

Coding of abstract quantity by ‘number neurons’ of the primate brain

Andreas Nieder

Received: 13 August 2012/Revised: 25 September 2012/Accepted: 26 September 2012
© Springer-Verlag Berlin Heidelberg 2012

Abstract Humans share with nonhuman animals a quantification system for representing the number of items as nonverbal mental magnitudes. Over the past decade, the anatomical substrates and neuronal mechanisms of this quantification system have been unraveled down to the level of single neurons. Work with behaviorally trained nonhuman primates identified a parieto-frontal cortical network with individual neurons selectively tuned to the number of items. Such ‘number neurons’ can track items across space, time, and modality to encode numerosity in a most abstract, supramodal way. The physiological properties of these neurons can explain fundamental psychophysical phenomena during numerosity judgments. Functionally overlapping groups of parietal neurons represent not only numerable-discrete quantity (numerosity), but also innumerable-continuous quantity (extent) and relations between quantities (proportions), supporting the idea of a generalized magnitude system in the brain. These studies establish putative homologies between the monkey and human brain and demonstrate the suitability of nonhuman primates as model system to explore the neurobiological roots of the brain’s nonverbal quantification system, which may constitute the evolutionary foundation of all further, more elaborate numerical skills in humans.

Keywords Single-neuron recordings · Parietal cortex · Prefrontal cortex · Rhesus monkey · Abstract categories

Abbreviations

aITC	Anterior inferior temporal cortex
BOLD	Blood-oxygenation-level-dependent
BS	Broad spiking neuron
fMRI	Functional magnetic resonance imaging
IPS	Intraparietal sulcus
JND	Just noticeable difference
LIP	Lateral intraparietal area
NS	Narrow spiking neuron
PFC	Prefrontal cortex
PPC	Posterior parietal cortex
SPL	Superior parietal lobule
VIP	Ventral intraparietal area

Introduction

The year 2002 marks the beginning of the investigation of numerical cognition at the level of single cells in awake animals. At that time, two laboratories working with behaviorally trained monkeys reported the presence of neurons in the association cortices that selectively responded to the number of objects or events. Nieder et al. (2002) found neurons responding preferentially to the number of visual items, whereas Sawamura et al. (2002) demonstrated cells that were activated by a specific number of self-performed hand movements. Based on these neurons’ encoding of numerical quantity, they have been referred to as ‘number neurons’ (Piazza and Dehaene 2004; Dehaene 2011). This article recapitulates the progress that has been made in our understanding of the neurophysiological foundation of numerical cognition over the last decade; it shows how this line of research deciphered behaviorally relevant response properties of neurons in

A. Nieder (✉)
Animal Physiology, Institute of Neurobiology,
University of Tübingen, Auf der Morgenstelle 28,
72076 Tübingen, Germany
e-mail: andreas.nieder@uni-tuebingen.de

nonhuman primates, but also helped to gain insights into number processing in the human primate brain. Since 10 years is a relatively short time span for brain research, and despite the many new findings, a multitude of exciting and pressing research questions remain elusive, some of which to be outlined throughout this article.

The physiological findings highlighted here stem from work in behaviorally trained rhesus monkeys (*Macaca mulatta*). Just as 10 years ago, this nonhuman primate is still the only model animal available to study how the activity of single cells and ensembles of neurons give rise to numerical competence. Neurophysiological experiments in awake, behaving monkeys have always been—and will remain—an essential approach to understand the brain and its cognitive abilities (Jasper et al. 1960; Evarts 1966). Monkeys can be trained with operant conditioning techniques to perform numerical tasks, such as discriminating and memorizing numerosities, or processing numerical information according to behavioral principles. During the animals' performance, the electrical activity of individual nerve cells can be monitored by means of microelectrodes positioned at known locations within the brain. Noninvasive methods lack the required high spatial and temporal resolution to measure the electrical signal of single neurons. This signal indispensably needs to be understood, because it is the electrical activity of single neurons embedded in neuronal networks that acts as physical carrier of information in the brain, thus “the neuron remains the important unit of function for developing a rational account of how behavior is generated” (Barlow 1995). In addition, recording neuronal activity simultaneously with behavioral performance presents a rich opportunity for experimental analysis of the neuronal foundations of cognitive functions (such as numerical competence) that would not be possible in untrained animals.

Behavior

Before addressing the neurophysiological correlate of any behavioral capacity in an animal model, this faculty first needs to be demonstrated in such animals. Can animals truly count and deal with natural numbers? In a strict sense, they cannot. Only humans are endowed with symbolic (linguistic) abilities as a prerequisite of a full-blown number theory (Nieder 2009). However, behavioral research over the last decade has shown that basic numerical competence does not depend on language and thus is present in animals. The pioneering work of German zoologist Koehler (1941, 1951) in the middle of the last century demonstrated for the first time convincingly that birds and mammals can discriminate stimuli based on the number of items (a capacity he termed ‘innominate counting’).

Nowadays, a plethora of studies demonstrates that animals are able to nonverbally and approximately estimate the number of objects and events (Davis and Pérusse 1988). Although an exhaustive review of the behavioral literature is beyond the scope of this review, example studies from different taxa indicate that numerical competence is a widespread phenomenon in the animal kingdom. Amongst vertebrates, not only mammals have been tested successfully, but also birds, such as pigeons (Scarf et al. 2011) and corvids (Smirnova et al. 2000; Bogale et al. 2011); because of the corvids' sophisticated cognitive capabilities (Emery and Clayton 2004; Hoffmann et al. 2011), these birds might be particularly suited to study the avian neuronal correlates of numerical competence. Moreover, spontaneous choice experiments revealed that amphibians (Uller et al. 2003) and fish (Agrillo et al. 2007) are able to pick larger sets over smaller ones. But even more distantly related animals like invertebrates show rudimentary magnitude discrimination: honey bees, for instance, can keep track of a small number of landmarks encountered sequentially during flight (Dacke and Srinivasan 2008). These examples indicate that numerical competence is of adaptive value for many animals from various taxa and with different brains. Currently, neuronal data of numerosity representations are only available for the primate brain, but the above-mentioned behavioral results postulate that also vertebrates without a neocortex (i.e., birds, reptiles, amphibians, and fish) or even invertebrates with altogether different brains (e.g., insects) must be able to assess quantity. Investigating convergent brain evolution in the realm of numerical competence will be highly interesting.

For nonhuman primates, the elegant work by Brannon and Terrace (1998) served as a catalyst also for subsequent neurophysiological studies, because it demonstrated with controlled behavioral techniques that rhesus monkeys exhibit a conceptual knowledge of numerical information. This numerical estimation system for representing number as language-independent mental magnitudes (‘analog magnitude system’) is a precursor on which verbal numerical representations build (Cantlon and Brannon 2006) and will later be discussed in detail. Whether an additional ‘subitizing’ (or ‘object tracking’) system in animals exists for the assessment of small numerosities up to 4 remains controversial (Nieder 2005). Numerical representations in laboratory animals that have been conditioned on numerosity discrimination exclusively show characteristics of the analog magnitude system (Weber-Fechner Law-signature) for both small and large numerosities (Nieder and Miller 2003; Cantlon and Brannon 2006; Beran 2007; Merten and Nieder 2009; Evans et al. 2009; Bogale et al. 2011).

In adult humans, this analog magnitude system is still present in subjects experimentally prevented from using

number symbols (Whalen et al. 1999; Merten and Nieder 2009) or never have learnt to count verbally (Gordon 2004; Pica et al. 2004). Beyond discrete quantities, nonhuman primates can also grasp continuous-spatial quantities, such as length (Tudusciuc and Nieder 2010) as well as relations between quantities resulting in proportions (Vallentin and Nieder 2008). In the realm of cognitive control, monkeys perform primitive arithmetic operations such as processing numerosities according to quantitative rules (Cantlon and Brannon 2005; Bongard and Nieder 2010). In sum, it is well accepted that numerical competence is rooted in biological primitives that can already be found in animals, thus opening the door for neurophysiological investigations (Nieder 2005).

Investigations of cognitive processing and its neuronal underpinning require subjects that are engaged in controlled behavioral tasks. To that aim, monkeys are trained to perform discrimination tasks based on numerical information. In the basic layout of the delayed match-to-numerosity task, monkeys viewed a sequence of two displays separated by a memory delay and were required to judge whether the second display (test) matches the first display (sample) with respect to the number of items shown on it. Thus, the monkeys are required to discriminate matching from non-matching numerosities to solve this task (Fig. 1a). To ensure that the monkeys solved the task by judging number per se rather than simply memorizing sequences of visual patterns or exploiting low-level visual features that correlate with number, sensory cues (such as position, shape, overall area, circumference, and density) were varied considerably and controlled for (Nieder et al. 2002).

In such tasks, monkeys and other animals can discriminate numerosities, but they do so in an approximate way (Nieder and Miller 2003). Unlike counting in human adults who represent the number of items in a precise way, animals can only nonverbally estimate numerosity. Thus, when animals discriminate a sample numerosity from smaller or larger (nonmatch) numerosities, it is difficult for them to discriminate numerosities close to the target numerosity (say, 5 vs. 6), but progressively easier to dissociate numerically remote quantities (such as 2 vs. 6). Because of this *numerical distance effect*, the discrimination performances result in peak distributions centered around the target (sample) numerosity (Fig. 1b). In addition, the behavioral discrimination distributions also grew broader with increasing target numerosities, an indication of the *numerical size effect*. This size effect captures the finding that pairs of numerosities of a constant numerical distance are easier to discriminate if the quantities are small (for example, 2 vs. 3), but more difficult if large (e.g., 5 vs. 6). This size effect is in accord with Weber's Law, stating that the *just noticeable difference*, JND (ΔI),

between magnitudes is proportional to the magnitude of the physical stimulus (I); thus the ratio of ΔI and I , the Weber fraction, is a constant. The numerical distance and size effects together with a constant Weber fraction are clear signatures of the analog magnitude system present in monkeys (Fig. 1d, f) and man (Fig. 1e, g).

Neurons encoding numerical quantity

Recordings in monkeys actively discriminating visual numerosity (Fig. 1a) demonstrated the capacity of single neurons in the lateral prefrontal cortex (PFC) and posterior parietal cortex (PPC) (Fig. 2a) to encode cardinality (Nieder et al. 2002, 2006; Nieder and Miller 2004a). Numerosity-selective neurons were tuned to the number of items in a visual display (Fig. 2b–g), that is, they showed maximum activity to one of the presented quantities—a neuron's "preferred numerosity"—and a progressive drop off as the quantity became more remote from the preferred number (Nieder et al. 2002; Nieder and Merten 2007). Importantly, changes in the physical appearance of the displays had no effect on the activity of numerosity-selective neurons (Nieder et al. 2002, 2006; Nieder and Miller 2004a). About 30 % of randomly selected PFC neurons encoded numerosities (Nieder et al. 2002). In the PPC, numerosity-selective neurons were sparsely distributed in several areas, but with around 20 % relatively abundant in the fundus of the intraparietal sulcus (IPS), area VIP (Colby et al. 1993). There were few such cells in the anterior inferior temporal cortex (aITC) (Nieder and Miller 2004a).

