Available online at www.sciencedirect.com
ScienceDirect
Current Opinion in Neurobiology

Neural constraints on human number concepts

Andreas Nieder

True counting and arithmetic abilities are unique to humans and are inextricably linked to symbolic competence. However, our unprecedented numerical skills are deeply rooted in our neuronal heritage as primates and vertebrates. In this article, I argue that numerical competence in humans is the result of three neural constraints. First, I propose that the neuronal mechanisms of quantity estimation are part of our evolutionary heritage and can be witnessed across primate and vertebrate phylogeny. Second, I suggest that a basic understanding of number, what numerical quantity means, is innately wired into the brain and gives rise to an intuitive number sense, or number instinct. Third and finally, I argue that symbolic counting and arithmetic in humans is rooted in an evolutionarily and ontogenetically primeval neural system for non-symbolic number representations. These three neural constraints jointly determine the basic processing of number concepts in the human mind.

Address
Animal Physiology Unit, Institute of Neurobiology, University of Tübingen, Auf der Morgenstelle 28, 72076 Tübingen, Germany

Corresponding author: Nieder, Andreas (andreas.nieder@uni-tuebingen.de)

Current Opinion in Neurobiology 2020, **60**:28–36

This review comes from a themed issue on **Neurobiology of behavior**

Edited by **Richard Mooney** and **Michael Brecht**

For a complete overview see the Issue and the Editorial

Available online 4th December 2019

https://doi.org/10.1016/j.conb.2019.10.003

Introduction

To represent numbers exactly, and to calculate with them, we use a symbolic system of representation that is unique to humans [1]. Importantly, this symbolic number system is not functioning right from the start of our lives. Instead, we painstakingly have to learn over many years of training what number symbols — numerals and number words — mean and how they can be used.

However, in the absence of symbolic number representations we are not ignorant of numerical quantity. We can conceive of the approximate number of items in a set, its cardinality or numerosity, by estimating it nonsymbolically. The mental/brain system responsible for nonsymbolic quantity representations is called 'approximate number system (ANS)'. In addition to allowing an approximation of small and large numerical value, the ANS is characterized by two more behavioral characteristics. One is the 'numerical distance effect' which says that numerically distant numbers are easier to discriminate than numerically closer numbers. The other is the 'numerical size effect', meaning that at a given numerical distance, it is easier to discriminate numbers with low values than numbers with high values; discrimination is a function of value ratio, that is, is 'ratio-dependent'. Both of these phenomena are signatures of Weber's law, and the ANS obeys it. A nonsymbolic precursor of symbolic numerical competence is not only seen during human ontogeny in human infants and children [2], but also across different species in animal phylogeny [3,4]. Thus, without formal number training, and in a state of symbolic nescience, we humans and other animals can still grasp numerosity.

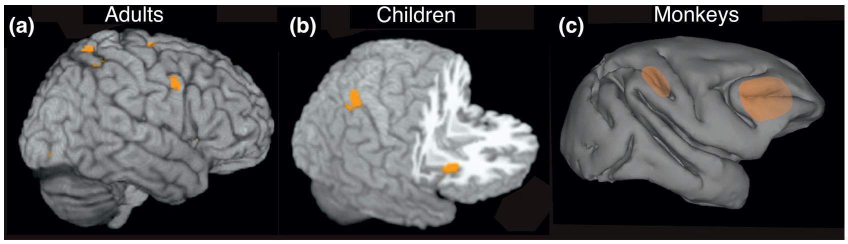
The past two decades have seen an impressive progress in locating different number skills in the human brain, both those relaying on the ANS and the symbolic number system. Examinations of brain-damaged patients and brain imaging studies identified regions primarily of the posterior parietal and frontal lobes as key areas of both nonsymbolic and symbolic number processing (Figure 1a) [5,6]. Complementing these findings in humans, neurophysiological studies in monkeys deciphered neuronal principles of numerical competence down to single neurons [7]. From these insights acquired at different levels of neuroscience, neural constraints emerge which are implemented in the human brain by evolution and development. This review highlights three neural constraints realized in ontogeny and phylogeny that determine how the human mind can conceive of basic numbers.

Evolutionary constraints on number processing

Monkey single-neuron recordings

Macaques and humans share many features of brain organization and physiology due to a relatively recent last common ancestor roughly 30 Mio years ago [8]. For instance, as mammals all primates share a six-layered neocortex as endbrain integration center, but also a primate-specific granular dorsolateral prefrontal cortex [9]. Equipped with a cerebral cortex, advanced monkeys exhibit high-level cognitive skills [10,11] and numerical capabilities [12,13]. Assuming that the human capability to estimate set size is primeval and dates back to a common ancestor with other primates, one would expect it to rely on homologous neural structures and coding mechanisms in primates.

Figure 1



Comparable brain areas are activated during number processing in primate ontogeny and evolution.
Reoccurring regions of fMRI BOLD activation during number processing in human adults **(a)** and children **(b)**, compared with areas of single-neuron activation in monkey **(c)**. Data for adults in (a) from Ref. [6], and for children in (b) from Ref. [60•].

Indeed, striking similarities between humans and monkeys indicate a common anatomical and physiological origin of numerical competence in primates which constrains where and how quantity information is processed in the human brain. In monkeys, just as in humans, the IPS and the PFC constitute the core areas for number representation and number processing [14–16] (Figure 1c). The dorsolateral prefrontal cortex (PFC) [17–19] and regions of the intraparietal sulcus (IPS) [20], most notably the ventral intraparietal area (VIP) [21–24], contain neurons responsive to numerical values (Figure 2b). The responses of such numerosity-selective neurons — or 'number neurons' — are tuned with maximum discharge rates to preferred numerical values while showing progressively decreasing activity to values more remote from the preferred one, a neuronal reflection of the numerical distance effect. Since different number neurons exhibit different preferred numerosities, the population of number neurons provides information which allows monkey to approximately discriminate all possible numerosities (Figure 2e) [25]. However, the tuning precision of number neurons deteriorates with an increase in preferred numerical values. This finding reflects a neuronal numerical size effect [5]. In addition to this Weber-law signature, the neurons' tuning functions are best described on a non-linearly compressed, logarithmic number scale [26], which mirrors the psychophysical Fecher-law observed in monkey and human behavior [27].

