcus; PS – principal sulcus. Based on [34••,35,65,66].

the animals. In summary, the monkeys understood the indexical reference of the shape-numerical value relation.

As seen in previous recordings, the responses of single neurons in both the prefrontal [43,44] and the intraparietal sulcus of the posterior parietal cortex [45,46] were tuned to the numerosity of the dot patterns. Only in the PFC, but not in the IPS, many of the same neurons were equally tuned to the numerical values assigned to the numeral shapes (Figure 3), thus representing the

Figure 3



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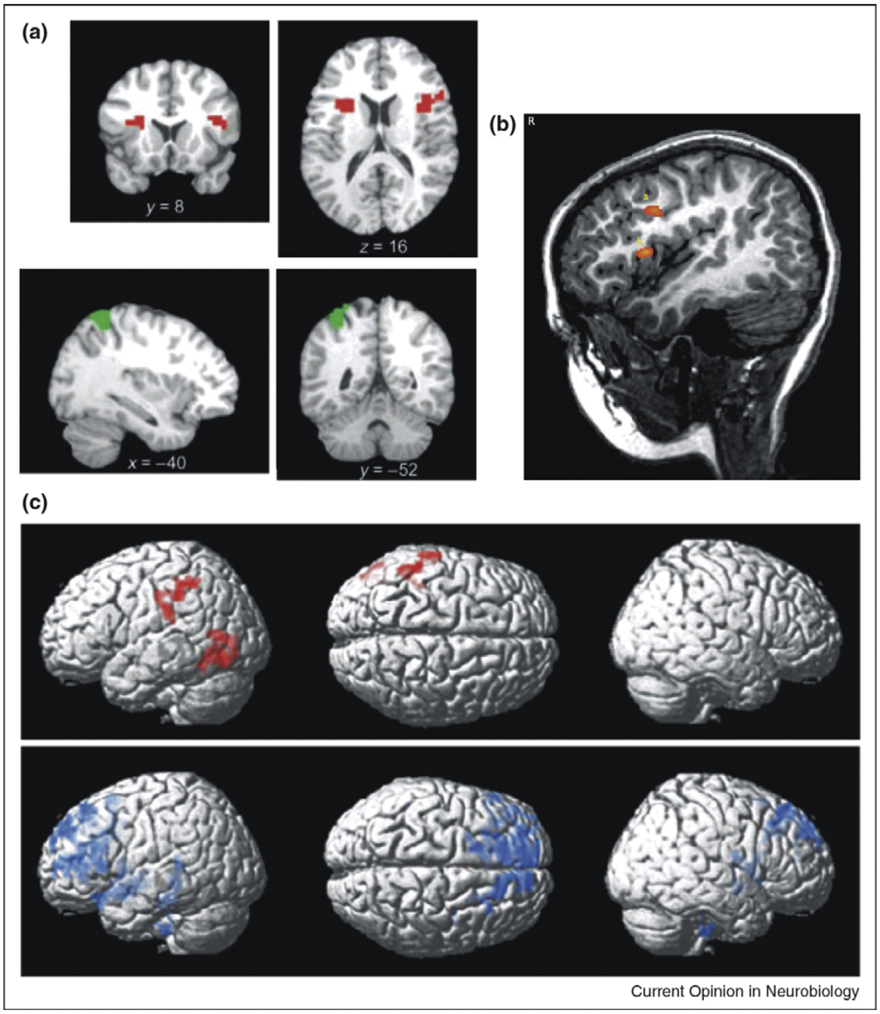
Semantic association neuron of the macaque dorsolateral prefrontal cortex. **(a,b)** Responses of the same single PFC neuron to both numerosities and associated numeral shapes (side panels in **(a)** and **(b)** illustrate sample stimuli). Neuronal responses in **(a)** and **(b)** are shown as dot-raster histograms (top, each dot represents an action potential) and smoothed spike density histograms (bottom, colors denote discharge to the corresponding sample numerical value 1–4). The first 500 ms indicate the fixation period. Black vertical lines mark sample-onset (500 ms) and offset (1300 ms). This neuron's preferred numerical value in the sample and delay period was 4. Note the similarity in the association neuron's temporal discharge profiles in response to the multiple-dot displays and the shape of Arabic numerals. **C**) Time course of the quality of numerical association. Cross correlation coefficients for the tuning behavior of the neuron to dots **(a)** and shapes **(b)**. The interval bordered by vertical dotted lines indicates the time phase of significant cross correlation (as determined by measures from signal detection theory) between tuning to numerical values in the multiple-dot displays and Arabic numerals; in this period, the neuron associated numerical values in the two protocols. The overall tuning functions of this neuron to dots and shapes are shown in the inset. After [42••].