Besides neurons representing visual numerosities, cells in the superior parietal lobule (SPL) have been reported to keep track of the number of movements (Sawamura et al. 2002, 2010). The authors trained monkeys to alternate between five arm movements of one type ('push') and five of another ('turn'). They found neurons in a somatosensory-responsive region (part of area 5) of the SPL that maintained the number of movements. Most movement-number representations (85%) found by Sawamura et al. (2002) were not abstract; number-selective activity depended on whether the monkey's movement was 'push' or 'turn'. By contrast, the visual numerosity representations found in the PFC and fundus of the IPS were abstract and generalized (Nieder et al. 2002, 2006; Nieder and Miller 2004a).

The activity of all numerosity-selective neurons, each tuned to a specific preferred visual or action numerosity, formed an array of numerically overlapping tuning functions (Fig. 3). Because such tuning functions represent the range of numerosities encoded, or filtered out, by the neurons, these neurons can be said in technical terms to form a bank of overlapping numerosity filters.

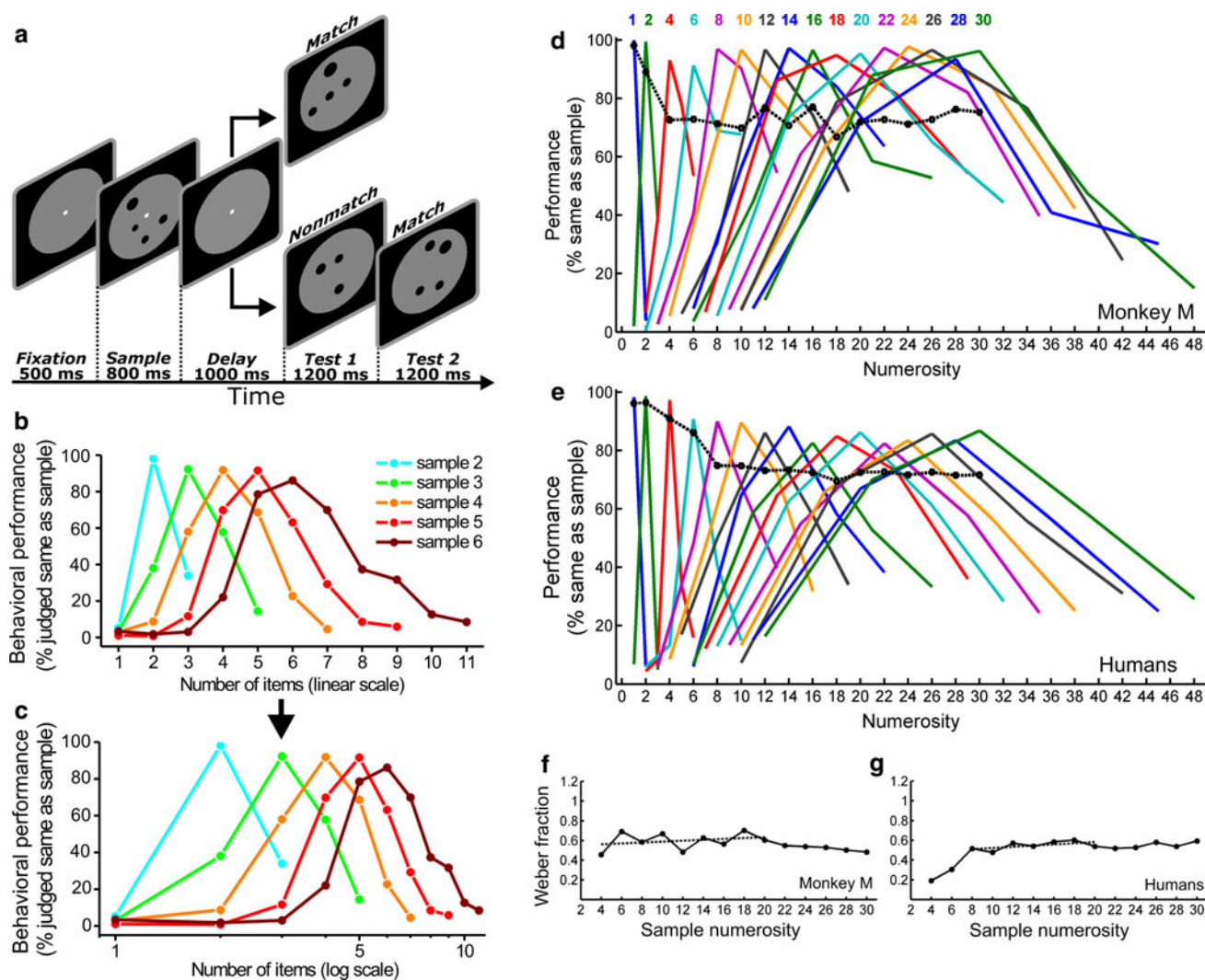


Fig. 1 Representation of visual cardinality in rhesus monkeys. **a** Delayed match-to-sample task with visually presented numerosity as the stimulus dimension of interest. A trial started when the monkey grasped a lever and fixated at a central target. After 500 ms of pure fixation, the sample stimulus (800 ms) cued the monkey for a certain numerosity it had to memorize during a 1,000-ms delay period. Then, the test 1 stimulus was presented, which in 50 % of cases was a match showing the same number of dots as cued during the sample period. In the other 50 % of cases the test 1 display was a non-match, which showed a different numerosity as the sample display. After a non-match test stimulus, a second test stimulus (test 2) appeared that was always a match. To receive a fluid reward, monkeys were required to release the lever as soon as a match appeared. Trials were pseudo-randomized and balanced across all relevant features. Monkeys were

required to maintain fixation throughout the sample and delay period. **b** Behavioral 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 color legend) indicate the sample numerosity at which each curve was derived. **c** The same behavioral performance functions plotted on a logarithmic scale resulted in symmetric functions (from Nieder and Miller 2003). **d** Behavioral performance functions of a single monkey M for sample numerosities 1 to 30. **e** Behavioral performance functions of humans for sample numerosities 1 to 30. **f** Weber fractions derived from the performance of monkey M shown in **d**. **g** Weber fractions derived from the performance of humans shown in **e** (from Merten and Nieder 2009)

The neuronal tuning functions (Fig. 3a) mirror the animals' behavioral performance functions (Fig. 1b). 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); they need to be sequentially ordered to allow meaningful quantity assignments.

The discrimination precision between numerosities relying on peak tuned numerosity detectors would benefit from sharp, and thus only mildly overlapping tuning functions. We thus hypothesized that the local interactions between neuron classes in the PFC could help to shape numerical representations (Diester and Nieder 2008). The two main classes of neurons in the neocortex are excitatory pyramidal cells (projection cells; ca. 80% of all neocortical

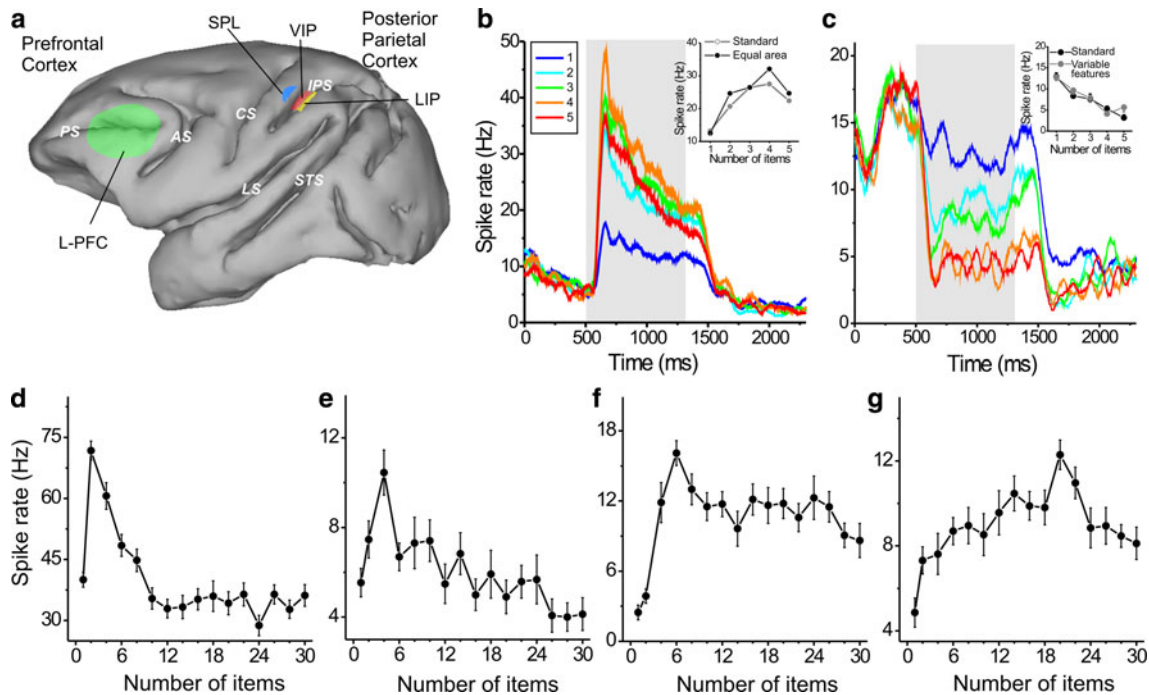
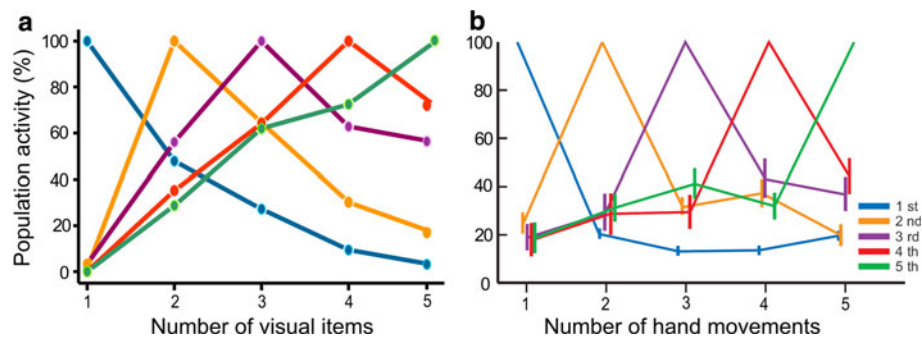