Human neuroimaging

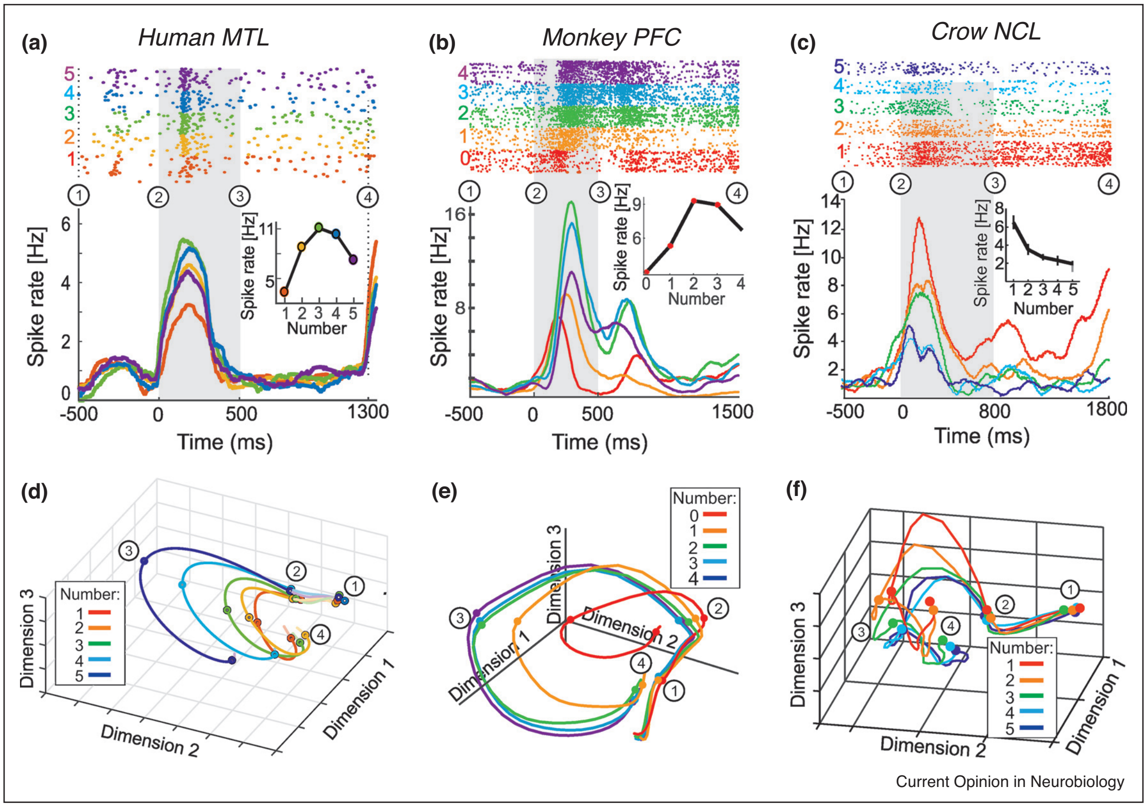
Human number representations are found in very similar and probably homologous regions of the posterior parietal and prefrontal cortex (Figure 1a,c) [5]. Lesions in the posterior parietal lobe are not only detrimental for symbolic number tasks, but also cause problems in nonsymbolic number estimation [28,29]. As a proxy for neural responses, blood oxygen level-dependent (BOLD) activity measured with functional magnetic resonance imaging (fMRI) is modulated by nonsymbolic and symbolic numerical values [6].

In order to retrace the putative tuning of number neurons underlying the BOLD signal, specific fMRI adaptation protocols were applied. This protocol exploits the electrophysiological finding that neurons decrease their firing rates to repeated presentation of the same preferred stimulus [30]. In fMRI adaptation, the subjects' BOLD activity in number-related brain areas to a certain, task-irrelevant numerosity is adapted by repeated presentation of (controlled) dot arrays of a constant number of items. When deviant numerosities are occasionally presented, a systematic release from adaptation of the BOLD signal as a function of the numerical distance from the habituated numerosity is observed. In several studies exploiting fMRI adaptation, the subjects' BOLD responses to numerical changes formed an upside-down peaked curve indicative of neurons tuned to specific numerosities. This kind of spontaneous tuning based on BOLD activity was shown primarily in and around the intraparietal sulcus (IPS), but also the lateral prefrontal cortex (PFC) [31–33].

Human single-neuron recordings

The functional imaging literature suggested that tuned number-selective neurons also existed in the human brain. However, human imaging methods are limited in drawing conclusions about neuronal responses [34]. Recently, the electrical activity of number neurons could be directly recorded in patients who underwent treatment for pharmacologically intractable epilepsy and were implanted with chronic depth electrodes in the medial temporal lobe (MTL) [35••]. Although the MTL is not considered part of the core number network, imaging studies show that the hippocampal system represents numerical information when children learn to count and perform arithmetic [36]. In this recording study, the patients performed simple sequential addition and subtraction tasks with operands of small numerical values [35••]. In half of the trials, the numerical values were presented non-symbolically as dot numerosities. A substantial 16% of the randomly

Figure 2



Single neuron and population responses in human MTL (left), monkey PFC (middle), and crow NCL (right) represent numerosity.
(a) Responses of an example human MTL neuron selective to numerosity 3. Top panel shows dot-raster histograms (each dot represents an action potential), bottom panel depicts averaged spike density functions (activity averaged and smoothed). Each colored line shows the time course of activity for the five tested quantities 1–5. The first 500 ms represent the fixation period (baseline). Gray shading represents the sample period in which the numerosity display was shown. The tuning curve insets indicate the mean activity of the neurons to the numerosities in the sample period. **(b)** Example numerosity-selective neuron recorded from monkey PFC. Same layout as in (a). (Note the slightly different range of tested numerosities from 0 to 4). **(c)** Example numerosity-selective neuron recorded from crow NCL. Same layout as in (A). **(d)** Dynamics of neuronal population of human MTL neurons based on state-space analysis. Average state-space trajectories, reduced to the three principal dimensions for visualization, depict the activity of many numerosity-selective neurons (n = 92) in three-dimensional space. Each trajectory shows the temporal evolution of population activity. Encircled numbers indicate boundaries between task periods as shown in (a). The trajectories diverge after numerosity presentation, indicating increased neuronal discriminabilty between numerosities. **(e)** Dynamics of the population of monkey PFC neurons. Same layout as in (D). **(f)** Dynamics of the population of crow NCL neurons Same layout as in (d). Data in (A,D) from [35], data in (b,e) from [25], data in (c) from Ref. [48], data in (f) from Ref. [50].