indexical sign reference [42••]. Interestingly, individual neurons' tuning to dot numerosities and corresponding numerical signs was significantly impaired whenever the monkeys made errors in assigning dot numerosities to the appropriate shape. In other words, if the PFC neurons did not associate numerosities with the correct shape, the animals were prone to errors, supporting the relevance of prefrontal 'association neurons' for the semantic mapping process.

Thus, in nonhuman primates, both prefrontal and parietal neurons represent numerical values but, unlike parietal neurons, only prefrontal neurons have the additional capacity to associate numerosity and an Arabic numeral shape as its indexical referent [42••]. These findings suggest the PFC as the prime source in the mapping process of initially meaningless shapes to semantic categories, giving rise to an indexical understanding of signs. The prefrontal region is strategically situated for such associations; it receives input from both the anterior inferotemporal cortex encoding shape information [47] as well as the posterior parietal cortex [48] that contains numerosity-selective neurons [45,46].

Support for this assumption comes from recent fMRI studies with children. When comparing numerical values in symbolic (numerals) and nonsymbolic notation (sets of dots), children at the ages of six and seven invoke the same cortical networks previously described for adults, with parietal brain regions as key structures. Interestingly, however, children also recruit the inferior frontal cortex (granular frontal cortex BA 44/45) for notation-independent numerical processing to a much greater degree than adults [49,50]. Similarly, a greater engagement of frontal brain regions during Arabic numeral judgments [51•] and symbolic arithmetic tasks [52] has been described in children than in adults (Figure 4). These results point to the PFC as the cardinal structure in acquiring a symbolic number concept during ontogeny. Only with age

Figure 4



Recording of fMRI activation in children and adults during numerical operations. **(a)** Statistical comparison of BOLD activation in 6–7-year old children and adults during nonsymbolic and symbolic number comparison. Unlike adults, who showed greater activity in the left superior parietal cortex (green color), children exhibited the strongest effect of notation-independent numerical processing in the inferior frontal gyrus (red color). In children, this region generated a positive response to both Arabic numeral and dot array conditions, a robust numerical ratio effect, and a strong correlation with behavioral performance [50]. **(b)** In 10-year-old children judging the relative magnitude oft two single-digit Arabic numerals, numerical distance was found to have significant effects on areas in the dorsolateral and ventrolateral prefrontal cortex (activation in red). From [51•]. **(c)** Participants ranging from 8 to 19 years old were asked to verify the correctness of arithmetic equations (such as 5 + 3 = 9). Regions in red indicate areas (such as the supramarginal gyrus) that were activated to a greater extent in adults, whereas mainly prefrontal areas (blue) were recruited in younger subjects. From [52].

and proficiency, the activation seems to shift to parietal areas.

This frontal-to-parietal shift has been interpreted as a result of increasing automaticity in number tasks. The PFC could, thus, be ontogenetically and phylogenetically the first cortical area to establish semantic associations. In human adolescents, number representations might be relocated to the parietal cortex [53,54,55•] in parallel with maturing language capabilities that ultimately endow our species with a sophisticated symbolic system. The posterior parietal cortex of adults seems to store representations of number symbols in particular. In contrast, non-numerical configurational association between environmental stimuli and behavioral context, or even written words, are thought to be stored in the temporal lobe [56]; in both cases, however, the active retrieval of semantic associations seems to be under the control of the PFC.