Fig. 2 Numerosity-selective neurons in the monkey brain. **a** Dorsolateral view of a rhesus macaque brain. The *colored areas* represent regions in which neurons that respond to numerosities have been identified via single-cell recordings. Areas include the lateral prefrontal cortex (LPFC), the SPL, the ventral intraparietal area (VIP), which is located at the fundus of the intraparietal sulcus, and the lateral intraparietal area (LIP) (AS arcuate sulcus, CS central sulcus, IPS intraparietal sulcus, LS lateral sulcus, LS lunate sulcus, PS principal sulcus, STS superior temporal sulcus). **b, c** Responses

of single neurons that were recorded from the PFC (**b**) and the IPS (**c**). Both neurons show graded discharge during sample presentation (interval shaded in *gray*, 500–1,300 ms) as a function of numerosities 1 to 5 (color-coded averaged discharge functions). The *insets* in the *upper right corner* 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**) (after Nieder et al. 2002). **d–g** PFC neurons tuned to preferred numerosities 2 (**d**), 4 (**e**), 6 (**f**), and 20 (**g**) (from Nieder and Merten 2007)

Fig. 3 Overlapping population tuning functions of numerosity-selective neurons. **a** Averaged single-cell numerosity-tuning functions (from PFC) to visual numerosities (after Nieder and Miller 2003). **b** Averaged single-cell responses (from area 5 of the SPL) tuned to the number of self-performed hand movements (after Sawamura et al. 2010)



neurons) and inhibitory interneurons (local cells), which differ in various aspects (Markram et al. 2004; Wonders and Anderson 2006).

Importantly, combined evidence from different approaches suggests that that longer action potential wavelengths stem from putative pyramidal cells, whereas shorter waveforms are derived from inhibitory interneurons (Connors and Gutnick 1990). Diester and Nieder (2008) analyzed the extracellularly recorded waveforms of single cells and classified them into narrow spiking (NS, putative

inhibitory interneurons) and broad spiking (BS, putative pyramidal cells) neurons (Fig. 4a).

Both cell types were tuned to numerosity. Interestingly, NS–BS pairs recorded simultaneously at the same electrode were mainly characterized by inverse numerosity tuning and negative cross-correlations of spike timing, indicating inhibitory interactions (Fig. 4b, c). BS–BS cell pairs, however, exhibited similar numerosity tuning and positive cross-correlations of spike occurrence (Fig. 4d, e). This confirms excitatory connections causing spiking

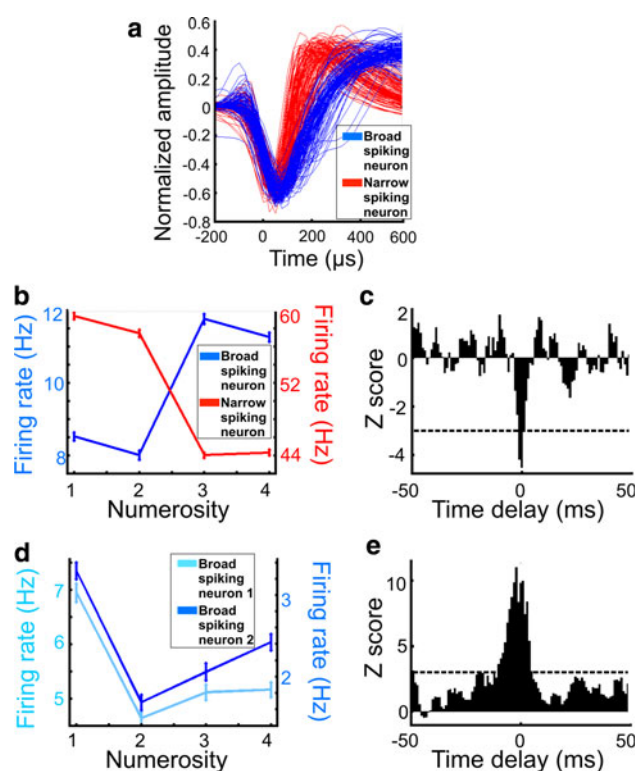


Fig. 4 Synchronization patterns of adjacent numerosity-selective neurons. **a** Normalized average waveforms of a random subset of 130 neurons aligned by their minimum showing narrow (NS)- and broad-spiking (BS) neurons, respectively. **b** Example NS-BS cell pair recorded at the same electrode with opposite numerosity tuning relative to each other. **c** When tested with a cross-correlation analysis on spike timing, the cell pair in (b) showed a significant cross-correlation trough. This indicates that both cells are functionally connected and one cell provides inhibitory input to the other. **d** Example BS-BS cell pair recorded at the same electrode with equivalent numerosity preferences. **e** Cross-correlation analysis for the cell pair in d resulted in a positive correlation peak, suggesting common input (after Diester and Nieder 2008)

synchronization in neighboring BS cells. Together, these results suggest that inhibitory input by putative interneurons sharpens the categorical numerosity tuning of possible PFC pyramidal cells. These findings favor feedforward mechanisms subserving cognitive categorization.

Encoding of numerosity by peaked tuning functions with a preferred numerosity is termed a “labeled-line code”. Such a labeled-line code with ‘number neurons’ tuned to a preferred numerosity have been predicted based on the *neural filtering model* by Dehaene and Changeux (1993) and has been repeatedly shown to exist in the monkey brain (Nieder et al. 2002; Sawamura et al. 2002, 2010; Nieder and Miller 2004a). In many network models, however, the final tuned numerosity detectors receive input from preceding “summation units”, i.e., neurons monotonically increasing and decreasing discharge rates as a function of numerosity (“summation code”) (Dehaene and Changeux 1993; Verguts and Fias 2004; Stoianov and Zorzi 2012).

A putative physiological reflection of ‘summation units’ was found in the parietal lobe, the lateral intraparietal area LIP (Roitman et al. 2007). Monkeys performed a delayed saccade task in which sets of dots provided implicit information about the reward magnitude a monkey was to receive. The responses of many neurons resembled the output of accumulator neurons with response functions that systematically increased or decreased with increase of stimulus set size. Thus, monotonic magnitude coding of LIP neurons may provide input to neurons in the PPC and PFC that compute cardinal numerical representations via tuning to preferred numerosities. Alternatively, the representation of quantity may change if it is encoded as a behaviorally relevant, explicit category.

In sum, the parietal cortex, and the IPS in particular, might be the first cortical stage that extracts visual numerical information because its neurons require shorter latencies to become numerosity selective than PFC neurons (Nieder and Miller 2004a). As PPC and PFC are functionally interconnected (Quintana et al. 1989; Chafee and Goldman-Rakic 2000), that information might be conveyed directly or indirectly to the PFC where a larger proportion and more selective neurons represent numerosity, particularly during the working memory phase, to gain control over behavior. Of course, numerosity-selective neurons need not exclusively encode numerical information. As discussed later, evidence from single-cell recordings in monkeys and imaging studies in humans suggests that single neurons have diverse coding capacities and thus can be members of partly overlapping neuronal populations encoding different types of abstract magnitudes.

Abstract numerosity detectors: enumeration across space, time, and modality

Numerical quantity is a most abstract concept, it applies equally well to items and events laid out in space or time, and across all sensory modalities. Three apples and three calls all belong to the cardinality ‘three’. Where in the brain might such abstract numerosity detectors be implemented? Obviously, the ideal candidate brain areas integrate information multimodally across time and space. As classical association cortices, the prefrontal and posterior parietal cortices fulfill these criteria. The PPC hosts neural circuitry dedicated to the representation of abstract spatial information (Colby and Goldberg 1999), and neurons in both areas are activated across time to integrate sensory cues with goal-directed actions (Fuster 2001). PFC and PPC receive highly processed multimodal input (Lewis and Van Essen 2000; Bremmer et al. 2001; Miller and Cohen 2001). Both the PPC and the PFC, in particular, are cardinal processing stages for executive functions

(e.g., categorization, working memory, decision making, goal-directed behavior, etc.) (Freedman et al. 2001; Wallis et al. 2001; Stoet and Snyder 2004, Merten and Nieder 2012). Moreover, functional imaging in the human primate points towards the prefrontal and posterior parietal cortices as key structures for abstract counting processes (Dehaene et al. 1999, 2004).

Within the visual modality, the number of items and events can be determined in two fundamentally different spatio-temporal presentation formats. When presented simultaneously as in multiple-item patterns (i.e., $\cdot \cdot$), numerosity can be estimated at a single glance in a direct, perceptual-like way from a spatial arrangement. On a behavioral level, constant reaction times and equal numbers of scanning eye movements to individual items (Nieder and Miller 2004b) indicate parallel processing mechanisms for quantity assessments from multiple-dot patterns. Moreover, the response latencies of single neurons are indifferent across numerosities (Nieder et al. 2002). In contrast to a simultaneous presentation, the elements of a set can be presented one by one (i.e., $\bullet - \bullet - \bullet$, etc.) and, thus, need to be enumerated successively across time (Meck and Church 1983; Whalen et al. 1999; Cordes et al. 2001). Sequential enumeration is cognitively more demanding; it incorporates multiple encoding, memory and updating stages, and bears an ordinal aspect (numerical rank) in addition to the cardinal component (numerical quantity) (Jacob and Nieder 2008). Sequential enumeration may even be regarded as a form of addition of one.

