

COUNTING ON NEURONS: THE NEUROBIOLOGY OF NUMERICAL COMPETENCE

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Abstract | Numbers are an integral part of our everyday life — we use them to quantify, rank and identify objects. The verbal number concept allows humans to develop superior mathematical and logic skills that define technologically advanced cultures. However, basic numerical competence is rooted in biological primitives that can be explored in animals, infants and human adults alike. We are now beginning to unravel its anatomical basis and neuronal mechanisms on many levels, down to its single neuron correlate. Neural representations of numerical information can engage extensive cerebral networks, but the posterior parietal cortex and the prefrontal cortex are the key structures in primates.

“The truths of arithmetic govern all that is numerable. This is the widest domain of all; for to it belong not only the existent, not only the intuitable, but everything thinkable. Should not the laws of number, then, be connected very intimately with the laws of thought?”¹

We are surrounded by numbers. We use them for counting items, telling the time, calculating prices, encoding credit cards, solving equations, keeping score of sports games, identifying flights, ranking journals and so on. What makes numbers special is their incredible flexibility; they can be used to quantify, rank and identify virtually everything imaginable, be it fact or fiction. With the support of language, we process numerical information with infinite precision and in endless applications.

Although true counting and mathematics are cultural achievements that are bound to language, it has become evident over recent decades that animals that lack language also possess basic numerical capabilities. Comparative psychologists have shown that animals discriminate numerical information, and developmental psychology experienced a breakthrough when tapping numerical cognition in human infants of only few months of age. These developments indicate that numerical competence did not emerge *de novo* in linguistic humans, but built up on a biological precursor system^{2–4}.

This article reviews the considerable progress that has been made in our understanding of basic numerical competence and its anatomical and functional machinery. Historically, case studies of the pathology of numerical competence provided the first insights into its neural roots. Acquired calculation deficits (acalculia) were found to occur after brain damage near the parieto-occipito-temporal junction^{5,6} or in the frontal lobe⁷. With the increase in functional imaging techniques, investigation of numerical processing in the intact human brain became possible. Recently, studies with behaviourally trained nonhuman primates complemented the emerging picture with single-neuron correlates and mechanisms.

Numerical concepts

The concept of number encompasses different aspects of numerical cognition. A particularly illustrative example of possible number assignments is the following sentence: “Despite a seventy-eight yard run by number thirty-four the Bears lost by two touchdowns and dropped into sixth place.”⁸

This sentence shows that number assignments can be classified into three categories⁹. Cardinal number (cardinality or ‘numerosity’) refers to quantitative number assignment and, therefore, applies to the elements of a set,

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doi:10.1038/nrn1626
Published online
15 February 2005

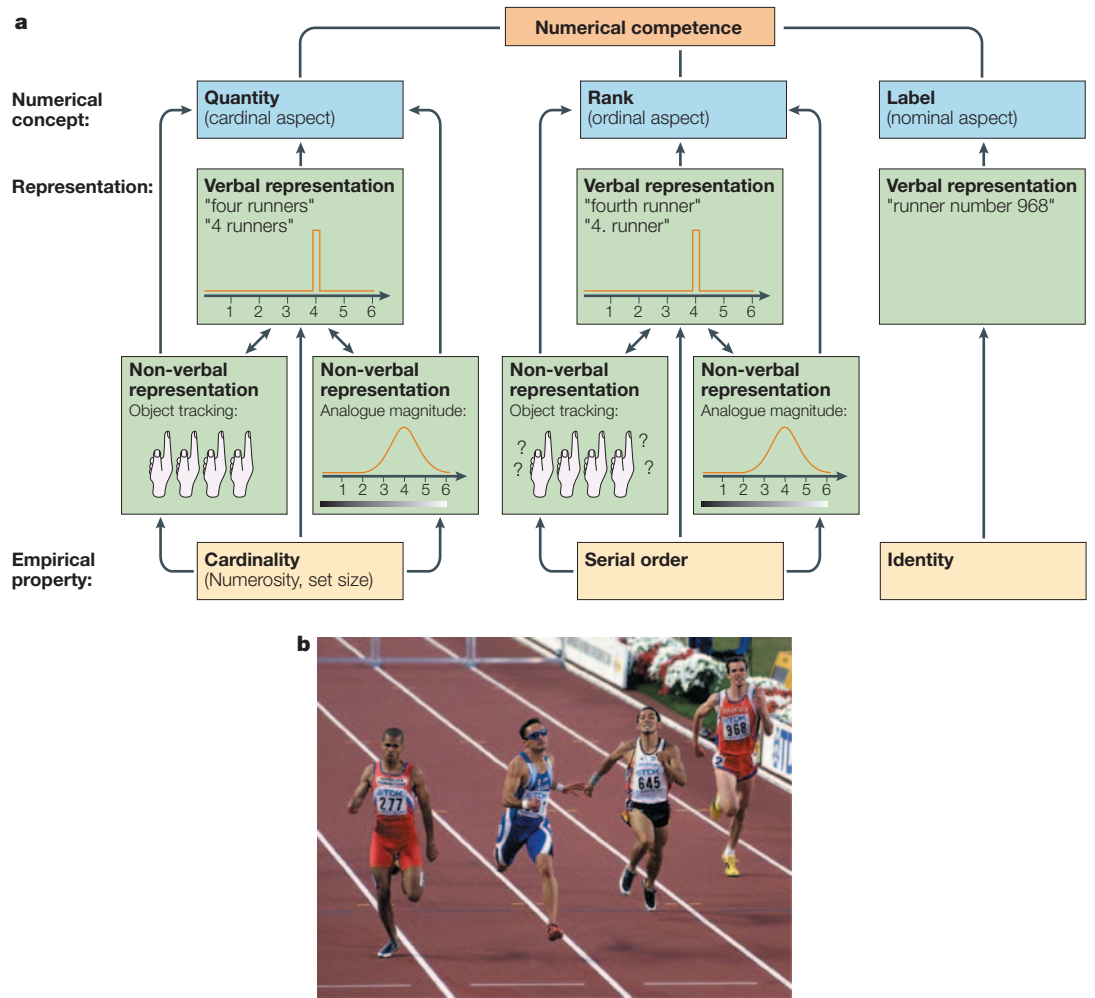


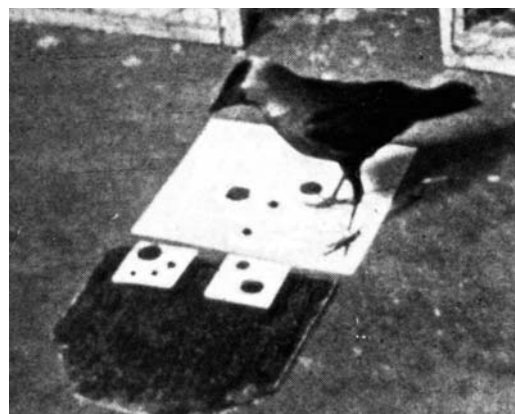
Figure 1 | Schematic illustration of how object properties are represented verbally and non-verbally according to the three numerical concepts — quantity, rank and label. a | Cardinality and serial order are non-verbally represented as approximate analogue magnitude, which is indicated by the Gaussian probability density function, in this example representing four objects. Small numerosities are also thought to be represented by object tracking processes (indicated by the pointing finger). Object tracking might also be used to represent serial order. Through language-based number words and symbols (such as a true number concept), the information of numerical quantity and rank are represented in a more precise ('digital') way, which is illustrated by a unit impulse function. The nature of the interactions between non-verbal and verbal representations, as indicated by the arrows, is only tentative and beyond the scope of this article. A numerical label can only be assigned through language for the purpose of identification (no number line is needed because numerical labels do not need to be sequentially arranged). **b** | The picture of four racing men illustrates the different numerical assignments. The cardinality of the set of men is 4. The men can be sequentially ordered according to their speed; in this example, the runner dressed in red on the right is assigned rank 4. Ordering the runners according to spatial arrangement from left to right would also assign the same runner rank 4. Although the individual correlations between numbers and the empirical elements in a set (the runners) are irrelevant for cardinal assignments, such correlations between the runners and the number are the ordinal numbers. The runner on the right, dressed in red, is labelled number '968', illustrating the nominal number assignment that is used for identification.

and concerns the questions: 'How many?' and 'How much?'. It refers to discrete set sizes ('two touchdowns') and continuous measures ('seventy-eight yard run'). Ordinal number applies to the rank of an individual element in a sequence ('sixth place'), and concerns the question, 'Which one?'; and nominal number identifies objects within a set — numbers that are used like proper names ('number thirty-four'). In a way, nominal number assignments are atypical (or even 'non-numerical'⁸). They are exclusively verbal and are found only in linguistic humans. As a result, nominal number will not be considered in this review.