To establish a full-fledged number theory, meaningful associations (semantics) are not sufficient. Sign–object associations must be accompanied by rules guiding the structuring of signs (syntax). Syntax refers to the rules governing structure in natural language sentences, but also the behavior of mathematical systems, such as arithmetic, logic or artificial programming languages. Syntax and semantics of individual sign–sign relations are inextricably linked. Syntax establishes relations between signs that determine the meaning of an expression. 'It is the essence of symbolic associations that their reference is determined by general rules, logical relationships that have application across all possible combinations in the system' [15]. Order, for instance, is a crucial aspect of syntax. In natural language, order may determine the agent and the patient of an expression. The sequence of the words 'man' and 'lion' in a 'killing-event' determines completely different meanings ('the man killed the lion' versus 'the lion killed the man'). Similarly, the order of numbers matters in calculation (e.g. '8–4' versus '4–8').

As with semantic sign–object relations, precursors of symbolic syntactical structures can also be identified in animal behavior, for example, in monkey communication. For instance, Zuberbühler [57] found that Campbell's male monkeys give acoustically distinct alarm calls to leopards and crowned-hawk eagles, and Diana monkeys respond to these calls with their own corresponding alarm calls. However, in less dangerous situations, Campbell's males emit a pair of low, resounding 'boom' calls before their alarm calls. Boom-introduced Campbell's alarm calls no longer elicited alarm calls in Diana monkeys, indicating that the booms have affected the semantic specificity of the subsequent alarm calls in a way that there was no normal immediate antipredator response require. Generally speaking, an understanding of which stimuli, thoughts or actions need to go together according to given rules is obligatory to achieve behavioral goals. Such circuitry is also hosted by the DLPFC: Single neurons in the primate DLPFC encode sequence plans [58,59] and abstract rules [60]. Such neuronal circuits in the primate DLPFC could readily have been adopted in the course of primate evolution for syntactic processing in human symbol systems.

That complex syntactical representations may have impinged on inferior frontal cortex networks is supported by fMRI studies investigating language grammar [61]: simple, non-recursive grammar (finite stage grammar) that can also be sensed by monkeys [62], activated the phylogenetically older frontal operculum, that is premotor cortex. In contrast, the computation of recursive hierarchical sequences (phrase-structure grammar) that characterize human language additionally recruited a phylogenetically younger region of prefrontal cortex, namely Broca's area (BA 44 and 45). BA 44/45 may thus not only be crucial for the processing of semantics, but also syntactically complex sentence hierarchies in natural languages [61]. Interestingly, mirroring findings with number symbols, both semantic and syntactic language processing demands a higher involvement of the IFG in 6-year-old children than in adults [63]. In adult humans, however, a lesion study suggests that recursive syntax of calculations can be sustained independently of language grammar [64]; maybe with age and proficiency there is also a frontal-to-parietal shift for syntactical representations, just as for symbolic number representations

Conclusion

Symbol systems are of paramount importance to human cognition, they fundamentally transform the way we think. During human ontogeny, numerical sign competence passes from an iconic to an indexical and finally symbolic stage. Animals such as nonhuman primates do not have the capacity to transcend indexical reference, they do not understand symbolic, high-order sign–sign relations. But because indexical reference constitutes the basis for high-order symbolic reference, neurobiological finding in monkeys are instructive for the evolution of symbol systems. In both young children and monkeys, neurons in the granular prefrontal cortex, a novel brain structure evolved in primates, allows extra processing abilities, such as sign and symbol acquisition and manipulation. Our understanding of number signs and symbols seems to depend on prefrontal neurons that establish links between nonsymbolic numerosities and arbitrary shapes that, together with syntactic rules guiding the structuring of signs, arrive at a symbol system in adult humans.

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