To address the neuronal representation of an abstract counting-like accumulation of sensory events and to compare it to the encoding of numerosity in simultaneous displays, Nieder et al. (2006) recorded single-cell activity in area VIP while monkeys performed a delayed match-to-sample task in which sample numerosity was specified either by single dots appearing one by one to indicate the number of items in sequence ('sequential protocol', Fig. 5a) or by multiple-dot patterns ('simultaneous protocol', Fig. 1a). It was ensured that temporal or spatial cues could not be used by the animals to solve the task. In addition to the previously described neurons selective to numerosity in multiple-dot patterns, roughly 25 % of the neurons in the fundus of the IPS also encoded sequentially presented numerical quantity (Fig. 5c, g). However, numerical quantity was represented by distinct populations of neurons during the ongoing spatial or temporal enumeration process (i.e., in the sample phase); cells encoding the number of sequential items were not tuned to numerosity in multiple-item displays, and vice versa. Once the enumeration process was completed, though, and the monkeys had to store information in mind, a third population of neurons coded numerosity both in the sequential and simultaneous protocol; about 20 % of the cells were

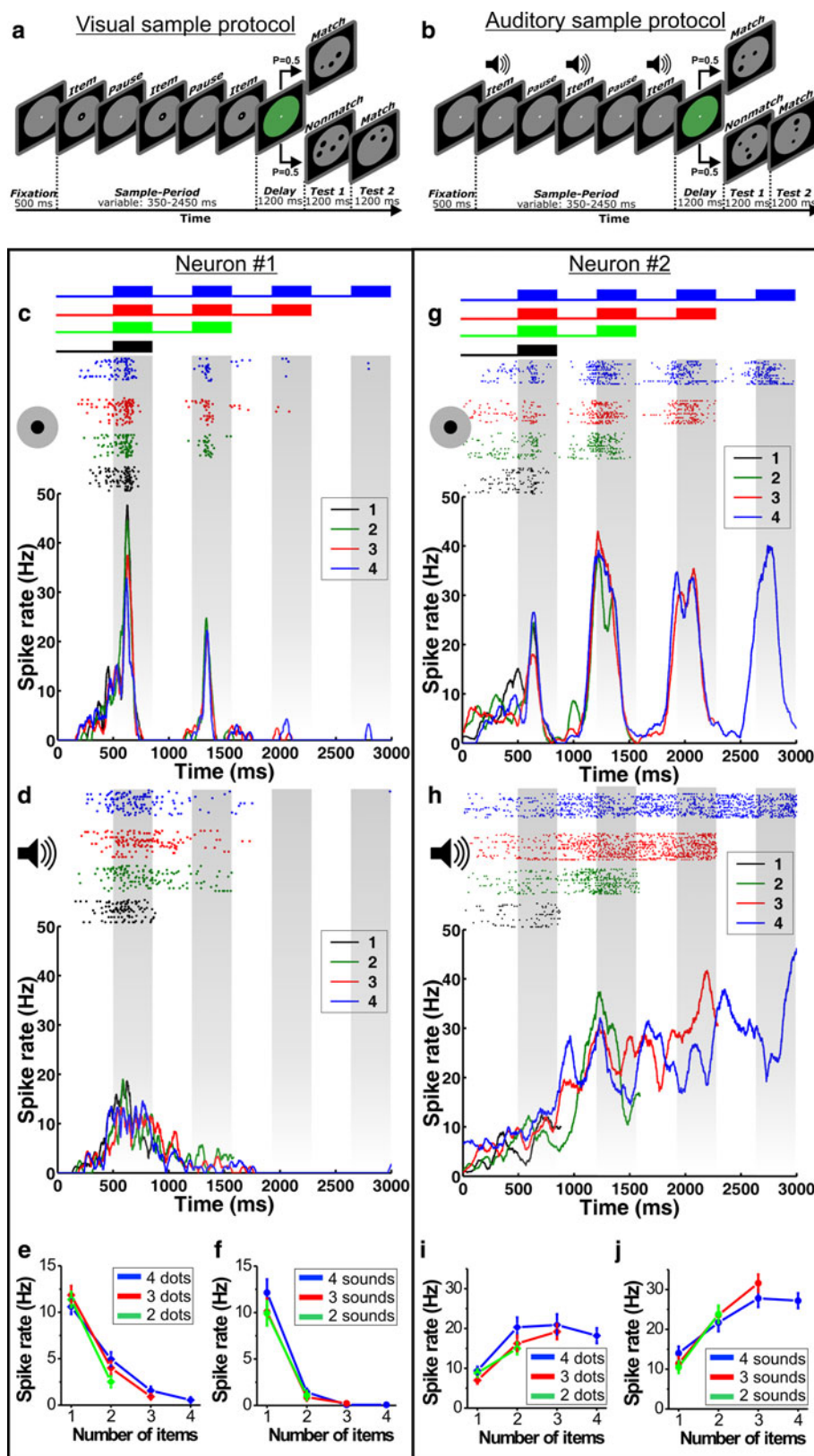
tuned to numerosity irrespective of whether it was cued simultaneously or in sequence. This argues for segregated processing of numerosity during the actual encoding stage in the parietal lobe, but also for a final convergence of the segregated information to form most abstract quantity representations. The intermediate numerosity of an ongoing quantification process and the storage of the final cardinality seem to be accomplished by different neuronal populations.

As an abstract magnitude, numerosity not only needs to be encoded across time and space, but is also independent of sensory modality ('supramodal'). Three light flashes or three calls are both instances of 'three'. To address whether neurons encode the number of items/events irrespective of the items' modality, numerosity selectivity needs to be compared across different sensory modalities in one and the same experiment. In a recent combined psychophysical and electrophysiological study, rhesus monkeys were trained to assess and discriminate both the number of visual dots (Fig. 5a) and auditory sounds (Fig. 5b) within the same session (Nieder 2012). While the monkeys performed this task, the activity of individual neurons in the lateral prefrontal and ventral intraparietal cortices was recorded. Groups of neurons in the VIP and PFC encoded either the number of auditory pulses, visual items, or both. Figure 5 displays the detailed activity of one PFC neuron (#1) that was tuned to both one dot and one sound (Fig. 5c–f), and another PFC neuron (#2) supramodally tuned to numerosity 3 (Fig. 5g–j). Interestingly, supramodal tuning to each of the four tested numerosities (1 to 4) was only present in the PFC; VIP only represented numerosity 1 supramodally. A truly abstract and behaviorally relevant supramodal representation of numerosity is thus first present in the PFC; neurons in the VIP seem to be more limited in this respect. In humans, supramodal coding of numbers also in the fundus of the IPS has been inferred from a functional imaging study (Eger et al. 2003). Supramodal numerosity detectors might provide a computational advantage: they could easily be linked to visual shapes or auditory sounds to establish symbolic representations of numbers in humans, such as numerals and number words. This is also postulated by the influential triple-code model (Dehaene 1992). According to this framework, numerical cognition initially involves a lower step of modality-specific analysis, followed by a higher processing stage where these representations reach an abstract, amodal estimation module.

Behavioral significance of numerosity-selective neurons

Three lines of evidence support the notion that numerosity-selective neurons constitute the neuronal basis for

Fig. 5 Supramodal coding of numerosity. **a** Visual sample protocol. The sample numerosity (here numerosity 3) was cued by sequentially presented items temporally separated by pauses containing no items. The temporal succession and duration of individual items were varied within and across quantities. **b** Auditory sample protocol. Same stimulus sequence, but with sound pulses in the sample phase to be enumerated. **c–f** Supramodal responses of example neuron #1 selective to quantity 1 (only one presented temporal protocol shown for clarity). **c** Responses of neuron #1 to a sequence of visual dots (see protocol in **a**). *Top panel* illustrates the temporal succession of individual items (*square* pulses represent single items). Below, the corresponding latency-corrected discharges for many repetitions of the protocol are plotted as dot-raster histograms (each *dot* represents an action potential, spike trains are sorted and *color-coded* according to the sample proportion illustrated by example stimuli on the *left*). The *bottom panel* shows the averaged spike density functions. The first 500 ms represent the fixation period. Corresponding *colors* were used for the stimulation illustration and the plotting of the neural data. *Gray-shaded areas* denote item presentation of individual items. **d** Responses of neuron #1 to a sequence of auditory pulses (see protocol in **b**). Same layout of neuronal responses as in **c**. **e** Tuning functions of neuron #1 to visual numerosities 1 to 4. **f** Tuning functions of neuron #1 to auditory numerosities 1 to 4. **g–j** Supramodal responses of example neuron #2 tuned to quantity 3. Same layout as in **c–f** (from Nieder 2012)



numerosity-related behavior: firstly, a direct correlation between psychophysical performance and neuronal response properties; secondly, the decrease of the neurons'

coding capacities whenever the monkeys make behavioral errors; and thirdly, selective disturbance of performance caused by inactivation of number neurons.

The response properties of numerosity-selective cells in both parietal and prefrontal cortices can explain basic psychophysical phenomena in monkeys, such as the numerical distance and size effect (Fig. 1b). As mentioned earlier, the activity of all numerosity-selective neurons, each tuned to a specific preferred numerosity, formed an array of numerically overlapping filter functions. The *numerical distance effect* results from the fact that the neural filter functions that are engaged in the discrimination of adjacent numerosities heavily overlap (Nieder and Miller 2003). As a consequence, 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 where the animal has to discriminate sets of a larger numerical distance. The behavioral consequences of the numerical size effect therefore in accord with Weber's Law. The *numerical size effect* is directly related to the precision of the neuronal numerosity filters: the widths of the tuning curves (or neuronal numerical representations) increase linearly with preferred numerosities (that is, on average, tuning precision deteriorates as the preferred quantity increases). Hence, more selective neural filters that do not overlap extensively are engaged if a monkey has to discriminate small numerosities (say, 1 and 2), which results in high signal-to-noise ratios and few errors in the discrimination. Conversely, if a monkey has to discriminate large numerosities (such as 4 and 5), the filter functions would overlap considerably. Therefore, the discrimination has a low signal-to-noise ratio, which leads to poor performance.

Weber's Law predicts that the behavioral performance functions—the monkeys' behavioral numerical representations—are best described (i.e., symmetrical) on a non-linear, possibly logarithmically compressed scale, or 'number line'. This finding is formally captured by Fechner's Law which states that the perceived magnitude (S) is a logarithmic function of stimulus intensity (I) multiplied by a modality and dimension-specific constant (k). In fact, both the behavioral performance functions (Fig. 1c) and the neuronal tuning functions (Fig. 3a) are better described by a logarithmic, as opposed to a linear scale (Nieder and Miller 2003; Nieder and Merten 2007; Merten and Nieder 2009). Therefore, single-neuron representations of numerical quantity in monkeys obey the Weber-Fechner Law, just as the behavioral discrimination performance does.

An important piece of evidence for the contribution of numerosity-selective neurons to behavioral performance came from the examination of error trials. When the monkeys made judgment errors, the neural activity for the preferred quantity was significantly reduced as compared to correct trials (Nieder et al. 2002, 2006; Nieder and

Miller 2004a; Nieder and Merten 2007). As a result of this (and the ordered representation of quantity), the activity to a given preferred numerosity on error trials was more similar to that elicited by adjacent non-preferred quantities on correct trials. In other words, if the neurons did not encode the numerosity properly, the monkeys were prone to mistakes.

The most direct evidence for the importance of parietal numerosity-selective cells in representing quantity information was recently collected by Sawamura et al. (2010). These authors transiently and focally inactivated parietal area 5 (by application of muscimol) to test its functional contributions to numerosity-based action selection in monkeys trained to push or turn a handle a variable number of times in response to a visual stimulus. As a consequence of chemical inactivation, the error rate in the numerical task increased significantly, mainly based on omissions. A control task showed that the errors were not caused by motor deficits or impaired ability to select between actions. These results indicate that parietal area 5 is crucial for selecting actions on the basis of numerical information.