It is important to distinguish between the empirical properties that numerical concepts refer to, and the verbal and non-verbal representations of these properties (FIG. 1). Numerical quantity refers to the cardinality of objects (the size of a set), and is represented non-verbally by analogue magnitude or object tracking mechanisms (see below for further discussion of these representational formats). Numerical rank refers to serial order, which is also thought to be represented by analogue magnitude mechanisms (and possibly object tracking) on a non-verbal level. Numerical labels, which refer to the identity of objects, can only be represented through language.

Box 1 | The legacy of Otto Koehler (1889–1974)

The German zoologist Otto Koehler was first to convincingly show numerical competence in animals¹²⁵. He proposed that animals might have two rudimentary capabilities — a visuo-spatial one and a temporal one^{126,127}. Depending on whether the items to be enumerated needed to be encountered simultaneously or sequentially, he classified the first capability as “simultaneously seeing the number of items” as opposed to “successively acting upon the number of items”. For example, he tested the animals’ judgment of simultaneously presented items using a matching-to-sample protocol, in which the sample numerosity was indicated by the number of ink dots (or pebbles and plasticine beads). The subject’s task was to find the one of two possible test lids that showed the same number of dots, and lift it to find a food reward in the pot underneath it. One way Koehler tested the second, sequential capability was by training birds to peck a certain number of grains from two piles of grain. For example, a bird trained on ‘five’ could eat all three grains from a small pile and two additional grains from a second, larger pile, before flying off, leaving the rest of the grains untouched. The animals also learned to combine both the simultaneous and the sequential task.



Koehler was aware of potential non-numerical cues that the birds might have relied on to solve the tasks, so he eliminated figural, positional and temporal cues to the best of his knowledge. To avoid giving the animals unconscious cues, the experimenter was out of sight of each animal throughout the sessions. An automatic spring-loaded device shooed the birds if they made errors. The experimental sessions were videotaped and thoroughly analysed off-line. Most notably, Koehler introduced transfer tests in which the punishment contingency was removed. During such transfer tests, the birds successfully applied the learned numerosity discriminations to novel situations without feedback for their behaviour.

Over the years, Koehler and his students tested eight animal species in the numerical competence project and derived upper numerosity-discrimination limits — 5 for pigeons, 6 for budgerigars and jackdaws and 7 for ravens, African gray parrots, Amazones, magpies, squirrels¹²⁸ and humans. His work, which was published in many scientific articles, served as the basis for all the following investigations into non-verbal numerical competence and its neural foundation.

Only the human faculty of language provides the cognitive capacity that is required to develop a full-blown, systematic number concept, because it allows verbal representations that link relations between numbers with relations between objects or events¹⁰. Like language itself¹¹, counting and counting ‘words’ are based on recursive rules. For that reason, the terms ‘counting’ and ‘number (word)’ will not be used in the context of infant and animal studies in this review, but will be used exclusively in studies that investigate adult humans with a linguistic number concept.

However, animals and humans are nonetheless able to non-verbally grasp the numerical properties of objects and events, namely cardinality and serial order. This article deals mainly with the non-verbal behavioural and neural representations of these two properties.

Numerical quantity (cardinality)

Animal behaviour. Animals can discriminate the cardinality of sets. Historically, the work of Otto Koehler (BOX 1) provided the first positive evidence that birds and mammals can be trained to discriminate simultaneously viewed sets of objects based on their cardinality, and can keep track of the numerosity of performed actions. Over the past six decades or so, a number of birds (for example, pigeons, budgerigars, amazones, African gray parrots, canaries, magpies and ravens) and mammals (for example, rats, raccoons, dolphins, dogs, capuchins, rhesus monkeys, orangutans and chimpanzees) have

successfully been trained to perform several numerical tasks in different modalities (for a review of the classic literature, see REF 12).

A valid concern in all these studies is that conditioned animals might merely respond to well-known stimuli that they have been trained with (usually for an extensive period of time). However, Brannon and Terrace¹³ showed that monkeys are able to transfer their numerical knowledge to numerosities that they have never seen. Two monkeys were trained to respond to visual displays that showed the numerosities of 1 to 4 by touching the displays in ascending numerical order. Non-numerical visual cues were painstakingly excluded. When the animals were subsequently tested with the novel numerosities of 5 to 9, they correctly responded in an ascending order, without reinforcement of choice behaviour. This indicates a true understanding of the concept of cardinalities and their sequential arrangement.

Impressive as such capabilities are, it has been suggested that the numerical competence observed in these animals was either a laboratory artefact or a last-resort strategy that the animals adopted when all non-numerical cues were eliminated. Therefore, researchers left the laboratory to study the spontaneous behaviour of wild animals. The data collected for different species indicate that quantity information is indeed exploited by animals to allow them to make informed choices in their natural environment (BOX 2). The work of Hauser and colleagues^{14–16}, in particular, showed that primates

Box 2 | **Ecological significance of numerical assessments**

The assessment of numerical information ensures an animal's fitness and survival. This is particularly evident in social interactions (fight or flight decisions in contests), foraging (exploiting the richer food patch) and parenting (allowing an animal to discriminate its own offspring).

Based on playback experiments, it has been suggested that when female lions hear another pride roaring, they decide whether to respond aggressively or to retreat from the perceived threat by comparing the number of different roars they hear with the number of individuals in their own group¹²⁹. The importance of numerical assessments in severe inter-group contests is also confirmed in male chimpanzees¹³⁰, which defend their resources and sometimes even kill members of a neighbouring community. Chimpanzees are willing to enter into a contest only if they outnumber the opposing side by a factor of 1.5 — a finding that can be mathematically modelled based on Lanchester's theory of combat¹³¹.

In a natural environment, an animal is constantly faced with the problem of optimising its energy intake. Untrained, free-ranging rhesus monkeys choose a container with the greater number of apple slices when the comparisons are one versus two, two versus three or three versus four¹³².

In a recent study of conspecific brood parasitism¹³³, it was shown that American coots (an aquatic rail) lay eggs up to an optimal clutch size based on the number of their own eggs that are already in the nest. In doing so, these birds are able to ignore parasitic eggs (based on visual cues) that other coots might smuggle into their nest. So, coots seem to assess the set size of their own eggs while ignoring the set size of all the eggs (their own and those that are parasitic) together.

Similar to cardinality discriminations, spontaneous ordinal judgments are evident in wild animals. For example, establishing the serial order of individuals according to their status is important in hierarchical societies, and members of baboon groups seem to rank their companions according to their dominance¹³⁴.

These examples illustrate that numerical judgments are of considerable ecological significance for wild animals, and are made spontaneously in their natural environment.

spontaneously perform rudimentary tasks on cardinality, such as adding and subtracting small sets of items. So, studies under controlled conditions and investigations of spontaneous behaviour in the wild complement each other and form a clear picture of numerically competent animals.

Infant behaviour. Not only non-verbal animals, but also pre-verbal human infants of several months of age have the capacity to represent cardinality, both in the visual and the auditory domain (for a recent review see REF. 17). Developmental psychologists have invented several methods of deriving behavioural data from babies, including the HABITUATION-DISHABITUATION PROTOCOL (which can also be applied to untrained animals). Infants can also engage in rudimentary arithmetic, which was first shown in experiments in which five-month-old infants were shown basic addition and subtraction operations with small sets of objects¹⁸. To test the babies' reactions, the numerical outcome (the number of objects) was in some cases consistent with the operation (for example, 2 for 1 + 1) and in other cases inconsistent (for example, 1 for 1 + 1). Based on an infant's tendency to look longer at unexpected events, looking time served as an indirect measure of the infants' expectations about the results of the operations they witnessed. On average, looking time was significantly longer for the unexpected (and numerically inconsistent) outcome, which supports the idea that humans have an ontogenetically early and pre-verbal capacity to understand simple arithmetic.

HABITUATION-DISHABITUATION PROTOCOL

When repeatedly confronted with displays of a given number of visual objects (for example, two), infants will habituate to this numerosity and their looking time to the displays will decrease, but they will regain interest (dishabituate) if they are then presented with a display containing a different numerosity (for example, three).