selected MTL neurons responded to the number of items in the first operand, irrespective of the dot array layout. Each selective cell was tuned to a preferred numerosity (Figure 2a). The bell-shaped number tuning curves also explained the rather large numerical distance effect found for non-symbolic numerosity comparisons in humans [37] Using computational decoding analyses, numerosities could reliably be predicted from the population of MTL neurons (Figure 2d). These findings provide evidence for these neurons as the physiological correlate of numerosity representations. What is more, this code present in the human brain was exactly the type of approximate number code previously seen in monkeys [7], thus suggesting an evolutionarily conserved code.

Recordings in corvid songbirds

As primates, humans and monkeys share profound neural similarities for number processing. However, if the roots of numerical competence reach even deeper in evolution, one may expect similar computational principles in vertebrates that are only distantly related to mammals and primates, and may even exhibit a very different brain anatomy.

Birds are ideal models to address this question. The high-level cognitive feats corvid songbirds [38,39•] includes the ability to judge and process numerical quantity with considerable precision [40,41]. However, the prehistoric reptilian-like last common ancestor of birds and primates lived already about 320 million years ago [42,43]. During this long time of parallel evolution, the avian endbrain evolved differently from mammals and realized nuclear-organized circuits rather than a layered cerebral cortex found in mammals [44•,45]. In this nuclear avian endbrain, the associative endbrain area termed 'nidopallium caudolaterale (NCL)' is considered to be the functional equivalent of the primate prefrontal cortex (PFC) [46,47].

Electrophysiological recordings in behaving crows have shown that the corvid brain has implemented exactly the same code as primates to represent numerical quantity. Crow NCL neurons are tuned to individual numerosities by discharging strongest to their respective preferred numerosity (Figure 2c) [48•,49]. The characteristics of both the neuronal and the behavioral tuning functions as well as the responses of the population of numerosity-selective neurons in NCL nicely explain the numerical distance and size effects seen in crow behavior (Figure 2f) [50].

The positive results from the crow brain could indicate one of two evolutionary scenarios: Either the same computational principles for number processing were independently implemented twice (or more) in remotely related vertebrates based on convergent evolution. Alternatively, canonical endbrain microcircuits giving rise to specific computational mechanisms may have evolved in a common sauropsid ancestor around 320 Mio years ago and were inherited since then with certain modifications by modern mammals and birds [44]. In any case, remotely related vertebrates with distinctly developed endbrains adopted similar physiological solutions to common computational problems in number processing.

Innate wiring in the brain

Numerical representations in number nescience

The human mind is not a blank slate when we are born, and this applies also to the realm of numerical quantity. Newborn human infants at the age of 50 hours already discriminate numerosity across sensory modality and sequential and simultaneous presentation formats [51]. The newborns showed the ratio-dependent numerical performance characteristic for the approximate number system (ANS) and its Weber's law signature that are frequently encountered in children, adults, and animals.

Analogous experiments very early in development have been performed in birds. The young domestic chick is an extremely precocial species and has been tested for numerical competence right after hatching from the egg and thus with a minimum of visual experience. Chicks have been shown to discriminate visual numerosity and even perform rudimentary calculations [52,53]. It may therefore not come as a surprise that also animals in the wild without any specific training, are endowed with numerical capabilities [54••].

The study of newborns and infants represent a radical case of counting nescience. But such a condition can also be found in adult humans. Indigenous people who have not attended school and cannot count can nevertheless discriminate quantity approximately and even perform rough calculations with set sizes [55–57]. As a classic signature of the ANS, discrimination performance in indigenous people becomes less precise with increasing target numbers. Of course, it is notoriously difficult to disentangle numerical information from other visual magnitudes, such as surface area, particularly when testing spontaneous numerosity discrimination behavior in infants and animals. In fact, the internal representation of number is tightly bound to the representation of other magnitudes [58] which become negligible with number training [59]. In general, however, visual number dominates the perception of other quantitative visual features in sets of objects both in humans and animals [60•,61•,62].

Numerical fMRI activation in young children before formal use of number

In agreement with behavioral findings in infants and young children, the neuronal machinery to extract number information is already in place early in ontogeny. When four-year-old children were presented with dot arrays in an fMRI adaptation protocol, activations in the posterior parietal and frontal lobes were found that were strikingly similar to those observed in adult participants tested under identical conditions [63]. Even in six-month-old [64] and three-month-old infants [65], very similar cortical areas were recruited for non-symbolic number processing, long before formal schooling has begun. A recent meta-analysis combining 32 imaging studies showed that number performance in children younger than 14 years emerges from known core areas of the cortical number network, such as posterior parietal and prefrontal cortices (Figure 1b) [66•]. In order to go beyond localization and to decipher the neural mechanism of number processing in children before formal number training, three-year-old to six-year-old children were tested with an fMRI adaptation protocol [67••]. Just as in adults and as predicted by single-neuron data, the children's BOLD responses to numerical changes formed an upside–down curve. Functional number neurons seem to be already at work by 3–4 years in humans, and most likely even earlier.

Number neurons in numerically naïve animals

If the brain is spontaneously endowed with the capacity to extract numbers, then number-selective neurons should be present without specific numerical training. This was indeed demonstrated in monkey that had never been trained to discriminate numerosity [68]. In monkeys ignorant of the number of dots in stimuli, about 10% of the randomly sampled neurons in PFC and VIP selectively responded to number. The number neurons in numerically naïve monkeys were spontaneously tuned to preferred numerosities and showed the same code as in trained animals [7].

