

62 From Number Neurons to Mental Arithmetic: The Cognitive Neuroscience of Number Sense

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ABSTRACT Digits and number words are a very recent cultural invention in the evolution of the human species. Indeed, they arise from the specifically human and evolutionary recent ability to create and mentally manipulate complex symbols. However, the sense of numerosity is older. A sensitivity to numerical properties of the world is present in numerous nonhuman species as well as in babies. In this chapter we consider the most relevant findings on the cognitive neuroscience of number sense, showing how data from different domains, from cognitive psychology to electrophysiology, and in different species, from rats to humans, are providing us with complementary information on how the brain represents and manipulates numbers. In particular, we show how such sensitivity to numbers is rooted on a distinct neural circuitry, which has been reproducibly identified in different subjects and species with convergent methods. These observations lead to the hypothesis that an elementary number system is present very early in life in both humans and animals and constitutes the start-up tool for the development of symbolic numerical thinking that permeates so deeply our western technological societies.

Let us imagine a lioness with her pride on the Serengeti Plains, in Tanzania. One night, while alone, she hears a roar from an intruding lioness. Should she try to drive the intruder off? That would be an even match, thus ending in a possibly fatal fight. She decides not to act. The following night, when she is with four sisters, they hear the roars of three intruder lionesses. This time it is three versus five. The lionesses peer into each other's eyes, then launch the attack. But by the time they reach the expected location, they find no intruder. The roaring sounds they had heard came from loudspeakers set up by a researcher investigating the numerical capacity of animals. This research shows that generally, animals decide to attack back only when the number of defenders is superior to the number of intruders (McComb, Packer, and Pusey, 1994). The decision-making process of these animals seems to be based on a multimodal comparison between the number of defenders as perceived

visually and the number of defenders as perceived auditorily. This suggests that the internal representation of number in animals can be quite abstract.

Numbers might be considered a very recent cultural invention in the evolution of the human species. Indeed, number words and digits arise from the specifically human and evolutionarily recent ability to create and mentally manipulate complex symbols. However, the sense of numbers is older. A sensitivity to numerical properties of the world is present in numerous nonhuman species, as well as in human babies, and its strong adaptive value is suggested by our lioness example. Such a sensitivity to numbers also seems to be rooted in a distinct neural circuitry that has been reproducibly identified in different subjects and species with convergent methods. These observations lead to the hypothesis that an elementary number system is present very early in life in both humans and animals, and constitutes the start-up tool for the development of the symbolic numerical thinking that permeates Western technological societies (Dehaene, 1997).

In this chapter, we consider the most relevant findings on the cognitive neuroscience of number sense, showing how data from different domains, from cognitive psychology to electrophysiology, provide complementary information on how the brain represents and manipulates numbers. We first consider how behavioral data have shed light on such a number sense in nonverbal organisms, either in animals or in human infants. Then we show how functional imaging and neuropsychology clarify the cerebral substrates of numerical ability. Finally, we explore the nature of the neural coding of numbers, as clarified by recent electrophysiological studies in monkeys.

Behavioral evidence for analogical representation of number

The ability to make numerical judgments has been tested in many different species of animals, including pigeons, rats, racoons, dolphins, and monkeys, in the wild and in more controlled experimental settings in laboratory, and using

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very different types of paradigms. Typically, animals are trained to respond differently to a variety of numerically defined stimuli, such as the number of visual stimuli, tones, motor responses, or reinforcements. However, because number usually covaries with some of the physical attributes of the stimuli, such as brightness, density, time, or hedonic value, reports of numerical abilities in animals are often met with skepticism. How can one be sure that animals are processing number rather than any other parameters of the stimulus? Two arguments have been used to demonstrate genuine numerical competence. First, animals can transfer numerosity between different modalities. For example, rats initially trained on distinct auditory and visual numerosity discrimination tasks could later generalize to novel sequences in which auditory and visual sequences were mixed (Church and Meck, 1984). This observation suggests that animals possess an abstract, amodal representation of number. Second, animals are able to generalize numerically relevant behavior to novel, nondifferentially rewarded stimuli (Meck and Church, 1983; Brannon and Terrace, 2000; Nieder, Freedman, and Miller, 2002; Sawamura, Shima, and Tanji, 2002). This finding indicates that they bring to the task more knowledge of numerical invariance than training alone could provide. For example, rats were trained to press one lever in response to a short two-tone sequence and another in response to a long eight-tone sequence. Although duration discrimination was sufficient for that initial performance, subsequently the rats generalized their behavior to novel, nondifferentially rewarded sequences in which duration was fixed and only number varied. This suggests that the animals were representing number during the initial training phase (Meck and Church, 1983).