Humans lacking number words. Human adults can reliably compare the cardinality of sets (arrays of dots, sequences of flashes or sound pulses, or motor actions) under conditions that prevent or discourage verbal counting (for example, in dual-task situations or when severe time limits are in place)^{19–21}. However, in contrast to precise verbal counting, non-verbal discrimination performance is inaccurate, or noisy. Some indigenous human cultures that lack number words or have a restricted concept of verbal counting rely completely on non-verbal cardinality assessment^{22–24}. For example, the people of the Pirahã tribe in South America have not developed a true number word system, and only use words to designate very small set sizes ('about one'), somewhat larger set sizes ('about two') and sets of many items (a one-two-many system of 'counting'). If asked to match the number of items placed before them with an equal number of objects, the Pirahã show only an imprecise capability to enumerate, with decreasing precision as the numbers become higher. Speakers of Mundurukú, another Amazonian language, lack words for numbers beyond five, but are still able to compare and imprecisely add large sets of items that are far beyond their naming range²³. So, humans without a linguistic number concept can only estimate the number of items by means of a non-verbal quantification system. In summary, human adults who lack a verbal counting system, pre-verbal infants and non-verbal animals show an evolutionarily ancient quantification system that operates independently of language.

Non-verbal systems of numerical quantity assessments. So far, it has been widely assumed that two non-verbal systems are used to assess numerosity^{17,25} (FIG. 1). The first system treats cardinality — the discrete number of objects — as analogous to continuous magnitudes²⁶. This system, which allows an animal or human to estimate set sizes, has been termed the analogue magnitude system. It has no upper limit of the number of items it can encode, but does become systematically less precise with increasing cardinality (FIG. 2e). So, like representations of sensory magnitude, the hallmark of analogue magnitude representations is that they obey Weber's Law^{27,28} (BOX 3). Two general effects that are seen in analogue magnitude representations are the numerical distance effect (discrimination between two cardinalities improves with increasing numerical distance between them) and the numerical magnitude effect (discrimination of two numerosities of a given numerical distance becomes more difficult as the absolute values of the two sets get higher)^{27,29–31}.

The second non-verbal system is thought to be an object tracking system (also known as 'subitizing'³²) that yields relatively discrete representations. This system keeps track of a small number of items (originally set to 6 (REF. 32), but later restricted to 3 or 4 items³³) by assigning 'markers' (also known as 'fingers', 'pointers', 'symbols', 'tokens' or 'files') to individual elements³⁴. These markers are thought to be derived from object segregation processes that take place in parallel in a pre-attentive stage of vision. Based on a limited number of markers,

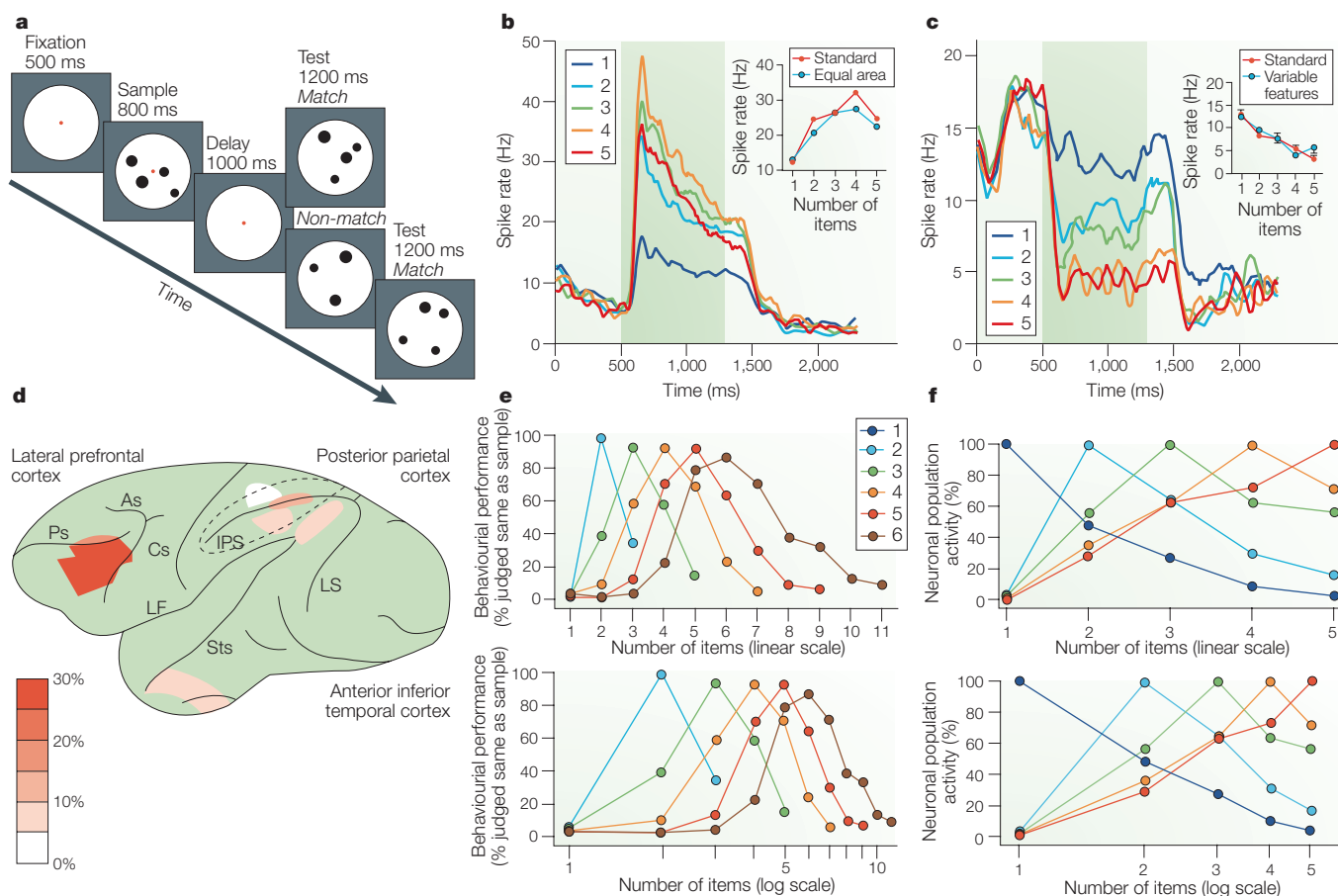


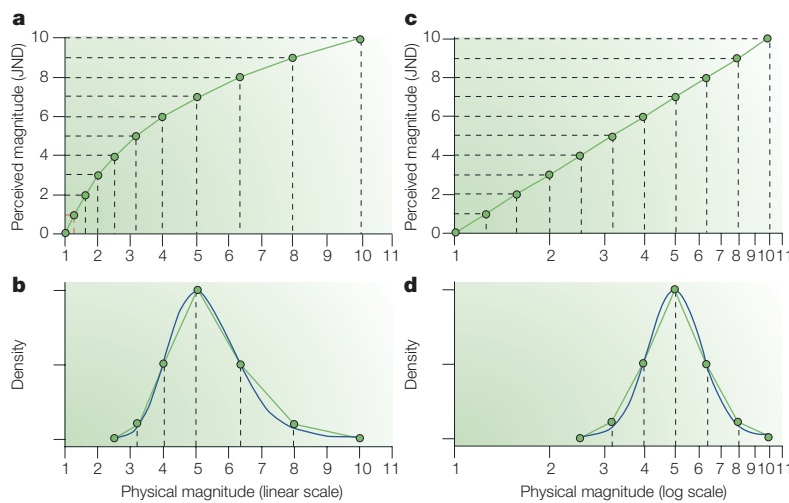
Figure 2 | Representation of visual cardinality in rhesus monkeys. **a** | A behavioural task. Monkeys carried out a delayed match-to-numerosity task. They were required to extract the numerosity in a visual array, memorize it briefly and match it to a test display that showed the same numerosity (but with a different visual pattern). To the best of their discriminatory abilities, the monkeys should not respond to the non-match test stimulus, which was presented in 50% of the trials. **b,c** | Responses of single neurons that were recorded from the prefrontal cortex (PFC) (**b**) and the intraparietal sulcus (IPS) (**c**). Both neurons show a graded discharge during sample presentation (interval shaded in green, 500–1,300 ms) as a function of numerosities 1 to 5 (colour coded average-discharge functions). The insets in the upper right corners show the tuning of both neurons and their responses to different control stimuli. The preferred numerosity was '4' for the PFC neuron (**b**), and '1' for the IPS neuron (**c**). Surface area of all items was equal across all numerosities in the 'equal area' condition. **d** | Lateral view of a monkey brain that shows the recording sites in the lateral prefrontal cortex, the posterior parietal cortex and the anterior inferior temporal cortex. The proportions of numerosity-selective neurons in each area are colour coded according to the scale shown. As, arcuate sulcus; Cs, central sulcus; LF, lateral fissure; LS, lunate sulcus; Ps, principal sulcus; Sts, Superior temporal sulcus. **e** | The graphs show the behavioural numerosity discrimination functions of two monkeys. The curves indicate whether they judged the first test stimulus (after a delay) as containing the same number of items as the sample display. The function peaks (and the colour legend) indicate the sample numerosity at which each curve was derived. Behavioural filter functions are skewed on a linear scale (top), but are symmetric on a logarithmic scale (bottom). **f** | The averaged single-cell numerosity-tuning functions (from the PFC) are also asymmetric on a linear scale, but symmetric after logarithmic transformation. Panels **a,c,d** adapted, with permission, from REF. 48 © (2004) National Academy of Sciences, USA. Panels **b,f** adapted from REF. 47 © (2002) American Association for the Advancement of Science. Panel **e** adapted from REF. 27 © (2003) Elsevier Science.