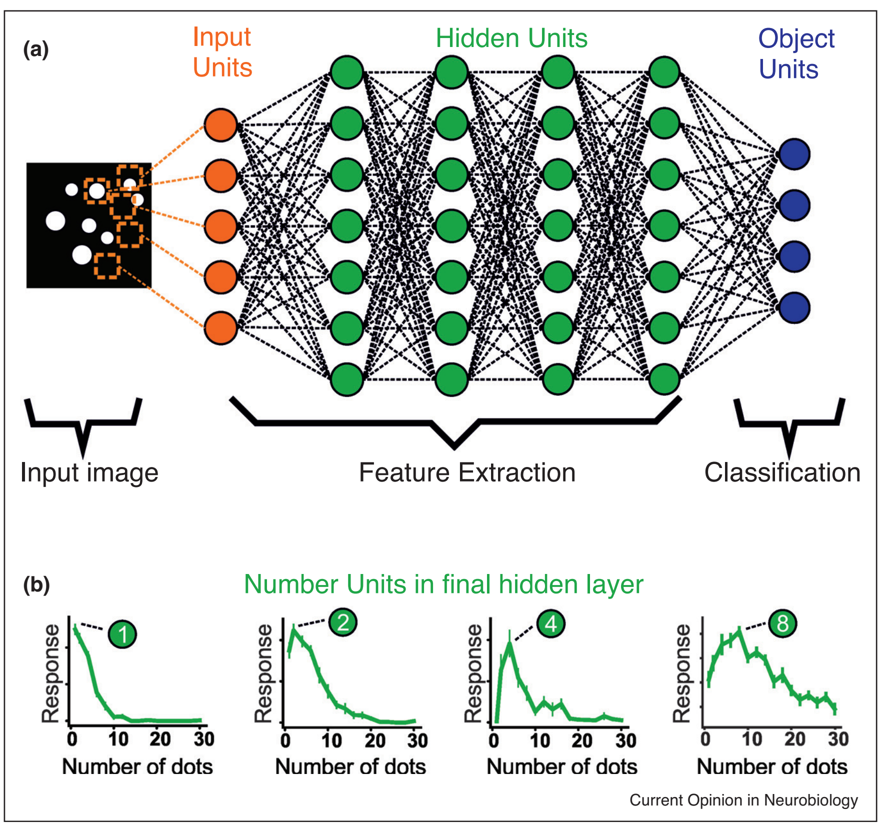
When the same initially numerically naive monkeys were later retrained to now actively discriminate visual numerosities, PFC neurons became more responsive and more selective during active discrimination, whereas none of these effects were observed for VIP neurons [69]. This indicates that PFC neurons become more engaged when the task requires it, whereas VIP neurons continue to encode numerosity as a visual stimulus regardless of behavioral relevance. The spontaneous existence of number neurons is not confined to the cerebral cortex because such neurons were also found in in the NCL of numerically naïve crows [70] Overall, this suggests number neurons to be present across phylogeny in any numerically competent animal.

Spontaneous visual number representations in neural networks

Considering that the visual system is by nature primarily concerned with visual objects, how can this capability to spontaneously extract numerical quantity be explained? In recent years, deep neural networks that mimic processing in the visual system have provided insights to the workings of the number system. Generative neural networks, a class of deep networks that learn to form an internal model of the sensory input, became sensitive to numerosity; however, such networks could not explain the emergence of real tuned number neurons [71].

Recently, therefore, so-called 'hierarchical convolutional neural networks (HCNN)', a class of biologically inspired models were used to understand how vision might give rise to numerical competence [72,73]. In one study, a HCNN was trained on a visual object recognition task unrelated to numbers (Figure 3a) [74••]. Although this HCNN was merely trained to classify natural images, about 10% of the network units spontaneously exhibited numerosity selectivity with characteristics virtually identical to real neurons (Figure 3b). In agreement with neurophysiology [17,23,35,48], the network units were tuned to preferred numerosities, exhibited approximate tuning that decreased in precision with increasing numbers, and were best described on a logarithmically

Figure 3



Number neurons spontaneously emerge in a deep neural network only trained for object recognition.
(a) Simplified architecture of the hierarchical convolutional neural network (HCCN) that consisted of a feedforward hierarchy of layers, in which visual input (controlled dot arrays) was received by network units in the first layer and propagated through multiple layers along the hierarchy. The network can be conceptually divided into two parts: a feature extraction network (green) and a classification network (blue). **(b)** Numerosity-tuned units emerging in the hidden units (green) of the feature extraction network of the HCNN. Four example network unit tuned to 1, 2, 4 and 8 are depicted. in agreement with real number neurons, the network units exhibited approximate tuning that decreased in precision with increasing numbers, and was best described on a logarithmically compressed number line. Data in (b) from Ref. [74].

compressed number line. Moreover, the network's numerosity-tuned units allowed for reliable categorization of the number of items in dot displays and showed all the characteristics expected based on the Weber-Fechner law [7].

Collectively, these findings in numerically naïve children, adults, animals, and neural networks suggest that the spontaneous emergence of the visual number sense is based on mechanisms inherent to the visual system. Visual numerosity-selectivity can emerge as a by-product of exposure to natural visual stimuli, without requiring any explicit training for numerosity estimation.

Of course, this is not to say that the brain's abstract number system is fully explained by these findings in the visual domain. The spontaneous visual numerosity representations that are at work right after birth or in neural networks cannot be regarded as abstract and cross-modal number representations. In addition to visual numerosities, also auditory and tactile number has to be extracted, most likely by the auditory and somatosensory system, respectively. In addition, sensory numerosity representations by themselves do not suffice because — like no other abstract magnitude — numerical information needs to be processed according to abstract principles to become behaviorally meaningful. Thus, both the merging of putative unimodal number representations and the processing of numbers requires true association brain areas that show some specialization for numerical information, such as the parieto-frontal core number network. Moreover, the neural substrates for numerical quantity remain flexible and experience modifications, in particular with regard to symbol usage in humans [75]. Thus, the currently identified innate 'visual number sense' is best considered a subcomponent of an abstract number network in the brain.

Human symbolic number concepts rooted in non-symbolic representations

Whether or not the approximate number system (ANS) acts as a start-up tool for symbolic counting is an intense debate [76,77]. However, almost all scientists working in the field would agree that one way or another, the ANS must play a key role because only the ANS provides information about cardinality, that is, what numerical quantity means. This suggests that symbolic counting is, at least partly, grounded in non-symbolic quantity representations [1], as outlined below.