In sum, the activity of numerosity-selective neurons gives rise to numerical competence in highly trained monkeys. But can such numerosity detectors also be expected in the brains of animals that have not specifically been trained to discriminate cardinalities? The necessary experiments to answer this question with certainty have not been performed yet. However, even without training in the laboratory, animals in the wild routinely make decisions based on numerical information (McComb et al. 1994; Lyon 2003; Benson-Amram et al. 2011; Wilson et al. 2012). This is only possible if the brain can represent numerosity, i.e., the brain must contain neurons encoding set size even in animals that did not receive specific training in the laboratory. With training and increased behavioral relevance of numerosity, the frequency and maybe response properties of numerosity-selective neurons may change, but a *de novo* emergence seems highly unlikely. The putative neuronal changes from a numerically untrained to a numerically experienced monkey need to be explored in future studies.

Beyond number: coding of abstract magnitudes

Cardinality, the number of items in a set, is a most abstract magnitude category. However, not only enumerable, but also continuous abstract magnitudes, such as size (spatial magnitude) or temporal intervals (temporal magnitude), need to be represented and processed. Interestingly, the representation of numerical magnitudes and spatial and/or temporal magnitudes share many features and are not completely segregated. In a number comparison task, for

example, interference between number and size can be shown: choosing the numerically larger number takes significantly longer if the numeral is smaller in size compared to the numerically smaller number (e.g., in the comparison 2 vs. 7) (Henik and Tzelgov 1982; Washburn 1994; Pinel et al. 2004). Functional imaging studies in humans suggest that anatomical vicinity (Fias et al. 2003; Pinel et al. 2004; Castelli et al. 2006; Dormal et al. 2012) or even a common magnitude system (Walsh 2003) for the representation of numerical (discrete) and spatial/temporal (continuous) quantity in the parietal cortex might be responsible for behavioral interference phenomena between different types of quantities.

Besides the numerosity representations mentioned above (Nieder et al. 2002; Sawamura et al. 2002), also time interval judgements in macaques activate regions in both the prefrontal (Genovesio et al. 2006), pre-supplementary motor (Mita et al. 2009), and the posterior parietal (Leon and Shadlen 2003) cortices. In a more extensive investigation of the brain activity related to time interval judgment, functional imaging data in monkeys (Onoe et al. 2001) show that the fronto-parietal cortical regional cerebral blood flow co-varies with time interval judgment. This suggests a fronto-parietal network of neurons engaged in time processing.

To investigate how continuous quantity is encoded by single nerve cells and how it relates to numerosity representations, Tudusciuc and Nieder (2007, 2010) trained two rhesus monkeys in a delayed match-to-sample protocol to discriminate both the number of (one to four) items in multiple-dot displays or the length of a line (out of four different lengths) in random trial alternations. After the monkeys solved more than 81 % of the trials correctly for both the length and the numerosity protocols, single unit activity from area VIP in the depth of the IPS was analyzed while the animals performed the task. About 20 % of anatomically intermingled single neurons in the monkey IPS each encoded discrete-numerical (Fig. 6a), continuous-spatial (Fig. 6b), or both types of quantities (Fig. 6c). Thus two partly overlapping populations of neurons within this area may give rise to quantity judgments, suggesting ‘distributed but overlapping’ neural coding of quantitative dimensions in the IPS (Pinel et al. 2004). Analyses using a population decoding technique (Laubach 2004) based on an artificial neuronal network (Kohonen 1997) showed that the relatively small population of quantity-selective neurons carried most of the categorical information. By exploiting the classical spike-rate measure which contributes to the monkeys’ quantity discrimination performance (Nieder et al. 2002, 2006; Nieder and Miller 2004a), the classifier was able to accurately and robustly discriminate both continuous and discrete quantity classes in a behaviorally relevant way. Subsequent recordings in the PFC

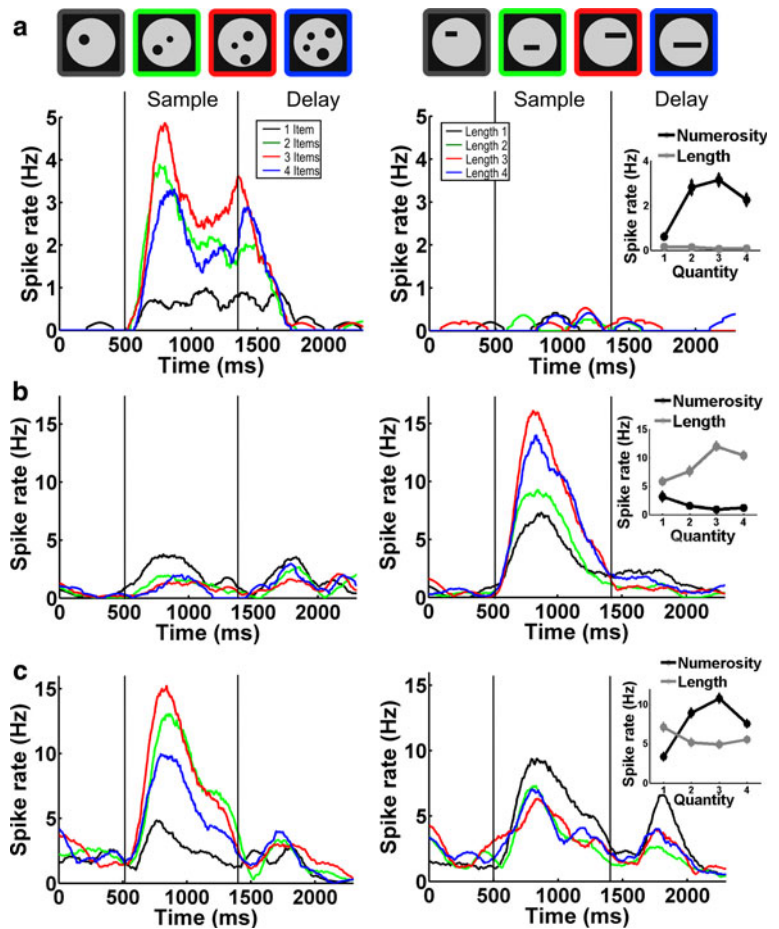
showed similarly anatomically intermingled neurons encoding either length, numerosity, or both types of quantities (Tudusciuc and Nieder 2009). A comparison of the response characteristics between parietal and frontal areas revealed a larger proportion of VIP neurons representing each quantity type in the early sample phase, in addition to shorter response latencies to quantity for VIP neurons.

Not only absolute distances (or lengths) are encoded by PFC neurons, but also relative distances. Genovesio et al. (2011) trained monkeys to sequentially judge the distance of two stimuli relative to a reference point on a computer screen. After a delay period, the same two stimuli reappeared (as choice stimuli), and the monkeys’ task was to choose the one that had appeared farther from the reference point during its initial presentation. Most PFC neurons encoded relative distance, with categorical representations (“farther”) predominating over parametric ones (“how much farther”). Relative-distance coding was most often abstract, independent of its position on the screen.

Many vital decisions in animals require an estimation of the relation between two quantities, or proportion (Jacob et al. 2012). Vallentin and Nieder (2008, 2010) demonstrated that rhesus monkeys were able to grasp proportionality in a delayed match-to-sample test. They trained two rhesus monkeys to judge the length ratio (proportion) between two lines, a reference and a test line. The length ratios between the test and reference lines were 1:4, 2:4, 3:4, and 4:4 (Fig. 7). After demonstrating that the monkeys could discriminate spatial proportions, Vallentin and Nieder (2010) investigated this capacity’s neuronal underpinning and recorded from neurons of the PFC while the animals performed the proportion discrimination task. Both during the sample and delay presentation, 25 % of the tested neurons were significantly tuned only to proportion, irrespective of the absolute lengths of the test and reference bars. Each of the selective neurons preferred one of the four tested proportions. Just as with numerosities or lines, a labeled-line code was found for the coding of proportions, with neurons exhibiting peaked tuning curves and preferred proportions. The areas where such proportion-selective neurons were found coincided with PFC regions that also house numerosity-selective neurons. These data suggest that the perception of relational quantity is represented by the same frontal network and magnitude code as absolute quantity in the primate brain.

In sum, neurons in the prefrontal and posterior parietal cortices are selectively tuned to different types of abstract quantity. The putative parietal semantic quantification system occupies a fixed location (namely, deep in the IPS fundus) relative to other parietal areas involved in sensory, motor, and attentional functions (Nieder and Dehaene 2009). However, it is highly unlikely that (most) of the

Fig. 6 Neuronal coding of continuous and discrete quantity. **a–c** Three example neurons exhibiting selectivity for quantity. *Top panels in a* illustrate the four different numerosities (*left*) and four different line lengths (*right*) used as stimuli. *Left and right graphs illustrate the discharge rates (displayed as smoothed spike density histograms) of the same neuron in the numerosity and length protocol, respectively.* The first 500 ms represent the fixation period. The area between the two *black vertical bars* represents the sample presentation, the following 1,000 ms indicate the delay phase. *Colors* correspond to the quantity dimensions. The *insets* between two histograms depict the tuning functions of each of the three neurons to numerosity and length.



numerosity-selective neurons found in these regions are exclusively encoding numerical information. Rather, single neurons encoding quantity seem to be members of partly overlapping ensembles of neurons, resulting in ‘distributed but overlapping’ neural coding of magnitude dimensions.

Putative homologous primate substrates for numerosity representations

Can findings about numerical competence in the nonhuman primate brain be transferred to the human brain? Historically, case studies of the pathology of numerical competence provided the first insights into its neural roots and pointed to association cortices in the parietal and frontal lobes. Acquired calculation deficits (“acalculia”) were found to occur after brain damage near the parieto-occipito-temporal junction (Henschen 1919; Gerstmann 1940) or in the frontal lobe (Luria 1966). With the advent of functional imaging techniques, most notably functional magnetic resonance imaging (fMRI), investigation of numerical processing in the intact human brain became possible.