this system can only represent a limited number of items (~4) and fails for larger numbers. Importantly, object tracking mechanisms can represent cardinality only implicitly, through markers³⁵.

Whether the experimental data support the existence of two separate non-verbal mechanisms for cardinality assessment remains controversial — the data might alternatively be explained by a sole magnitude mechanism. In infants, numerical competence was believed to be grounded almost exclusively in object tracking processes. Recently, however, large-numerosity

tasks have been solved by babies who apparently used analogue magnitude representations^{36,37}. In animals, the presence of an object tracking mechanism was proposed on the basis of spontaneous discrimination behaviour in wild monkeys that showed a set size limitation of about 4 objects in early studies^{14,15,38,39}. However, more recently it was shown that untrained monkeys and apes can also discriminate and compute larger numerosities based on analogue magnitude representations^{40,41}. Moreover, numerical representations seen in laboratory animals that have been conditioned

Box 3 | **Discrimination and scaling of magnitude**



In 1834, the German physiologist E. H. Weber¹³⁵ discovered that two relatively heavy weights must differ by a greater amount than two relatively light weights for one weight to be perceived as heavier than the other. In other words, heavier weights are harder to discriminate. The ‘Just Noticeable Difference’ (JND or ΔI) — the minimum amount by which stimulus magnitude must be changed in order to produce a noticeable variation in sensory experience — is a constant fraction (c) of the level of stimulus intensity (I). So, Weber’s Law, which has wide generality across different sensory magnitudes and modalities, is expressed as: $\Delta I/I = c$

In 1860, G. T. Fechner¹³⁶ proposed an extension based on Weber’s Law: as the stimulus intensity increases, it takes greater and greater changes in intensity to change the perceived magnitude by some constant amount. So, the perceived magnitude (S) is a logarithmic function of stimulus intensity (I) multiplied by a modality and dimension specific constant (k). This relationship is expressed in Fechner’s Law: $S = k \cdot \log(I)$

Plotting the number of psychological units (such as JNDs of numerosities) against the physical stimulus magnitude (such as number of items) shows that equal increments in perceived magnitude correspond to larger and larger increases in physical magnitude (panel a). Based on multiple JNDs at arbitrary thresholds (data points in panels b and d), the schematically-derived probability density function (which can be regarded as the mental representation of a magnitude) is skewed (panel b). However, if the perceived magnitude is plotted against the logarithm of physical magnitude, it yields a linear relationship (panel c), which results in a symmetric density function (panel d).

These fundamental laws are usually valid for general sensory phenomena and can account for many properties of sensory neurons¹³⁷. The action potential rate (in slowly adapting receptors) is generally a function of the logarithm of the stimulus intensity¹³⁸. Although the response characteristics of receptor cells can explain the logarithmic compression of sensory experiences (Fechner’s Law), it is not yet clear why cognitive magnitudes (such as numerical quantity) obey the same law.

on a numerosity discrimination task exclusively show characteristics of the analogue magnitude system, even for small set sizes^{27,31}. Furthermore, several behavioural studies in humans did not find discontinuities between small and large number representations^{20,24,42}. To add to the debate, the question of how cardinality might be derived within an object tracking framework remains theoretically challenging. Pylyshyn⁴³ suggests that judging the numerosity of a set of items might involve two different processing stages: an individuation stage that might derive object entities of a (visual) scene in parallel, and a (serial) enumeration stage, used to judge the numerosity of individuated items. However, according

to this explanation, the first, individuation stage (object tracking) is only a pre-processing stage that does not provide access to cardinality, and so might not be regarded as a system that assesses numerical information at all. This is probably one of the reasons why imaging of the neural substrates of object tracking has remained inconclusive^{44,45}. By contrast, serial counting from the cardinalities 4 and over activated a set of bilateral frontoparietal regions⁴⁶.

Single-neuron representations of non-symbolic cardinality.

Recent single-cell recordings in monkeys showed the capacity of single neurons to encode numerical quantity. In monkeys performing a visual delayed match-to-numerosity task (FIG. 2a), the highest proportion of numerosity-selective neurons was found in the lateral prefrontal cortex (31% of all randomly selected cells), irrespective of co-varying non-numerical parameters⁴⁷ (FIG. 2b). In the posterior parietal cortex, numerosity-selective neurons were most abundant in the fundus of the intraparietal sulcus (18%) — there were few in other posterior parietal cortex areas or in the anterior inferior temporal cortex (aITC)⁴⁸ (FIG. 2c). Neurons in a somatosensory-responsive region of the superior parietal lobule (part of area 5) have been reported to keep track of the number of movements⁴⁹, but in a movement-type dependent manner (that is, the neurons responded differently according to whether the monkey’s movement was ‘push’ or ‘turn’). Area 5 neurons were not found to encode numerosity in visual displays⁴⁸.

Numerosity-selective neurons in the prefrontal cortex and intraparietal sulcus were ‘tuned’ to the number of items on a visual display⁴⁷ — that is, they showed maximum activity in response to one of the five presented quantities — a neuron’s ‘preferred numerosity’ (FIG. 2b,c); together, all numerosity-selective neurons formed a bank of overlapping numerosity filters (FIG. 2f). Interestingly, the neurons’ sequentially-arranged, overlapping tuning curves preserved an inherent order of cardinalities. This is important because numerosities are not isolated categories, but exist in relation to one another (for example, 3 is greater than 2 and less than 4) and the numbers need to be sequentially ordered to allow meaningful quantity assignments⁹. This type of ‘labelled line code’ for numerical quantity contrasts with purely sensory magnitudes, which show monotonic discharge functions. When investigating the frequency of a tactile stimulus, for example, the discharge rate increases with increasing stimulus intensity^{50,51}. The fact that intraparietal sulcus neurons require shorter latencies to become numerosity selective than do prefrontal cortex neurons indicates that the intraparietal sulcus might be the first cortical stage to extract visual numerical information⁴⁸. As the posterior parietal cortex and prefrontal cortex are functionally interconnected⁵², that information might be conveyed directly or indirectly to the prefrontal cortex, where it could be amplified and maintained to gain control over behaviour⁵³.