Shared behavioral characteristics in children and adults

Numerate adults show shared behavioral characteristics for both nonsymbolic and symbolic number discriminations, such as the numerical distance and size effect and Weber's law [37,78,79]. More importantly, infants and children rely on the ANS during number symbol acquisition in development. Their precision for numerosity judgments improves continuously throughout childhood, and individual differences in achievement in mathematics are related to individual differences in the acuity of the ANS [80]. Thus, exercises that aim at enhancing addition and subtraction with numerosities have a positive effect for symbolic arithmetic [81]. A total of three meta-analyses found support for a modest but significantly positive relation between approximate numerosity estimation and math ability [82–84].

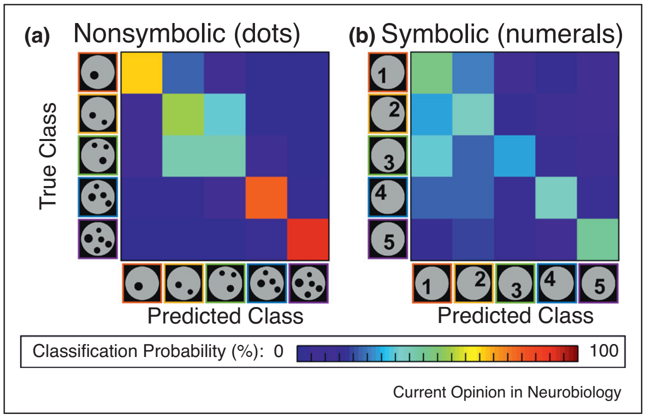
The ANS and the symbolic number system interact and rely on each other not only in healthy development but also when it is challenged. Math development is seriously handicapped when the ANS is inefficient. Dyscalculia, a severe disability in learning and performing arithmetic, is also known to be based on deficits in fundamental number skills, such as assessing small sets of objects [85] or comparing the numerosities of two-dot arrays [86]. Thus, problems with discriminating numerosities in preschool children can predict trouble with learning arithmetic later in school because deficits in higher-level mathematical skills may stem from impaired representations of basic numerical magnitudes by the ANS [87].

Dyscalculia brain research provides further links between the nonsymbolic and symbolic systems. In infants and young children, a parieto-frontal number network similar to the adult system is initially used to represent nonsymbolic quantity [66,67], but with number training learns to also represent number symbols. Compared to normally developing children, dyscalculic children showed decreased activation in some of the same brain areas related to quantity representations, as well as stronger activation in others [88]. Also, children with dyscalculia tend to have less robust number-related activations in the IPS, but also recruit more distributed brain regions, particularly in the frontal lobe [89].

Single-neuron in humans represent nonsymbolic and symbolic number

A link between nonsymbolic and symbolic number representations was recently also found at the level of single neurons. In the same intracranial recording study, in which patients performed calculations with nonsymbolic numerosities, patients also solved these arithmetic problems with number symbols (Arabic numerals) presented on half of the trials [35]. A small but significant proportion of neurons responded selectively to numerical values of numerals. Interestingly, the groups of MTL neurons responding to numerals or dot numerosities hardly overlapped. Thus, distinct groups of neurons represented either nonsymbolic or symbolic number formats, but not both number formats simultaneously. Whether segregated populations of such 'format-dependent' number neurons are a special feature of the MTL or the general way of how our brain encodes different formats of numbers needs to be addressed in the future.

Figure 4



Numerical values of numerosities and Arabic numerals can be read out from populations of tuned MTL neurons in the human brain.
A support vector machine-classifier was trained to classify numerical values using the firing rates of MTL neurons to a subset of numerosities **(a)** and Arabic numerals **(b)**, and then the classifier's performance was tested on held-out stimuli. The resulting confusion matrices show robust classification accuracy for the five numerosities in the nonsymbolic (a) and symbolic format (b) as represented by high performance values along the diagonal. As a reflection of the numerical distance effect, the probability of misclassification of trials increased the closer two classes were in the numerical space, in particular for the nonsymbolic number format. From Ref. [35].

The numeral-selective neurons were also tuned to preferred values, just like numerosity-selective neurons [35]. This suggests a labeled-line code, not only for non-symbolic, but also for symbolic numbers. Importantly, the population of numeral-selective neurons carried enough information to allow a statistical classifier to correctly assign numerical values above chance (Figure 4). The numeral-selective neurons' tuning functions were sharp and only mildly overlapped [35]. This means that tuning to number symbols was more selective than tuning to non-symbolic numbers and barely showed a numerical distance effect. This finding is in agreement with behavioral studies in humans and neural modeling, which show that the distance effect is substantial for the comparison of non-symbolic numerosities, but minute for judgments on exact number symbols [37,90]. The presence of a distance effect for number symbols again argues that high-level human numerical abilities are inherited from more basic non-symbolic number representations. Number symbols seem to acquire their numerical meanings by becoming linked to evolutionarily conserved set size representations during the course of cognitive development.

Conclusion

In summary, the data reviewed support an initial and at least partial grounding of the symbolic number system in the non-symbolic ANS. Given the recency of symbolic number capacities to the human species (a cultural invention dating to within a few thousand years [1]), it is hardly conceivable that the human brain could have evolved exclusively *de novo* neural mechanisms for the processing of numerical quantities. The current neurobiological findings suggest that number processing abilities must build upon, and thus be strongly constrained by, the prior evolution of the primate and vertebrate brain.

Conflict of interest statement

Nothing declared.

Acknowledgement

Supported by DFG grants NI 618/2-1, NI 618/3-1, NI 618/4-1, and NI 618/10-1.

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1. Nieder A: *A Brain for Numbers: The Biology of the Number Instinct*. Cambridge, USA: MIT Press; 2019.

2. Feigenson L, Dehaene S, Spelke E: **Core systems of number**. *Trends Cogn Sci* 2004, **8**:307-314.

3. Agrillo C, Miletto Petrazzini ME, Bisazza A: **Numerical abilities in fish: a methodological review**. *Behav Processes* 2017, **141**:161-171.