To address simple numerical representations without task demands, a so-called fMRI adaptation protocol that requires a subject simply to look at stimuli has been used. In such an fMRI adaptation protocol, human adults are repeatedly presented with numerical stimuli (dot patterns, line proportions or numbers) they have to watch passively. Single-cell studies in monkeys demonstrated that repetitions of the same stimulus over and over again cause habituation of selective neurons, i.e., the responses of selective neurons decreases (Desimone 1996). It is hypothesized that this suppression effect should be present also at the level of the vascular system: If number neurons also exist in the human brain, their activity should become suppressed with repetition of number stimuli. As a consequence, the blood-oxygenation-level-dependent (BOLD) signal measured by fMRI, a complex mass signal of the brain’s vascular system that is correlated with neuronal activity (Logothetis et al. 2001), is expected to decrease. If suddenly the value of the numerical stimuli is changed, other number neurons that have not been habituated would become active, causing a sudden relative increase (rebound) in BOLD activity. Following this logic and taking the peak tuning functions of monkey

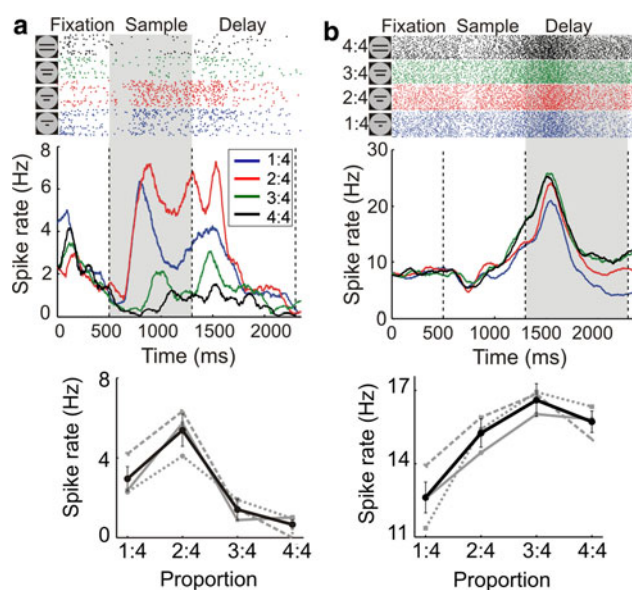


Fig. 7 Neuronal coding of line proportions. Single-cell responses of two example neurons during the fixation, sample, and delay period are shown. Neurons were proportion-selective during the sample (a) or delay (b) period (marked in gray). In the top panel, the neuronal responses are plotted as dot-raster histograms (each dot represents an action potential, spike trains are sorted and color-coded according to the sample proportion illustrated by example stimuli on the left). Middle panels show spike density functions (activity to a given proportion averaged over all trials and smoothed by a 150-ms Gaussian kernel). The first 500 ms represent the fixation period followed by an 800-ms sample and a 1,000-ms delay phase (separated by vertical dotted lines). Bottom panels depict the tuning functions of the respective neurons for each of the three stimulus protocols derived from the periods of maximum proportion selectivity (error bars represent SEM) (from Vallentin and Nieder 2008)

numerosity-selective neurons into account, the BOLD signal rebound should be a function of the numerical distance from the numerical value of the habituation stimulus. This rebound BOLD activity thus provides an indirect read-out of the shape of the tuning functions of putative human number neurons.

Consistent with this hypothesis, the two studies using this adaptation protocol with numerosities found that the BOLD signal decreased during the adaptation period and recovered as a function of the distance of the novel numerosity from the adaptation numerosity. Piazza et al. (2004) found this effect only in the IPS (Fig. 8a), whereas Jacob and Nieder (2009b) reported adaptation to numerosity in both the bilateral IPS and lateral PFC (Fig. 8b). Interestingly, the areas of BOLD activation to numerosities heavily overlapped with areas at which activity in response to dot and line proportions was detected (Fig. 8b). Using the same methodology but presenting fractions in symbolic notation, Jacob and Nieder (2009a) could also show tuning in human parietal cortex to preferred fractions that even generalize across the format of presentation.

While the above-mentioned studies all used visual stimuli, Eger et al. (2003) showed that BOLD activation is also supramodal in human IPS. The authors performed fMRI while subjects were asked to detect numerals, letters or colors 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

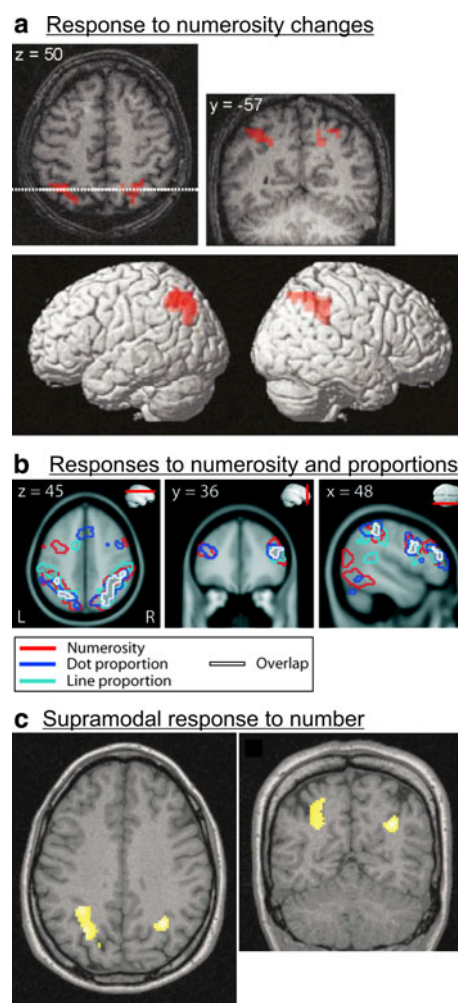


Fig. 8 Regions in the human brain responsive to different types of quantities. a Regions in the human brain that responded to numerosity changes, as measured by BOLD activation. Colored areas in the axial (top left) and coronal (top right) sections, as well as on the surface image indicate the IPS (from Piazza et al. 2004). b Substantial overlap (outlined in white) of BOLD activation in the human brain for numerosities, dot proportions and line proportions. Significant overlap was restricted to the bilateral parietal cortex surrounding the IPS, the precentral, and prefrontal cortex (modified from Jacob and Nieder 2009b). c Cortical localization of supramodal responses to numbers. Color-coded activation maps showing greater BOLD responses to visual and auditory numbers than to visual and auditory letters and colors superimposed onto horizontal (left) and coronal (right) anatomical images (from Eger et al. 2003)

non-target letters or colors. The IPS was the only region that showed higher activation for numerals, both visually and acoustically (Fig. 8c). This suggests 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 form) numerical activation in human IPS.

Together, these comparisons highlight striking similarities between human and monkey numerical representations. First, number neurons are found in comparable brain regions of the PFC and IPS. Second, number neurons in both species seem to be tuned to preferred numerosities. Third, number neurons exhibit a similar level of abstractness across modalities (at least for non-symbolic numerosities). This suggests that the parieto-frontal network for nonverbal numerical information constitutes a phylogenetic precursor for semantic quantity representations, a system that becomes vastly enhanced to also deal with number symbols and arithmetic in literate humans.

Towards symbolic number representations: semantic shapes-numerosities associations

In contrast to other animals, humans invented number symbols (numerals and number words) as mental tools that enable us to create precise quantity representations and perform exact calculation. But even though number symbols are of paramount importance in our today's scientifically and technologically advanced culture, their invention dates back only a couple of thousand years (Ifrah 2000). Given the time scale of brain evolution, a *de novo* development of brain areas with distinct, culturally dependent number symbol functions is more than unlikely (Dehaene 2005). Rather, it is conceivable that brain structures that originally evolved for other purposes are built upon or 'recycled' in the course of continuing evolutionary development (Gould 1982; Dehaene and Cohen 2007). In children learning to count, long-term associations between initially meaningless shapes (that later become numerals) and inherent semantic numerical categories must be established as a prerequisite for the utilization of signs as numerical symbols (Nieder 2009). This necessary, but by no means sufficient step towards the utilization of number symbols in humans can also be mastered by different animal species (Boysen and Berntson 1989; Washburn and Rumbaugh 1991; Matsuzawa 1985; Xia et al. 2001).

To investigate the single-neuron mechanisms of associating the quantity meaning of a set to an arbitrary visual shape (semantic association), Diester and Nieder (2007, 2010) trained two monkeys to associate the a priori meaningless visual shapes of Arabic numerals with the inherently meaningful numerosity of multiple-dot displays.

After this long-term learning process was completed, a relatively large proportion of PFC neurons (24 %) encoded plain numerical values, irrespective of whether they had been presented as a specific number of dots or as a visual sign. Such 'association neurons' showed similar tuning during the course of the trial to both the direct numerosity in dot stimuli and the associated numerical values of signs. Again, the activity of association neurons predicted the monkeys' judgement performance; if the monkeys failed to match the correct number of dots to the learned signs, the tuning behavior of a given neuron to numerosities and their associated visual shapes were severely disrupted. These findings argue for PFC association neurons as a neuronal substrate for the semantic mapping processes between signs and categories. In contrast to PFC, only 2 % of all recorded IPS neurons associated signs with numerosities. The conclusion drawn from these results is that—even though monkeys use the PFC and IPS for non-symbolic quantity representations—only the prefrontal part of this network is engaged in semantic cardinality-to-shape associations.

The prefrontal region is strategically situated to establish semantic associations (Miller and Cohen 2001); it receives input from both the anterior inferotemporal cortex encoding shape information (Tanaka 1996) as well as the PPC that contains numerosity-selective neurons (Nieder and Miller 2004a; Nieder et al. 2006). Previous studies showed that neurons in the PFC encode learned associations between two purely sensory stimuli without intrinsic meaning (e.g., the association of a certain color with a specific sound, or pairs of pictures) (Rainer et al. 1999; Miller et al. 1996; Fuster et al. 2000). Miyashita and co-workers found evidence that the PFC is important for active retrieval of associative representations (Tomita et al. 1999). Our findings (Diester and Nieder 2007) demonstrate that neurons in the PFC represent semantic long-term associations not only between pairs of pictures, but also between arbitrary shapes and systematically arranged categories with inherent meaning (i.e., the ordered cardinalities of sets). In that respect, the PFC of primates may not only control the retrieval of long-term associations, but may in fact constitute a crucial processing stage for abstract semantic associations.

The importance of the PFC for monkey numerical competence seems at odds with the dominant role of the posterior parietal lobe in adult humans (but see also Doricchi et al. 2005; Jacob and Nieder 2009b; Dormal et al. 2012, for PFC involvement). However, learning and experience over the years of an individual may partly specialize the IPS of adult humans for the representation of quantity. Interestingly, the PFC is more intensely engaged early in ontogeny in human infants. Children at the ages of six and seven recruit the inferior frontal cortex for notation-

independent numerical processing to a much greater degree than adults (Kaufmann et al. 2006; Cantlon et al. 2009). Similarly, a greater engagement of frontal brain regions during Arabic numeral judgments (Ansari et al. 2005) and symbolic arithmetic tasks (Rivera et al. 2005) has been described in children compared to adults. These results point to the PFC as the cardinal structure in acquiring a symbolic number concept during ontogeny. Only with age and proficiency, the activation seems to shift to parietal areas. Perhaps the neural correlates of nonverbal numerosity processing at a phylogenetically more ancient stage in nonhuman primates are more similar to those early in human ontogeny.