In terms of simple signal detection principles⁵⁴, the response properties of numerosity-selective cortical cells can explain basic psychophysical phenomena in

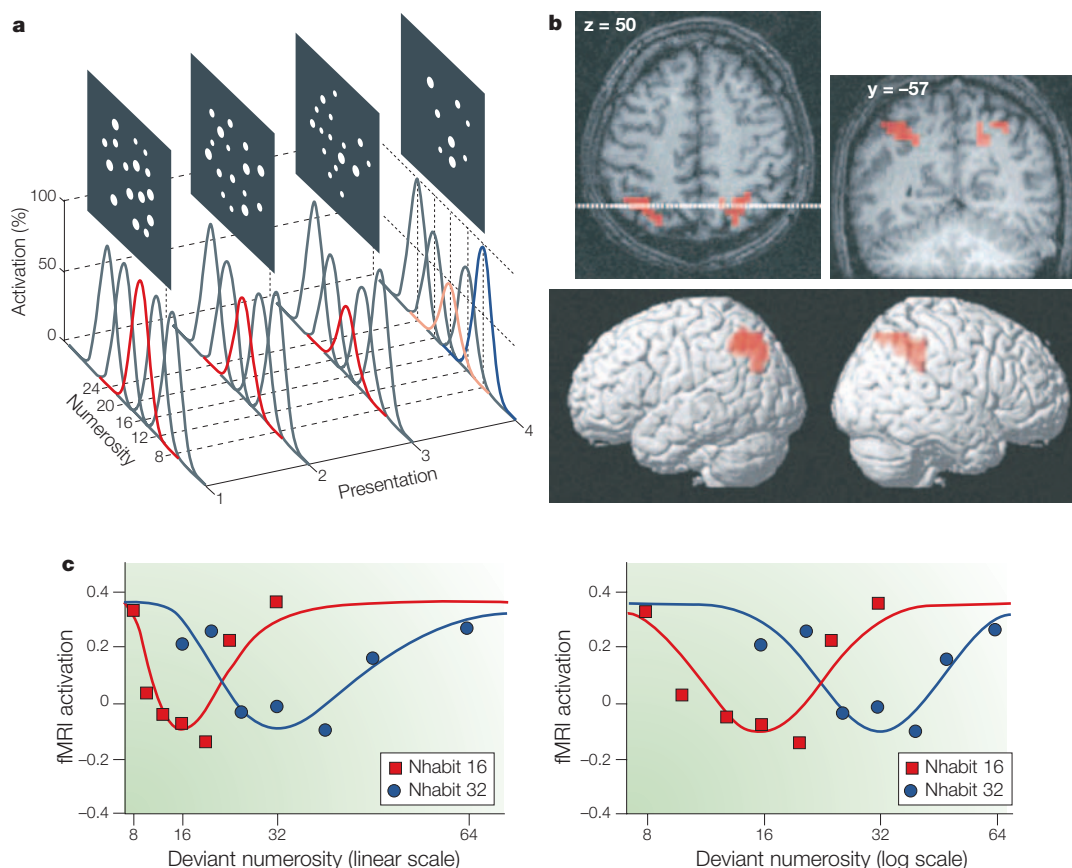


Figure 3 | Functional MRI adaptation with numerosities in humans. **a** | Subjects were repeatedly presented with several visual displays of a fixed numerosity (for example, 16 dots), without the requirement to discriminate them. If any region of the brain contains a population of numerosity-selective neurons that are tuned to a specific number of dots (illustrated by Gauss functions, below the dot patterns) and automatically detect numerical information, such a population of detectors should become habituated (that is, decrease its discharge) with repeated numerosity presentations. In this example, neurons tuned around numerosity 16 are activated (represented by red Gaussian) and should habituate, whereas neurons tuned to other numerosities should not be affected. Such a habituation effect was then 'read-out' by recording the event-related fMRI activation to a single deviant numerosity that was presented at the end of a display sequence (represented by blue Gaussian). The activation difference between the habituated pink and the non-habituated blue numerosity tuning curves was then measured. Figure courtesy of I. Diester, Hertie-Institute for Clinical Brain Research, Tübingen. **b** | fMRI was used to show the regions of the human brain that responded to numerosity changes. Coloured areas in the axial (top left) and coronal (top right) sections and on the surface image (bottom) indicate the involvement of the intraparietal sulcus. z and y values give ventral-dorsal and posterior-anterior Talairach coordinates. **c** | fMRI results of a habituation–dishabituation protocol in humans. The activation difference between habituation and deviant numerosities resulted in (inverted) numerosity-tuning curves that were more symmetrically fitted on a logarithmic (right) than on a linear (left) scale. Habituation numerosities ('Nhabit') 16 and 32 were used. Panels **b,c** reproduced, with permission, from REF. 55 © (2004) Elsevier Science.

monkeys, such as the numerical distance and size effect (FIG. 2e). The numerical distance effect results from the fact that the neural filter functions that are engaged in the discrimination of adjacent numerosities overlap heavily. As a result, the signal-to-noise ratio of the neural signal detection process is low, and the monkeys make many errors. On the other hand, the filter functions of neurons that are tuned to remote numerosities barely overlap, which results in a high signal-to-noise ratio and, therefore, good performance in cases in which an animal has to discriminate sets by a larger numerical distance.

The numerical size effect is based on the finding that neuronal tuning obeys Weber's Law: the widths of the tuning curves (or neuronal numerical representations)

increase linearly with preferred numerosities^{27,47} (that is, on average, neurons become less precisely tuned as the preferred quantity increases). So, selective neural filters that do not have considerable overlap are also engaged if a monkey has to discriminate small numerosities (such as 1 and 2), which results in high signal-to-noise ratios and few errors in discrimination. Conversely, if a monkey has to discriminate large numerosities (like 4 and 5), the filter functions would overlap considerably. Therefore, the discrimination would show a low signal-to-noise ratio, which would lead to poor performance.

In humans, the prefrontal cortex and the parietal lobe, in particular the intraparietal sulcus, have long

been regarded as the prime sources of numerical competence. However, this view was almost exclusively based on verbal and symbolic number tasks, which are only vaguely comparable to numerical magnitude estimation. If there are anatomical and functional similarities between the brains of monkeys and humans, equivalent areas in the brain should also be activated in humans when non-verbal cardinality is processed. By testing functional MRI (fMRI) adaptation with numerosities (FIG. 3), Piazza *et al.*⁵⁵ found a corresponding blood oxygenation level dependent (BOLD) activation in the intraparietal sulcus of humans (but see also REF. 56 for a negative result). The only region of the brain that was found to be significantly habituated to numerosity was the horizontal segment of the intraparietal sulcus. Piazza *et al.*⁵⁵ could indirectly trace the average numerosity-tuning curve of the underlying neural population, which also showed a clear Weber-fraction signature.

This raises an important question that concerns the scaling scheme of the 'mental number line', that is, are numerical judgments best described on a linear^{4,57,58}, or a nonlinear, possibly logarithmically compressed scale^{30,59,60}? The latter would be predicted if Fechner's Law holds (BOX 3). As the behavioural discrimination and single-unit tuning functions might be regarded as the monkeys' behavioural and neural numerical representations²⁷ (FIG. 2e,f), the crucial question then concerns which scaling scheme would provide symmetric (that is, Gaussian) probability density distributions. It turned out that both the performance and the single unit data for numerosity judgments are better described by a compressed scale (FIG. 2e,f), as opposed to a linear scale²⁷. Therefore, numerical representations in monkeys obey Fechner's Law. Similarly, fMRI tuning curves in human studies seem to be well described on a logarithmic scale⁵⁵, which indicates that the non-verbal 'number line' is nonlinearly compressed. Logarithmic encoding of numerosity is also indicated by neural network models^{61,62}.

One advantage of the use of such a compressed 'number line' would be that smaller cardinalities could be represented with many neurons to gain precision, whereas larger numerosities could be represented with a smaller proportion of neurons (although the representations would only be fuzzy in the latter case)⁶³. In any case, whether a monkey faces thirty or forty hostile opponents might not be that relevant, it should take to its heels anyway.

Symbolic representations of cardinality. Language allows humans to use symbolic representations, and numbers are the symbols that are used when dealing with numerical information. Several animal species (such as pigeons⁶⁴, parrots⁶⁵, macaques⁶⁶ and chimpanzees^{67,68}) have successfully been trained to use visual forms or vocalizations to denote the cardinality of sets. Although this association between form and numerosity is an important first step in mapping symbols to numerical magnitude, animals fail to show true symbolic, recursive number representations¹¹ that would allow them to use

numbers productively for true counting. Therefore, one might argue that linguistic quantity processing and non-verbal cardinality assessment are two completely independently operating neural systems. However, this does not seem to be the case; on the contrary, numerical values that are cued by number symbols and set size have been shown to activate corresponding structures in the brains of humans.