4. Nieder A: **Evolution of cognitive and neural solutions enabling numerosity judgements: lessons from primates and corvids**. *Philos Trans R Soc Lond B Biol Sci* 2017, **373**.

5. Nieder A, Dehaene S: **Representation of number in the brain**. *Annu Rev Neurosci* 2009, **32**:185-208.

6. Arsalidou M, Taylor MJ: **Is 2+2=4? Meta-analyses of brain areas needed for numbers and calculations**. *Neuroimage* 2011, **54**:2382-2393.

7. Nieder A: **The neuronal code for number**. *Nat Rev Neurosci* 2016, **17**:366-382.

8. Fleagle JG, Seiffert ER: **The phylogeny of primates**. In *Evolution of Nervous Systems*, edn 2, vol 3. Edited by Kaas JH. Academic Press/Elsevier; 2017:1-35.

9. Wise SP: **Forward frontal fields: phylogeny and fundamental function**. *Trends Neurosci* 2008, **31**:599-608.

10. Reader SM, Hager Y, Laland KN: **The evolution of primate general and cultural intelligence**. *Philos Trans R Soc Lond B Biol Sci* 2011, **366**:1017-1027.

11. Platt ML, Seyfarth RM, Cheney DL: **Adaptations for social cognition in the primate brain**. *Philos Trans R Soc Lond B Biol Sci* 2016, **371**:20150096.

12. Brannon EM, Terrace HS: **Ordering of the numerosities 1 to 9 by monkeys**. *Science* 1998, **282**:46-49.

13. Jordan KE, Maclean EL, Brannon EM: **Monkeys match and tally quantities across senses**. *Cognition* 2008, **108**:617-625.

14. Bongard S, Nieder A: **Basic mathematical rules are encoded by primate prefrontal cortex neurons**. *Proc Natl Acad Sci U S A* 2010, **107**:2277-2282.

15. Vallentin D, Bongard S, Nieder A: **Numerical rule coding in the prefrontal, premotor, and posterior parietal cortices of macaques**. *J Neurosci* 2012, **32**:6621-6630.

16. Eiselt AK, Nieder A: **Representation of abstract quantitative rules applied to spatial and numerical magnitudes in primate prefrontal cortex**. *J Neurosci* 2013, **33**:7526-7534.

17. Nieder A, Freedman DJ, Miller EK: **Representation of the quantity of visual items in the primate prefrontal cortex**. *Science* 2002, **297**:1708-1711.

18. Nieder A, Merten K: **A labeled-line code for small and large numerosities in the monkey prefrontal cortex**. *J. Neurosci* 2007, **27**:5986-5993.

19. Nieder A: **Supramodal numerosity selectivity of neurons in primate prefrontal and posterior parietal cortices**. *Proc Natl Acad Sci U S A* 2012, **109**:11860-11865.

20. Sawamura H, Shima K, Tanji J: **Numerical representation for action in the parietal cortex of the monkey**. *Nature* 2002, **415**:918-922.

21. Nieder A, Miller EK: **A parieto-frontal network for visual numerical information in the monkey**. *Proc Natl Acad Sci U S A* 2004, **101**:7457-7462.

22. Nieder A, Diester I, Tudusciuc O: **Temporal and spatial enumeration processes in the primate parietal cortex**. *Science* 2006, **313**:1431-1435.

23. Jacob SN, Nieder A: **Complementary roles for primate frontal and parietal cortex in guarding working memory from distractor stimuli**. *Neuron* 2014, **83**:226-237.

24. Okuyama S, Kuki T, Mushiake H: **Representation of the numerosity' zero' in the parietal cortex of the monkey**. *Sci Rep* 2015, **5**:10059.

25. Ramirez-Cardenas A, Moskaleva M, Nieder A: **Neuronal representation of numerosity zero in the primate parieto-frontal number network**. *Curr Biol* 2016, **26**:1285-1294.

26. Nieder A, Miller EK: **Coding of cognitive magnitude: compressed scaling of numerical information in the primate prefrontal cortex**. *Neuron* 2003, **37**:149-157.

27. Merten K, Nieder A: **Compressed scaling of abstract numerosity representations in adult humans and monkeys**. *J Cogn Neurosci* 2009, **21**:333-346.

28. Lemer C, Dehaene S, Spelke E, Cohen L: **Approximate quantities and exact number words: dissociable systems**. *Neuropsychologia* 2003, **41**:1942-1958.

29. Ashkenazi S, Henik A, Ifergane G, Shelef I: **Basic numerical processing in left intraparietal sulcus (IPS) acalculia**. *Cortex* 2008, **44**:439-448.

30. Desimone R: **Neural mechanisms for visual memory and their role in attention**. *Proc Natl Acad Sci U S A* 1996, **93**:13494-13499.

31. Piazza M, Izard V, Pinel P, Le Bihan D, Dehaene S: **Tuning curves for approximate numerosity in the human intraparietal sulcus**. *Neuron* 2004, **44**:547-555.

32. Jacob SN, Nieder A: **Tuning to non-symbolic proportions in the human frontoparietal cortex**. *Eur J Neurosci* 2009, **30**:1432-1442.32.

33. Demeyere N, Rotshtein P, Humphreys GW: **Common and dissociated mechanisms for estimating large and small dot arrays: value-specific fMRI adaptation**. *Hum Brain Mapp* 2014, **35**:3988-4001.

34. Nieder A: **The number domain- can we count on parietal cortex?** *Neuron* 2004, **44**:407-409.

35. •• Kutter EF, Bostroem J, Elger CE, Mormann F, Nieder A: **Single neurons in the human brain encode numbers**. *Neuron* 2018, **100**:753-761

The first intracranial single-unit recordings of numerosity-selective and numeral-selective neurons in the human brain in regions of the medial temporal lobe. It revealed striking similarities in number coding in the human brain compared to nonhuman primate brains.

36. Menon V: **Memory and cognitive control circuits in mathematical cognition and learning**. *Prog Brain Res* 2016, **227**:159-186.

37. Buckley PB, Gillman CB: **Comparisons of digits and dot patterns**. *J Exp Psychol* 1974, **103**:1131-1136.

38. Clayton NS, Emery NJ: **Avian models for human cognitive neuroscience: s proposal**. *Neuron* 2015, **86**:1330-1342.