Outlook

This review article illustrates that nonverbal numerical representations can engage a wide cortical network, with the PFC and the IPS, in particular, as key structures. Neurons in these areas are characterized by response properties that underlie basic psychophysical phenomena during cardinality judgments. But important as it is as a first step, the mere representation of magnitude does not, on its own, constitute a cognitive advantage to an organism. Quantities need to be further processed by integrating different sources of external and internal information before they can successfully influence behavior.

In nonhuman primates, PFC neurons can flexibly group information into behaviorally meaningful categories according to task demands. Such processes are commonly summarized as executive control functions (Miller and Cohen 2001; Fuster 2008; Stoet and Snyder 2009), and quantitative operations in particular require numerical information to be internally structured in accordance with contextual information, or rules. Recently, we showed that the activity of individual PFC neurons (Bongard and Nieder 2010) and neurons in the lateral premotor cortex (Vallentin et al. 2012) encoded the monkeys' capacity to flexibly switch between "greater than/less than" rules. It seems the brain operates with specific 'rule-coding' units that control the flow of information between sensory, memory, and motor stages.

The brain mechanism described in nonhuman primates may serve as an evolutionary precursor for mathematics in adult humans. Symbolic mathematical operations may co-opt or 'recycle' prefrontal circuits (Dehaene and Cohen 2007; Nieder 2009) to dramatically enrich and enhance our symbolic mathematical skills. Comparative work in nonhuman primates, children and adults should test this hypothesis. Single-cell electrophysiology in nonhuman primates, combined with behavioral and imaging studies in children and adults, is well positioned to answer this and

other important questions about the neural basis of numerical cognition in the years to come.

References

- Agrillo C, Dadda M, Bisazza A (2007) Quantity discrimination in female mosquitofish. *Anim Cogn* 10:63–70
- Ansari D, Garcia N, Lucas E, Hamon K, Dhital B (2005) Neural correlates of symbolic number processing in children and adults. *NeuroReport* 16:1769–1773
- Barlow H (1995) The neuron doctrine in perception. In: Gazzaniga, Michael S (eds) *The cognitive neurosciences*. MIT Press, Cambridge, pp 415–435
- Benson-Amram S, Heinen VK, Dryer SL, Holekamp KE (2011) Numerical assessment and individual call discrimination by wild spotted hyaenas, *Crocuta crocuta*. *Anim Behav* 82:743–752
- Beran MJ (2007) Rhesus monkeys (*Macaca mulatta*) enumerate large and small sequentially presented sets of items using analog numerical representations. *J Exp Psychol Anim Behav Process* 33:42–54
- Bogale BA, Kamata N, Mioko K, Sugita S (2011) Quantity discrimination in jungle crows, *Corvus macrorhynchos*. *Anim Behav* 82:635–641
- Bongard S, Nieder A (2010) Basic mathematical rules are encoded by primate prefrontal cortex neurons. *Proc Natl Acad Sci USA* 107:2277–2282
- Boysen ST, Berntson GG (1989) Numerical competence in a chimpanzee (*Pan troglodytes*). *J Comp Psychol* 103:23–31
- Brannon EM, Terrace HS (1998) Ordering of the numerosities 1 to 9 by monkeys. *Science* 282:746–749
- Bremmer F, Schlack A, Shah NJ, Zafiris O, Kubischik M, Hoffmann K, Zilles K, Fink GR (2001) Polymodal motion processing in posterior parietal and premotor cortex: a human fMRI study strongly implies equivalencies between humans and monkeys. *Neuron* 29:287–296
- Cantlon JF, Brannon EM (2005) Semantic congruity affects numerical judgments similarly in monkeys and humans. *Proc Natl Acad Sci USA* 102:16507–16511
- Cantlon JF, Brannon EM (2006) Shared system for ordering small and large numbers in monkeys and humans. *Psychol Sci* 17:401–406
- Cantlon JF, Libertus ME, Pinel P, Dehaene S, Brannon EM, Pelphrey KA (2009) The neural development of an abstract concept of number. *J Cogn Neurosci* 21:2217–2229
- Castelli F, Glaser DE, Butterworth B (2006) Discrete and analogue quantity processing in the parietal lobe: a functional MRI study. *Proc Natl Acad Sci USA* 103:4693–4698
- Chafee MV, Goldman-Rakic PS (2000) Inactivation of parietal and prefrontal cortex reveals interdependence of neural activity during memory-guided saccades. *J Neurophysiol* 83:1550–1566
- Colby CL, Goldberg ME (1999) Space and attention in parietal cortex. *Annu Rev Neurosci* 22:319–349
- Colby CL, Duhamel JR, Goldberg ME (1993) Ventral intraparietal area of the macaque—anatomical location and visual response properties. *J Neurophysiol* 69:902–914
- Connors BW, Gutnick MJ (1990) Intrinsic firing patterns of diverse neocortical neurons. *Trends Neurosci* 13:99–104
- Cordes S, Gelman R, Gallistel CR, Whalen J (2001) Variability signatures distinguish verbal from nonverbal counting for both large and small numbers. *Psychonom Bull Rev* 8:698–707
- Dacke M, Srinivasan MV (2008) Evidence for counting in insects. *Anim Cogn* 11:683–689

- Davis H, Pérusse R (1988) Numerical competence in animals: definitional issues, current evidence, and a new research agenda. *Behav Brain Sci* 11:561–615
- Dehaene S (1992) Varieties of numerical abilities. *Cognition* 44:1–42
- Dehaene S (2005) Evolution of human cortical circuits for reading and arithmetic: the “neuronal recycling” hypothesis. In: Dehaene S, Duhamel JR, Hauser MD, Rizzolatti G (eds) *From monkey brain to human brain*. MIT Press, Cambridge, pp 133–157
- Dehaene S (2011) The number sense: how the mind creates mathematics. Oxford University Press, Oxford
- Dehaene S, Changeux JP (1993) Development of elementary numerical abilities: a neural model. *J Cogn Neurosci* 5:390–407
- Dehaene S, Cohen L (2007) Cultural recycling of cortical maps. *Neuron* 56:384–398
- Dehaene S, Spelke E, Pineda P, Stanescu R, Tsivkin S (1999) Sources of mathematical thinking: behavioral and brain-imaging evidence. *Science* 284:970–974
- Dehaene S, Molko N, Cohen L, Wilson AJ (2004) Arithmetic and the brain. *Curr Opin Neurobiol* 14:218–224
- Desimone R (1996) Neural mechanisms for visual memory and their role in attention. *Proc Natl Acad Sci USA* 93:13494–13499
- Diester I, Nieder A (2007) Semantic associations between signs and numerical categories in the prefrontal cortex. *PLoS Biol* 5:e294
- Diester I, Nieder A (2008) Complementary contributions of prefrontal neuron classes in abstract numerical categorization. *J Neurosci* 28:7737–7747
- Diester I, Nieder A (2010) Numerical values leave a semantic imprint on associated signs in monkeys. *J Cogn Neurosci* 22:174–183
- Doricchi F, Guariglia P, Gasparini M, Tomaiuolo F (2005) Dissociation between physical and mental number line bisection in right hemisphere brain damage. *Nat Neurosci* 8:1663–1665
- Dormal V, Dormal G, Joassin F, Pesenti M (2012) A common right fronto-parietal network for numerosity and duration processing: an fMRI study. *Hum Brain Mapp* 33:1490–1501
- Eger E, Sterzer P, Russ MO, Giraud AL, Kleinschmidt A (2003) A supramodal number representation in human intraparietal cortex. *Neuron* 37:719–725
- Emery NJ, Clayton NS (2004) The mentality of crows: convergent evolution of intelligence in corvids and apes. *Science* 306:1903–1907
- Evans TA, Beran MJ, Harris EH, Rice DF (2009) Quantity judgments of sequentially presented food items by capuchin monkeys (*Cebus apella*). *Anim Cogn* 12:97–105
- Evarts EV (1966) Methods for recording activity of individual neurons in moving animals. In: Rushmer RF (ed) *Methods in medical research*. Year Book, Chicago, pp 241–250
- Fias W, Lammertyn J, Reynvoet B, Dupont P, Orban GA (2003) Parietal representation of symbolic and nonsymbolic magnitude. *J Cogn Neurosci* 15:47–56
- Freedman DJ, Riesenhuber M, Poggio T, Miller EK (2001) Categorical representation of visual stimuli in the primate prefrontal cortex. *Science* 291:312–316
- Fuster JM (2001) The prefrontal cortex—an update: time is of the essence. *Neuron* 30:319–333
- Fuster J (2008) *The prefrontal cortex*, 4th edn. Academic Press, London
- Fuster JM, Bodner M, Kroger JK (2000) Cross-modal and cross-temporal association in neurons of frontal cortex. *Nature* 405:347–351
- Genovesio A, Tsujimoto S, Wise SP (2006) Neuronal activity related to elapsed time in prefrontal cortex. *J Neurophysiol* 95:3281–3285
- Genovesio A, Tsujimoto S, Wise SP (2011) Prefrontal cortex activity during the discrimination of relative distance. *J Neurosci* 31:3968–3980
- Gerstmann J (1940) Syndrome of finger agnosia, disorientation for right and left agraphia and acalculia. *Arch Neurol Psychiatry* 44:398–408
- Gordon P (2004) Numerical cognition without words: evidence from Amazonia. *Science* 306:496–499
- Gould SJVE (1982) Exaptation: a missing term in the science of form. *Paleobiology* 8:4–15
- Henik A, Tzelgov J (1982) Is three greater than five: the relation between physical and semantic size in comparison tasks. *Mem Cogn* 10:389–395
- Henschen SE (1919) Über Sprach-, Musik und Rechenmechanismen und ihre Lokalisation im Großhirn. *Z. ges. Neurologie und Psychiatrie* 52:273–298
- Hoffmann A, Ruettler V, Nieder A (2011) Ontogeny of object permanence and object tracking in the carrion crow, *Corvus corone*. *Anim Behav* 82:359–367
- Ifrab G (2000) *The universal history of numbers: from prehistory to the invention of the computer*. Wiley, New York
- Jacob SN, Nieder A (2008) The ABC of cardinal and ordinal number representations. *Trends Cogn Sci* 12:41–43
- Jacob SN, Nieder A (2009a) Notation-independent representation of fractions in the human parietal cortex. *J Neurosci* 29:4652–4657
- Jacob SN, Nieder A (2009b) Tuning to non-symbolic proportions in the human frontoparietal cortex. *Eur J Neurosci* 30:1432–1442
- Jacob SN, Vallentin D, Nieder A (2012) Relating magnitudes: the brain’s code for proportions. *Trends Cogn Sci* 16:157–166
- Jasper HH, Ricci G, Doane B (1960) Microelectrode analysis of cortical cell discharge during avoidance conditioning in the monkey. *Int J Electroencephalogr Clin Neurophysiol Suppl* 131:137–156
- Kaufmann L, Koppelstaetter F, Siedentopf C, Haala I, Haberlandt E et al (2006) Neural correlates of the number-size interference task in children. *NeuroReport* 17:587–591
- Koehler O (1941) Vom Erlernen unbenannter Anzahlen bei Vögeln. *Naturwissenschaften* 29:201–218
- Koehler O (1951) The ability of birds to “count”. *Bull Anim Behav* 9:41–45
- Kohonen T (1997) *Self-organizing maps*, 2nd edn. Springer, Berlin
- Laubach M (2004) Wavelet-based processing of neuronal spike trains prior to discriminant analysis. *J Neurosci Meth* 134:159–168
- Leon MI, Shadlen MN (2003) Representation of time by neurons in the posterior parietal cortex of the macaque. *Neuron* 38:317–327
- Lewis JW, Van Essen DC (2000) Corticocortical connections of visual, sensorimotor, and multimodal processing areas in the parietal lobe of the macaque monkey. *J Comp Neurol* 428:112–137
- Logothetis NK, Pauls J, Augath M, Trinath T, Oeltermann A (2001) Neurophysiological investigation of the basis of the fMRI signal. *Nature* 412:150–157
- Luria AR (1966) *Higher cortical functions in man*. Tavistock, London
- Lyon BE (2003) Egg recognition and counting reduce costs of avian conspecific brood parasitism. *Nature* 422:495–499
- Markram H, Toledo-Rodriguez M, Wang Y, Gupta A, Silberberg G, Wu C (2004) Interneurons of the neocortical inhibitory system. *Nat Rev Neurosci* 5:793–807
- Matsuzawa T (1985) Use of numbers by a chimpanzee. *Nature* 315:57–59
- McComb K, Packer C, Pusey A (1994) Roaring and numerical assessment in contests between groups of female lions, *Panthera leo*. *Anim Behav* 47:379–387
- Meck WH, Church RM (1983) A mode control model of counting and timing processes. *J Exp Psychol: Anim Behav Process* 9:320–334
- Merten K, Nieder A (2009) Compressed scaling of abstract numerosity representations in adult humans and monkeys. *J Cogn Neurosci* 21:333–346