The intraparietal sulcus, which has been proposed to have a central role in basic quantity representations⁵⁵, is sometimes the only area that is specifically activated in simple number detection or comparison tasks. Eger *et al.*⁶⁹ performed fMRI while subjects were asked to detect numerals, letters or colours in visual sequences or acoustic streams. To avoid confusion between response selection and associated cognitive states (such as attention), the authors analysed the presentation of non-target numerals (numerals that were not required to be detected) and compared this with that of non-target letters or colours. The intraparietal sulcus was the only region that showed higher activation for numerals, both visually and acoustically. Therefore, numerical activation in the intraparietal sulcus seems to be automatic (task-independent), supramodal (visual and auditory) and notation-independent (irrespective of whether numerals are spoken or written, or presented in Arabic notation or spelled-out form⁷⁰). However, the intraparietal sulcus is also engaged in more general magnitude judgments. Pinel *et al.*⁷¹ used fMRI to scan subjects while they compared Arabic numerals for luminance, font size and numerical value. They observed strong overlap in the neural substrates for the three tasks. Number and size, but not luminance, activated a common parietal region, pointing towards an intimate relationship between spatial and numerical representations (BOX 4). This might mean that number-coding neurons are intermingled with other magnitude-coding neurons along the intraparietal sulcus^{71,72}. It remains a matter of debate whether the number domain is based on a distinct anatomical and functional substrate that exclusively processes numerical information, or whether it is also engaged in other cognitive tasks^{56,73,74}.

Beyond the mere encoding of quantity information *per se*, verbal numerical competence requires additional cognitive components. Dehaene and co-workers⁷⁵ suggest that verbal counting and calculation engage two more parietal regions: a posterior dorsal parietal area that is activated by shifts in spatial attention whenever subjects count, and a left angular gyrus area that is related to linguistic processing. Moreover, simple calculation tasks (such as subtraction) typically activate a distributed network that involves the parietal, prefrontal and premotor cortices^{69,76–80}.

Developmental studies confirm that impairments in arithmetical abilities correlate with abnormalities in the organization of parietofrontal networks, and the intraparietal sulcus in particular. Using voxel-based morphometry, Isaacs *et al.*⁸¹ compared the density of grey matter in adolescents who were born at equally

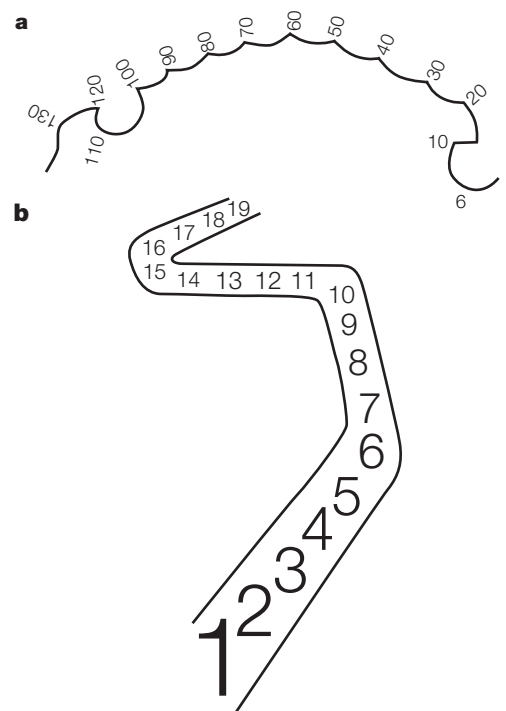
Box 4 | Numerical representations and space

Some people experience numbers automatically and consistently as being positioned at a fixed place within a mental spatial structure^{139,140}. In 1880, Francis Galton noticed that some people imagine ‘visualized numerals’¹⁴¹ when they think of numbers. Such ‘mental numbers’ are usually linearly organized — often arranged in a three-dimensional space — which supports the metaphor of a ‘mental number line’¹⁴² as a substrate for getting access to numbers (panels a,b).

The spatial numerical association of response codes (SNARC) effect¹⁴³ implicates a second close association between numerals and space. It describes the finding that the left hand responds faster to small numbers (one or two), whereas the right hand responds faster to relatively large numbers (seven or eight). The SNARC effect is thought to originate from the fact that quantity is spatially organized by numerical proximity, oriented from left to right, thereby causing a congruity between small numbers and left side-responses, and vice versa. This has led to the assumption of a left-to-right orientated mental number line in the case of left-to-right reading cultures (the opposite direction is found in cultures that read from right to left)¹⁴³. A similar effect has been discovered in a spatial attention task, where targets on the right side were detected faster when preceded by high digits and those on the left side were detected faster when preceded by low digits¹⁴⁴.

A third phenomenon that has been interpreted as showing a close link between number and space is the numerical distance effect — the discrimination between two numbers improves with increasing numerical distance between them. For example, it is easier (subjects respond faster and make less errors) to discriminate between two and eight than it is to discriminate between seven and eight. This effect has been found in animals^{27,29} and humans³⁰ when judging set size (cardinality) as well as numerals¹⁴⁵.

Support for an intimate relationship between space and number is also provided by lesion studies. Patients with hemispatial neglect resulting from brain damage to the right hemisphere have deficits in the perception and imagination of stimuli from the left side. When asked to indicate the midpoint of a line, they miss the midpoint and place it to the right (panel c). Similarly, these patients (who otherwise have intact numerical skills) misplace the midpoint of a numerical interval when asked to bisect it¹⁴⁶ (for example, they would state that six is the numerical midpoint between one and nine). They are also slower at judging smaller numerals relative to a reference numeral than larger ones¹⁴⁷. So, the notion of a ‘mental number line’ might be more than a simple metaphor; number lines and physical lines might be functionally isomorphic¹⁴⁶. Panel a reproduced from REF. 141 © (1880) Macmillan Magazines Ltd. Panel b reproduced from REF. 140 © (2001) Teubner Verlag.

**c Spatial neglect patients**

Where is the midpoint of the line?



severe grades of prematurity. Half of these individuals (with otherwise normal IQ) suffered from **DYSCALCULIA**, and the only region in the brain that showed reduced grey matter in association with arithmetical deficits was the left intraparietal sulcus. So, dyscalculia in children might be the result of specific disabilities in basic numerical processing, rather than the consequence of deficits in other cognitive abilities⁸². Arithmetical deficits are also found in certain genetic conditions, such as Turner syndrome (X monosomy)^{83,84}, **fragile X syndrome**⁸⁵ and **velocardiofacial syndrome**⁸⁶. In these conditions, fMRI hypoactivation (decreased BOLD activation) was found in the intraparietal sulcus and wider parietofrontal networks.

Numerical rank (serial order)

Behaviour. Numerical rank is the second main numerical concept that shows biological precursors. List learning — the ability to encode and then retrieve an arbitrary list of items in their correct order — opened a window for studying how the ordinal rank of objects is learned and stored by animals. Terrace and co-workers carried out a series of experiments that show that rhesus monkeys⁸⁷ (and, to a lesser extent, pigeons⁸⁸) could learn several lists of up to seven items (for example, photographs)⁸⁹. This provided the opportunity to evaluate the monkeys’ knowledge of the ordinal position of list items with ‘derived lists’. Derived lists are novel lists that are constructed by picking individual items from previously

DYSCALCULIA
Calculation deficits that are a result of developmental defects in the brain.