39. • Güntürkün O, Bugnyar T: **Cognition without cortex**. *Trends Cogn Sci* 2016, **20**:291-303

Comprehensive and up-to-date review on the anatomical basis of cognition in birds. During the long parallel evolution of mammals and birds, several neural mechanisms for cognition and complex behaviors may have converged despite an overall forebrain organization that is otherwise vastly different.

40. Bogale BA, Aoyama M, Sugita S: **Spontaneous discrimination of food quantities in the jungle crow, Corvus macrorhynchos**. *Anim Behav* 2014, **94**:73-78.

41. Ditz HM, Nieder A: **Numerosity representations in crows obey the Weber-Fechner law**. *Proc Biol Sci* 2016, **283**:20160083.

42. Kumar S, Hedges SB: **A molecular timescale for vertebrate evolution**. *Nature* 1998, **392**:917-920.43.

43. Hedges SB: **The origin and evolution of model organisms**. *Nat Rev Genet* 2002, **3**:838-849.

44. • Karten HJ: **Vertebrate brains and evolutionary connectomics: on the origins of the mammalian' neocortex'**. *Philos Trans R Soc Lond B Biol Sci* 2015, **370**:1684

Survey on the analysis of the nuclear organization of the avian brain, its connections, molecular properties and physiology, and organization of its pattern of circuitry and function relative to that of mammals, collectively referred to as 'evolutionary connectomics', by one of the grandmasters of comparative neuroanatomy. It describes how regions of the DVR, wulst and arcopallium of the avian brain contain telencephalic inputs and outputs remarkably similar to those of the individual layers of the mammalian 'neocortex', hippocampus and amygdala.

45. Dugas-Ford J, Ragsdale CW: **Levels of homology and the problem of neocortex**. *Annu Rev Neurosci* 2015, **38**:351-368.

46. Güntürkün O: **The avian' prefrontal cortex' and cognition**. *Curr Opin Neurobiol* 2005, **15**:686-693.

47. Nieder A: **Inside the corvid brain—probing the physiology of cognition in crows**. *Curr Opin Behav Sci* 2017, **16**:8-14.

48. • Ditz HM, Nieder A: **Neurons selective to the number of visual items in the corvid songbird endbrain**. *Proc Natl Acad Sci U S A* 2015, **112**:7827-7832

First demonstration of numerosity-tuned neurons outside of the primate lineage. The authors monitored single-neuron activity while crows performed a number-matching task. Neurons in the NCL were tuned to the numbers of visual items, regardless of the item's size or spatial arrangement.

49. Ditz HM, Nieder A: **Sensory and working memory representations of small and large numerosities in the crow endbrain**. *J Neurosci* 2016, **36**:12044-12052 http://dx.doi.org/10.1523/JNEUROSCI.1521-16.2016.

50. Ditz HM, Kupferman JK, Nieder A: **Neurons in the hippocampus of crows lack responses to non-spatial abstract categories**. *Front Syst Neurosci* 2018, **12**:33.

51. Izard V, Sann C, Spelke ES, Streri A: **Newborn infants perceive abstract numbers**. *Proc Natl Acad Sci U S A* 2009, **106**:10382-10385.

52. Rugani R, Regolin L, Vallortigara G: **Discrimination of small numerosities in young chicks**. *J Exp Psychol Anim Behav Process* 2008, **34**:388-399.

53. Rugani R, Fontanari L, Simoni E, Regolin L, Vallortigara G: **Arithmetic in newborn chicks**. *Proc Biol Sci* 2009, **276**:2451-2460.

54. •• Piantadosi ST, Cantlon JF: **True numerical cognition in the wild**. *Psychol Sci* 2017, **28**:462-469

Using data from wild baboons' troop movements to explain a variety of models of quantitative decision making, the authors find that baboos' decision making rely specifically on numerical representations. These numerical representations have key homologies with the psychophysics of human number representations. These findings provide the first robust evidence of true numerical reasoning in wild animals.

55. Gordon P: **Numerical cognition without words: evidence from Amazonia**. *Science* 2004, **306**:496-499.

56. Pica P, Lemer C, Izard V, Dehaene S: **Exact and approximate arithmetic in an Amazonian indigene group**. *Science* 2004, **306**:499-503.

57. Frank MC, Everett DL, Fedorenko E, Gibson E: **Number as a cognitive technology: evidence from Pirahã language and cognition**. *Cognition* 2008, **108**:819-824.

58. DeWind NK, Adams GK, Platt ML, Brannon EM: **Modeling the approximate number system to quantify the contribution of visual stimulus features**. *Cognition* 2015, **142**:247-265.

59. DeWind NK, Brannon EM: **Malleability of the approximate number system: effects of feedback and training**. *Front Hum Neurosci* 2012, **6**:68.

60. • Cicchini GM, Anobile G, Burr DC: **Spontaneous perception of numerosity in humans**. *Nat Commun* 2016, **7**:12536
Human subjects were shown to be far more sensitive to numerosity than to either density or area of dot arrays. Even in tasks where they were explicitly instructed to make density or area judgments, they responded spontaneously to number. The authors conclude that humans extract number information directly and spontaneously via dedicated mechanisms.

61. • Ferrigno S, Jara-Ettinger J, Piantadosi ST, Cantlon JF: **Universal and uniquely human factors in spontaneous number perception**. *Nat Commun* 2017, **8**:1-10
Adults and children, non-human primates, and numerate and innumerate Tsimane' adults were tested on a quantity task, in which they could choose to categorize sets of dots on the basis of number alone, surface area alone or a combination of the two. All subjects were universally biased to base their judgments on number as opposed to the alternatives. Humans and monkeys universally and spontaneously extract numerical information.

62. Anobile G, Guerrini G, Burr DC, Monti M, Del Lucchese B, Cicchini GM: **Spontaneous perception of numerosity in pre-school children**. *Proc Biol Sci* 2019, **286**:20191245.

63. Cantlon JF, Brannon EM, Carter EJ, Pelphrey KA: **Functional imaging of numerical processing in adults and 4-y-old children**. *PLoS Biol* 2006, **4**:e125.