- Merten K, Nieder A (2012) Active encoding of decisions about stimulus absence in primate prefrontal cortex neurons. *Proc Natl Acad Sci USA* 109:6289–6294
- Miller EK, Cohen JD (2001) An integrative theory of prefrontal cortex function. *Annu Rev Neurosci* 24:167–202
- Miller EK, Erickson CA, Desimone R (1996) Neural mechanisms of visual working memory in prefrontal cortex of the macaque. *J Neurosci* 16:5154–5167
- Mita A, Mushiaki H, Shima K, Matsuzaka Y, Tanji J (2009) Interval time coding by neurons in the presupplementary and supplementary motor areas. *Nat Neurosci* 12:502–507
- Nieder A (2005) Counting on neurons: the neurobiology of numerical competence. *Nat Rev Neurosci* 6:177–190
- Nieder A (2009) Prefrontal cortex and the evolution of symbolic reference. *Curr Opin Neurobiol* 19:99–108
- Nieder A (2012) Supramodal numerosity selectivity of neurons in primate prefrontal and posterior parietal cortices. *Proc Natl Acad Sci USA* 109:11860–11865
- Nieder A, Dehaene S (2009) Representation of number in the brain. *Annu Rev Neurosci* 32:185–208
- Nieder A, Merten K (2007) A labeled-line code for small and large numerosities in the monkey prefrontal cortex. *J Neurosci* 27:5986–5993
- Nieder A, Miller EK (2003) Coding of cognitive magnitude: compressed scaling of numerical information in the primate prefrontal cortex. *Neuron* 37:149–157
- Nieder A, Miller EK (2004a) A parieto-frontal network for visual numerical information in the monkey. *Proc Natl Acad Sci USA* 101:7457–7462
- Nieder A, Miller EK (2004b) Analog numerical representations in rhesus monkeys: evidence for parallel processing. *J Cogn Neurosci* 16:889–901
- Nieder A, Freedman DJ, Miller EK (2002) Representation of the quantity of visual items in the primate prefrontal cortex. *Science* 297:1708–1711
- Nieder A, Diester I, Tudusciuc O (2006) Temporal and spatial enumeration processes in the primate parietal cortex. *Science* 313:1431–1435
- Onoe H, Komori M, Onoe K, Takechi H, Tsukada H, Watanabe Y (2001) Cortical networks recruited for time perception: a monkey positron emission tomography (PET) study. *Neuroimage* 13:37–45
- Piazza M, Dehaene S (2004) From number neurons to mental arithmetic: the cognitive neuroscience of number sense. In: Gazzaniga M (ed) *The cognitive neurosciences*, 3rd edn. MIT Press, Cambridge
- Piazza M, Izard V, Pinel P, Le Bihan D, Dehaene S (2004) Tuning curves for approximate numerosity in the human intraparietal sulcus. *Neuron* 44:547–555
- Pica P, Lemer C, Izard V, Dehaene S (2004) Exact and approximate arithmetic in an Amazonian indigene group. *Science* 306:499–503
- Pinel P, Piazza M, Le Bihan D, Dehaene S (2004) Distributed and overlapping cerebral representations of number, size, and luminance during comparative judgments. *Neuron* 41:983–993
- Quintana J, Fuster JM, Yajeya J (1989) Effects of cooling parietal cortex on prefrontal units in delay tasks. *Brain Res* 503:100–110
- Rainer G, Rao SC, Miller EK (1999) Prospective coding for objects in primate prefrontal cortex. *J Neurosci* 19:5493–5505
- Rivera SM, Reiss AL, Eckert MA, Menon V (2005) Developmental changes in mental arithmetic: evidence for increased functional specialization in the left inferior parietal cortex. *Cereb Cortex* 15:1779–1790
- Roitman JD, Brannon EM, Platt ML (2007) Monotonic coding of numerosity in macaque lateral intraparietal area. *PLoS Biol* 8:e208
- Sawamura H, Shima K, Tanji J (2002) Numerical representation for action in the parietal cortex of the monkey. *Nature* 415:918–922
- Sawamura H, Shima K, Tanji J (2010) Deficits in action selection based on numerical information after inactivation of the posterior parietal cortex in monkeys. *J Neurophysiol* 104:902–910
- Scarf D, Hayne H, Colombo M (2011) Pigeons on par with primates in numerical competence. *Science* 334:1664
- Smirnova AA, Lazareva OF, Zorina ZA (2000) Use of number by crows: investigation by matching and oddity learning. *J Exp Anal Behav* 73:163–176
- Stoet G, Snyder LH (2004) Single neurons in posterior parietal cortex of monkeys encode cognitive set. *Neuron* 42:1003–1012
- Stoet G, Snyder LH (2009) Neural correlates of executive control functions in the monkey. *Trends Cogn Sci* 13:228–234
- Stoianov I, Zorzi M (2012) Emergence of a ‘visual number sense’ in hierarchical generative models. *Nat Neurosci* 15:194–196
- Tanaka K (1996) Inferotemporal cortex and object vision. *Annu Rev Neurosci* 19:109–139
- Tomita H, Ohbayashi M, Nakahara K, Hasegawa I, Miyashita Y (1999) Top-down signal from prefrontal cortex in executive control of memory retrieval. *Nature* 401:699–703
- Tudusciuc O, Nieder A (2007) Neuronal population coding of continuous and discrete quantity in the primate posterior parietal cortex. *Proc Natl Acad Sci USA* 104:14513–14518
- Tudusciuc O, Nieder A (2009) Contributions of primate prefrontal and posterior parietal cortices to length and numerosity representation. *J Neurophysiol* 101:2984–2994
- Tudusciuc O, Nieder A (2010) Comparison of length judgments and the Müller-Lyer illusion in monkeys and humans. *Exp Brain Res* 207:221–231
- Uller C, Jaeger R, Guidry G, Martin C (2003) Salamanders (*Plethodon cinereus*) go for more: rudiments of number in an amphibian. *Anim Cogn* 6:105–112
- Vallentin D, Nieder A (2008) Behavioural and prefrontal representation of spatial proportions in the monkey. *Curr Biol* 18:1420–1425
- Vallentin D, Nieder A (2010) Representations of visual proportions in the primate posterior parietal and prefrontal cortices. *Eur J Neurosci* 32:1380–1387
- Vallentin D, Bongard S, Nieder A (2012) Numerical rule coding in the prefrontal, premotor, and posterior parietal cortices of macaques. *J Neurosci* 32:6621–6630
- Verguts T, Fias W (2004) Representation of number in animals and humans: a neural model. *J Cogn Neurosci* 16:1493–1504
- Wallis JD, Anderson KC, Miller EK (2001) Single neurons in prefrontal cortex encode abstract rules. *Nature* 411:953–956
- Walsh V (2003) A theory of magnitude: common cortical metrics of time, space and quantity. *Trends Cogn Sci* 7:483–488
- Washburn DA (1994) Stroop-like effects for monkeys and humans: processing speed or strength of association? *Psychol Sci* 5:375–379
- Washburn DA, Rumbaugh DM (1991) Ordinal judgments of numerical symbols by macaques (*Macaca mulatta*). *Psychol Sci* 2:190–193
- Whalen J, Gallistel CR, Gelman R (1999) Nonverbal counting in humans: the psychophysics of number representation. *Psychol Sci* 10:130–137
- Wilson ML, Kahlenberg SM, Wells M, Wrangham RW (2012) Ecological and social factors affect the occurrence and outcomes of intergroup encounters in chimpanzees. *Anim Behav* 83:277–291
- Wonders CP, Anderson SA (2006) The origin and specification of cortical interneurons. *Nat Rev Neurosci* 7:687–696
- Xia L, Emmerton J, Siemann M, Delius JD (2001) Pigeons (*Columba livia*) learn to link numerosities with symbols. *J Comp Psychol* 115:83–91