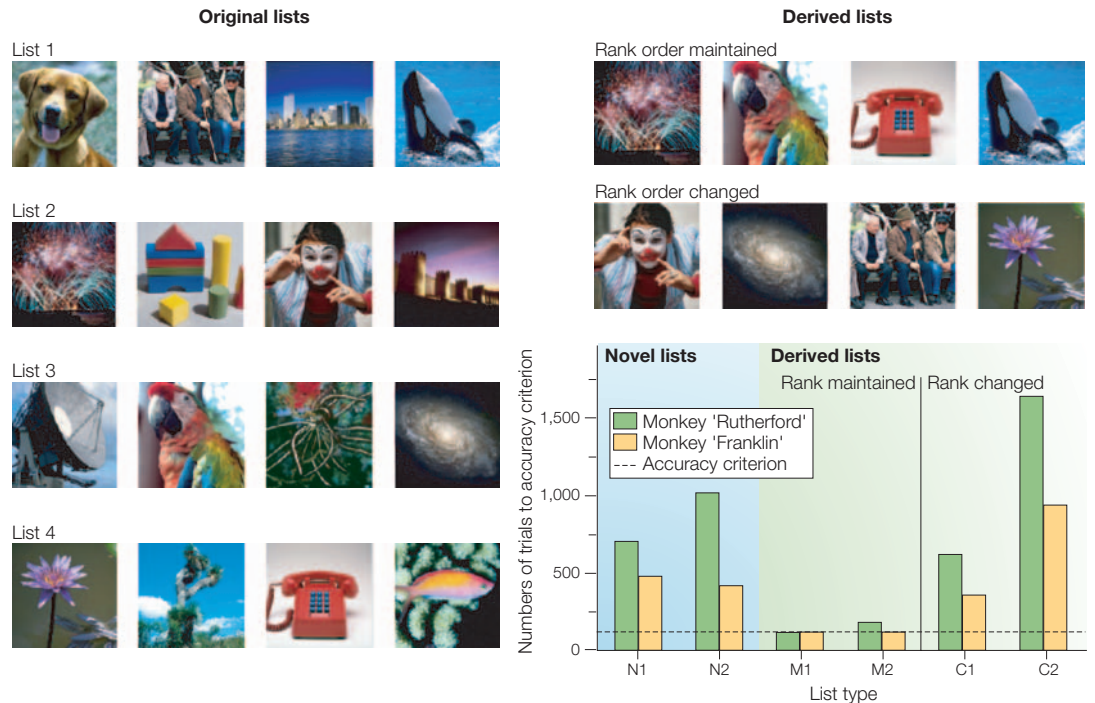


Figure 4 | **List learning experiments in rhesus monkeys.** The monkeys were trained to order original 4-item lists (left) by touching them in the correct order. Subsequently, they were tested with derived lists. Derived lists are novel lists that are constructed by picking individual items from previously learned lists and re-assembling them in such a way that two different modifications arise (right). In a rank order maintained list, the original ordinal position of all the items is maintained. For example, if a picture appeared at the second position in one of the original lists, it would also appear at position two in the derived list. However, in a rank order changed list, the list items are not only shuffled across lists, but also across rank positions, so that an item that occurs at position four in the original list would be placed at position two in the derived list. The graph shows the number of trials two monkeys needed to reach an accuracy criterion when learning novel lists. The monkeys needed few trials to learn derived lists when rank order was maintained (M), but mastering derived lists in which rank order had changed (C) took them as long as learning completely new lists. Graph reproduced, with permission, from REF. 92 © (1997) American Psychological Society.

learned lists and re-assembling them^{90,91} (FIG. 4). Interestingly, the derived lists on which each item's previous ordinal position was maintained were acquired rapidly by the monkeys without errors⁹². However, the monkeys needed as much time to learn the derived lists on which each item's ordinal position was changed as they did for completely novel lists. This result indicates that the monkeys acquired knowledge of each item's original ordinal position, and that they could exploit this knowledge in the order-maintained derived lists.

In a study that addressed monkeys' strategies for list recall, macaques were trained to report three-item lists with the sample items displayed in temporal sequence^{93,94}. After presentation of such a list, a test stimulus that showed the three items and a distractor item was presented, and the monkeys were required to touch the three items in the order that was previously shown to them, without touching the distractor. The distractor was taken from one of the other learned lists and so had a fixed ordinal position within its own list. Interestingly, the monkeys primarily mixed up a list item with a distractor if the distractor had the same ordinal position (in its own list) as the correct item. This indicates that monkeys intuitively categorize images in such lists by their ordinal number⁹³.

Neural representation of serial order. Ordinal categorization of visual items requires information about both the rank of an item (for example, based on temporal order) and its identity. Based on patient studies, the lateral prefrontal cortex has been implicated in maintaining temporal order information, which is an integral aspect of episodic memory^{95,96}. It is well known that damage to the human frontal cortex causes impairments in carrying out tasks that require recall of the temporal order of stimuli⁹⁷⁻⁹⁹. A similar ordering impairment results from lesioning the dorsolateral frontal cortex in monkeys¹⁰⁰, which supports the view that, in primates, the dorsolateral prefrontal cortex is important for maintaining information about the order of events.

fMRI studies in humans show that the prefrontal and parietal cortices are more strongly activated for order information (the order of words in a list) than for item information (the presence of words in a list)¹⁰¹⁻¹⁰⁴. In addition, Bengtsson *et al.*¹⁰⁵ found that the lateral frontoparietal areas, the basal ganglia and the cerebellum were preferentially involved in ordinal control of hand movements.

The single-neuron correlate of temporal rank order information in visual lists has recently been studied by Ninokura and co-workers^{106,107}. They trained monkeys

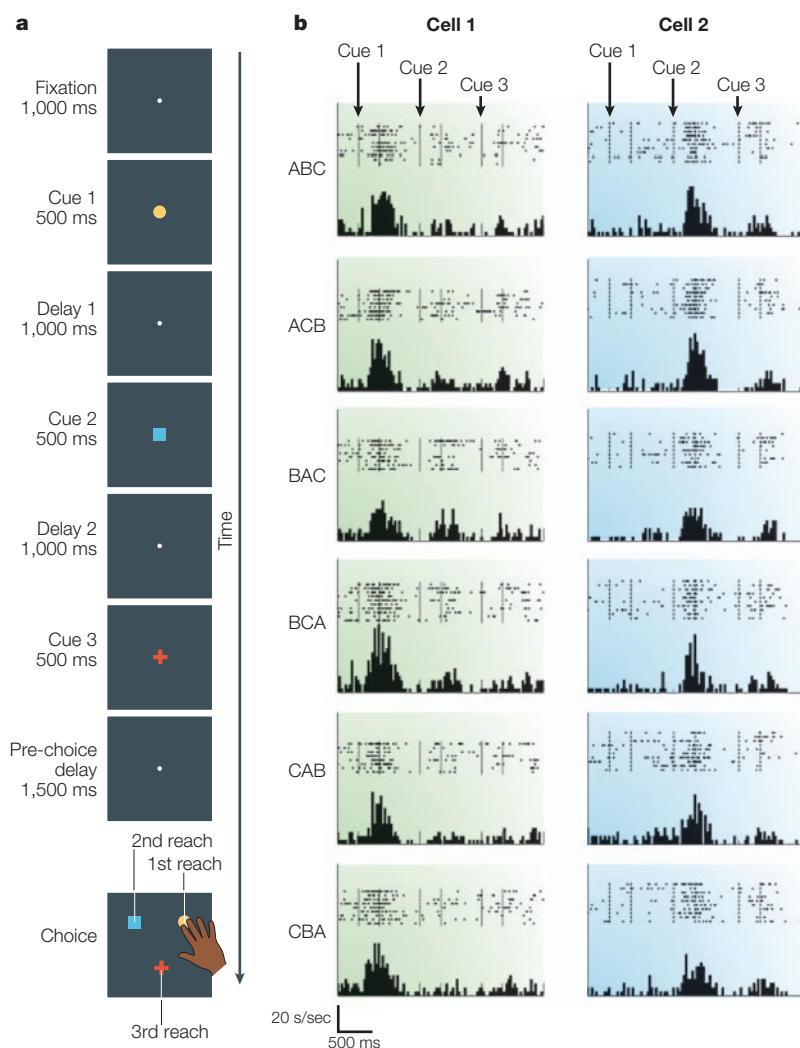


Figure 5 | Temporal ordering task and single cell responses from the prefrontal cortex. **a** | Monkeys were required to observe and remember the order in which three visual objects appeared, so that the animals could plan a subsequent triple-reaching movement in the same order. **b** | Two single neurons encoding the first (cell 1) and the second (cell 2) rank, irrespective of the order in which the three items (represented by the letters A, B and C) appeared. Neural responses are shown in dot-raster histograms (top panels, each dot represents an action potential), and averaged as peri-stimulus time histograms (bottom panels). s/sec, spikes per second. Panel **b** adapted, with permission, from REF. 107 © (2004) American Physiological Society.

to observe and remember the order in which three visual objects appeared, so that the animals could plan a subsequent triple-reaching movement in the same order (FIG. 5). Neurons in the ventrolateral prefrontal cortex were selectively for visual object properties (23% of the total sample), whereas neurons in the dorsolateral prefrontal cortex were selectively tuned to the rank order of the objects (44%), irrespective of the sensory properties of those objects; for example, a rank-order selective neuron would be active whenever the second item of the shuffled lists appears¹⁰⁷. A third class of neuron, found in the ventrolateral prefrontal cortex, showed the most complex response, which was characterized by integrating the objects' sensory and order information — such a

neuron would only discharge when a certain object appeared at a given position in the sequence. The inferior temporal cortex might also be a good candidate for representing ordinal information, as the medial temporal lobe is also involved in mnemonic function. Few neurons in the aITC signalled numerical information in a quantification task⁴⁸.