64. Hyde DC, Boas DA, Blair C, Carey S: **Near-infrared spectroscopy shows right parietal specialization for number in pre-verbal infants**. *Neuroimage* 2010, **53**:647-652.

65. Izard V, Dehaene-Lambertz G, Dehaene S: **Distinct cerebral pathways for object identity and number in human infants**. *PLoS Biol* 2008, **6**:e11.

66. • Arsalidou M, Pawliw-Levac M, Sadeghi M, Pascual-Leone J: **Brain areas associated with numbers and calculations in children: meta-analyses of fMRI studies**. *Dev Cogn Neurosci* 2018, **30**:239-250
Using quantitative meta-analyses of functional magnetic resonance imaging (fMRI) studies on children 14 years and younger, the authors identified concordant brain areas across articles that show activity to number tasks and calculation tasks, most notably areas of the parietal and frontal lobes.

67. •• Kersey AJ, Cantlon JF: **Neural tuning to numerosity relates to perceptual tuning in 3-6-year-old children**. *J Neurosci* 2017, **37**:512-522
Applying fMRI adaptation on 3–6-year-old children, the authors report neural tuning to cardinal numerosities in the IPS. The children's neural responses were accounted for by a model of numerosity coding that has been used to explain neural responses in the adult IPS. This research provides novel evidence of developmental continuity in the neural code underlying numerical representation and demonstrates that children's neural sensitivity to numerosity exists very early in ontogeny, and before formal education.

68. Viswanathan P, Nieder A: **Neuronal correlates of a visual "sense of number" in primate parietal and prefrontal cortices**. *Proc Natl Acad Sci U S A* 2013, **110**:11187-11192.

69. Viswanathan P, Nieder A: **Differential impact of behavioral relevance on quantity coding in primate frontal and parietal neurons**. *Curr Biol* 2015, **25**:1259-1269.

70. Wagener L, Loconsole M, Ditz HM, Nieder A: **Neurons in the endbrain of numerically naive crows spontaneously encode visual numerosity**. *Curr Biol* 2018, **28**:1090-1094.

71. Stoianov I, Zorzi M: **Emergence of a "visual number sense" in hierarchical generative models**. *Nat Neurosci* 2012, **15**:194-196.

72. Cadieu CF, Hong H, Yamins DL, Pinto N, Ardila D, Solomon EA, Majaj NJ, DiCarlo JJ: **Deep neural networks rival the representation of primate IT cortex for core visual object recognition**. *PLoS Comput Biol* 2014, **10**:e1003963.

73. Yamins DL, Hong H, Cadieu CF, Solomon EA, Seibert D, DiCarlo JJ: **Performance-optimized hierarchical models predict neural responses in higher visual cortex**. *Proc Natl Acad Sci U S A* 2014, **111**:8619-8624.

74. •• Nasr K, Viswanathan P, Nieder A: **Number detectors spontaneously emerge in a deep neural network designed for visual object recognition**. *Sci Adv* 2019, **5**:eaav7903
The authors show that network units tuned to abstract numerosity, and therefore reminiscent of real number neurons, spontaneously emerge in a biologically inspired deep neural network that was merely trained on visual object recognition. These findings explain the spontaneous emergence of the number sense based on mechanisms inherent to the visual system.

75. Dehaene S, Cohen L: **Cultural recycling of cortical maps**. *Neuron* 2007, **56**:384-398.

76. Piazza M: **Neurocognitive start-up tools for symbolic number representations**. *Trends Cogn Sci* 2010, **14**:542-551.

77. Carey S, Barner D: **Ontogenetic origins of human integer representations**. *Trends Cogn Sci* 2019, **23**:823-835.

78. Moyer RS, Landauer TK: **Time required for judgements of numerical inequality**. *Nature* 1967, **215**:1519-1520.

79. Dehaene S, Dupoux E, Mehler J: **Is numerical comparison digital? Analogical and symbolic effects in two-digit number comparison**. *J Exp Psychol Hum Percept Perform* 1990, **16**:626-641.

80. Halberda J, Mazzocco MMM, Feigenson L: **Individual differences in non-verbal number acuity correlate with maths achievement**. *Nature* 2008, **455**:665-668.

81. Park J, Brannon EM: **Training the approximate number system improves math proficiency**. *Psychol Sci* 2013, **24**:2013-2019.

82. Chen Q, Li J: **Association between individual differences in non-symbolic number acuity and math performance: a meta-analysis**. *Acta Psychol* 2014, **148**:163-172.

83. Fazio LK, Bailey DH, Thompson CA, Siegler RS: **Relations of different types of numerical magnitude representations to each other and to mathematics achievement**. *J Exp Child Psychol* 2014, **123**:53-72.

84. Schneider M, Beeres K, Coban L, Merz S, Susan Schmidt S, Stricker J, De Smedt B: **Associations of non-symbolic and symbolic numerical magnitude processing with mathematical competence: a meta-analysis**. *Dev Sci* 2017, **20**:e12372.

85. Landerl K, Bevan A, Butterworth B: **Developmental dyscalculia and basic numerical capacities: a study of 8–9-year-old students**. *Cognition* 2004, **93**:99-125.

86. Piazza M, Facoetti A, Trussardi AN, Berteletti I, Conte S, Lucangeli D, Dehaene S, Zorzi M: **Developmental trajectory of number acuity reveals a severe impairment in developmental dyscalculia**. *Cognition* 2010, **116**:33-41.

87. Reeve R, Reynolds F, Humberstone J, Butterworth B: **Stability and change in markers of core numerical competencies**. *J Exp Psychol Gen* 2012, **141**:649-666.

88. Kaufmann L, Wood G, Rubinsten O, Henik A: **Meta-analyses of developmental fMRI studies investigating typical and atypical trajectories of number processing and calculation**. *Dev Neuropsychol* 2011, **36**:763-787.

89. Price GR, Holloway I, Räsänen P, Vesterinen M: **Ansari D impaired parietal magnitude processing in developmental dyscalculia**. *Curr Biol* 2007, **17**:R1042-R1043.

90. Verguts T, Fias W: **Representation of number in animals and humans: a neural model**. *J Cogn Neurosci* 2004, **16**:1493-1504.