The lateral prefrontal cortex is an ideal region of the brain for encoding both sensory object properties and rank order information because it receives massive sensory input from the temporal and parietal lobes, and projects to pre-motor and motor areas of the frontal lobe⁵³. As a result, neurons that encode the ordinal positions of task-related hand or eye movements have frequently been found in the prefrontal¹⁰⁸ and various motor-related cortical areas in trained monkeys (FIG. 6). Joseph and co-workers^{109–112} identified order-selective neurons in the frontal eye field (FEF), caudate nucleus and anterior cingulate cortex (CGa) of monkeys that had been trained to sequentially order items based on a spatial arrangement. These neurons were only active when the monkeys reached for the 'first', 'second' or 'third' target, irrespective of the targets' locations and the precise type of hand movement. Clower and Alexander¹¹³ trained a monkey to position a cursor on a video display by moving a joystick clockwise or counterclockwise along a spatially-arranged four-item path. In the pre-supplementary motor areas (pre-SMA), more than two thirds of the recorded neurons showed significant effects of numerical order, but only about one third of the neurons showed an effect of rank order in the supplementary motor area (SMA). Rank order selectivity was also prevalent in the pre-SMA of monkeys that had been trained to sequentially perform three different hand movements ('push', 'pull' or 'turn') in four to six different orders, separated by waiting times^{114,115}. In the pre-SMA, the activity differed selectively according to the process of preparing the first, second or third movements in individual trials. The SMA, on the other hand, was more involved in linking the occurrence of two different movements and, therefore, in determining the order of the component movements in the sequence (relational order). The ordinal position of movements in the pre-SMA seems to be encoded in an effector-independent manner as in the case of eye-movement sequences¹¹⁶. Activity that reflected saccade sequence or the numerical position of a saccade within a sequence (rank) was more common in the supplementary eye field (SEF), whereas activity that reflected saccade direction was more dominant in the FEF¹¹⁷.

Interestingly, the processing of numerical-order information has not only been described in these pre-motor and supplementary motor areas, but also in the primary motor cortex. Carpenter and colleagues¹¹⁸ showed monkeys five spatially-arranged visual targets that appeared successively on a screen. After the target sequence was complete, the colour of one of the targets changed. The task required the monkeys to memorize the order in which the targets

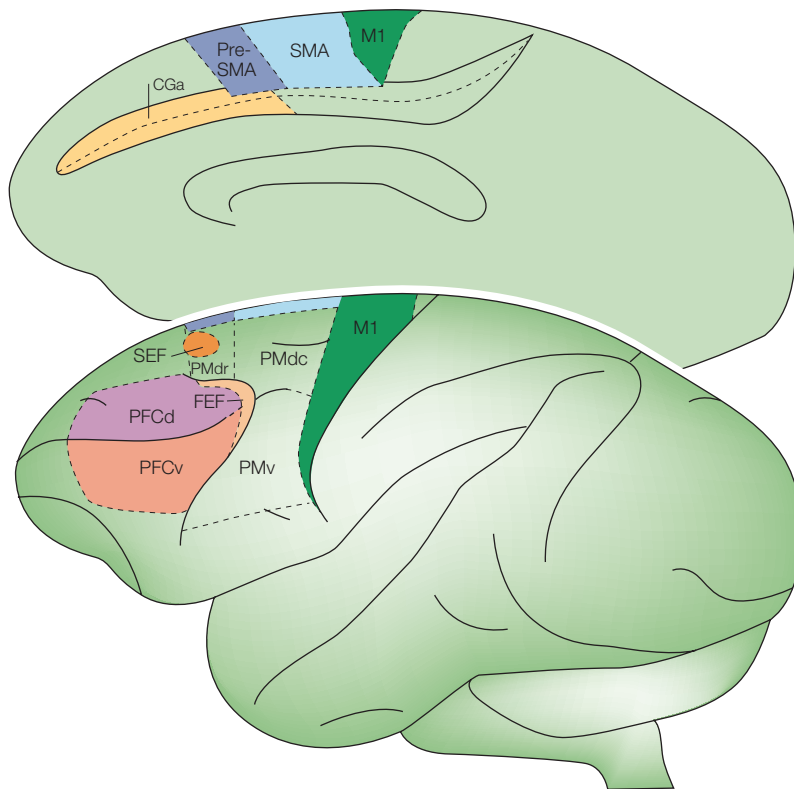


Figure 6 | Medial and lateral views of a rhesus monkey brain showing areas in which serial order activity has been reported. Medial view, top; lateral view, bottom. CGa, anterior cingulate cortex; FEF, frontal eye field; M1, primary motor cortex; PFCd/v, dorsal and ventral lateral prefrontal cortex; PMdc, dorsal premotor cortex, caudal; PMdr, dorsal premotor cortex, rostral; PMv, ventral premotor cortex; Pre-SMA, pre-supplementary motor area; SEF, supplementary eye field; SMA, supplementary motor area.

came up, and to point to the spot that had appeared just after the target that had changed in colour at the end of the list presentation. In approximately one third of the neurons recorded from the arm region of the topographically organized primary motor cortex (M1, FIG. 6), the ordinal position of the targets was the only factor that excited the neurons. Therefore, the motor cortex — an area that is traditionally regarded as pure motor executive — also participates in the processing of cognitive information about serial order within the context of a motor task. However, the authors point out that the motor cortex is probably just one component of a distributed network that encodes, stores and recalls a sequence¹¹⁸. Motor-related areas like M1, SMA, pre-SMA and FEF might receive numerical information that has been computed at earlier stages of the cortical hierarchy to perform appropriate serial order actions.

The representational formats of non-verbal serial order information are poorly understood. However, the behavioural and neuronal data indicate an imprecise representation of discrete numerical rank, which is reminiscent of an analogue magnitude mechanism that has been proposed for cardinality (FIG. 1). Whether an object tracking mechanism is involved in serial order representations is not clear.

Link between numerical quantity and rank

So far, numerical quantity and rank have mostly been studied separately, and the relationship between the mechanisms that underlie cardinality and serial order judgments remains indistinct. However, if these numerical capacities are two aspects of a common numerical faculty, there should be similarities between cognitive and neuronal processing.

At a behavioural level, a shared mechanism is indicated by the distance and the spatial numerical association of response codes (SNARC) effects (BOX 4), which have been reported for cardinality and serial order processing. These effects are not restricted to quantifiable dimensions, but have also been reported for other ordered series, such as letters of the alphabet and months of the year¹¹⁹. As with numerosities, the internal representation of ordered sequences might be spatially encoded. At the neural level, case studies of patients with brain lesions remain inconclusive about the common processing of quantity and rank information. Although one patient who showed the classical signs of Gerstmann's Syndrome (including acalculia) was unable to deal with large numbers and also showed impairment in processing ordered series (such as those of letters or days)¹²⁰, other case studies identified a dissociation between cardinal and ordinal number tasks^{121,122}. However, neurophysiological studies indicate that there might be shared neural substrates for cardinality and serial order processing. A study of event-related potentials shows that both the parietal and prefrontal cortices are activated in response to cardinal and ordinal tasks, but that the time course of activation is different¹²³. Similarly, fMRI studies show that a parieto-prefrontal network was activated during a letter ordering task¹⁰⁴, as seen in cardinal tasks^{76,77,79}. At the single cell level, both numerosity- and order-selective neurons have been identified in the prefrontal cortex of macaques^{47,106,107}. These data indicate that numerical quantity and rank order information probably share the same neural system.

Conclusion

Numerical competence *per se* is a sovereign faculty, and, as such, is found in animals, infants and human adults alike. It does not depend on language to operate, but without language it is limited to an approximate mode. Non-verbal numerical representations can engage a wide cortical network, and the prefrontal cortex and the intraparietal sulcus, in particular, are key structures. Neurons in these areas might underlie basic psychophysical phenomena in animals, human infants and adults during cardinality or serial order judgments. These non-verbal representations undergo a fundamental qualitative and quantitative transformation as soon as children learn to relate them to language. Based on the acquisition of numerical tools⁹ (symbols, such as numerals, and number words) and recursive rules, verbal numerical competence endows us with superior mathematical and logic skills¹²⁴. Understanding the neurobiological foundations of the powerful number faculty will, therefore, help to elucidate “the laws of thought”⁹¹.

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Acknowledgments

I thank I. Diester, O. Tudusciuc and K. Seymour for valuable comments on the manuscript. I. Diester provided figure 3a. My work is supported by a research group grant of the German Research Foundation and a career development award of the Human Frontier Science Program. Dedicated to Philipp.

Competing interests statement

The author declares no competing financial interests.

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