An ability to discriminate sets on the basis of their number is also present in preverbal human infants. With the classic method of habituation and recovery of looking time, both newborns and preverbal infants have been shown to discriminate sets of visual objects, as well as tones or words that differ in the number of syllables, on the unique basis of their numerosity (e.g., Xu and Spelke, 2000). Again, there is suggestive evidence of cross-modal numerosity matching (Starkey, Spelke, and Gelman, 1983), as well as of processing of the numerosity of abstract entities such as collections, whose physical attributes can be well controlled (Wynn, Bloom, and Chiang, 2002). Such animal and infant data, taken together, suggest that the sensitivity to the numerical aspect of the world does not depend on an acquired ability to manipulate symbols but is based on a nonverbal amodal representation of numerosity.

This representation can also be adduced in human adults. When prevented from using language and counting procedures, adult humans can make approximate numerosity judgments similar to those of animals and infants. They too can transfer numerosity from different modalities (visual and auditory) and modes of stimulus presentation (sequential

and simultaneous), and they do so without cost relative to a unimodal stimulus presentation (Barth, Kanwisher, and Spelke, 2003).

The parallels between human and animal behavior on number-related tasks are therefore numerous, but the most striking one is probably that they both seem to be governed by the very same metric (Gallistel and Gelman, 2000; figure 62.1). Number estimation performance in both humans and nonhuman animals is approximate, and becomes less and less accurate as the numbers increase. Furthermore, the variability in performance increases linearly with the size of the number involved, a property called scalar variability, or Weber's law, where the proportionality constant is called the Weber fraction. For example, rats instructed to press a lever a certain number of times will break off the sequence of lever presses with a probability that is roughly proportional to the percent deviation of the actual number of presses from the number of presses required to get the reward (Mechner, 1958; figure 62.1A). Likewise, monkeys instructed to judge whether successive visual displays have the same number of items make errors in direct proportion to the ratio of the two numbers. Thus, for larger numerical quantities, the two numerosities have to be numerically more distant for performance to reach the same level as the one obtained with smaller quantities (Nieder and Miller, 2003; figure 62.1B).

In humans, studies directly inspired by animal experiments show exactly the same type of metric. For example, Whalen, Gallistel, and Gelman (1999) presented numbers between 7 and 25 on a computer screen and asked subjects to press a button as fast as they could until they had felt they had made approximately the indicated number of button presses; verbal counting was prevented by asking subjects to recite words while performing the task. The results showed that both the mean estimate and its variability were proportional to target value, and that therefore the coefficient of variation (the ratio of the standard deviation to the mean) was constant across target size (figure 62.1C). Very similar results are found when humans were asked to estimate prices for different items; again, the standard deviation of price estimates was directly proportional to the mean price (Dehaene and Marques, 2002; figure 62.1D).

Moreover, Weber's law holds even when numerical judgments are not estimates but exact computations made over abstract numerical symbols, such as digits and number words. Such symbolic numerical judgments (e.g., choosing the larger number of 49 and 72) show magnitude effects exactly as nonsymbolic numerosity judgments do; they are influenced by the numerical difference between two values ("numerical distance effect") and by their absolute magnitude ("magnitude effect"), such that ultimately performance can be predicted by the ratio of the two numbers involved (Moyer and Landauer, 1967; Dehaene, 1992).

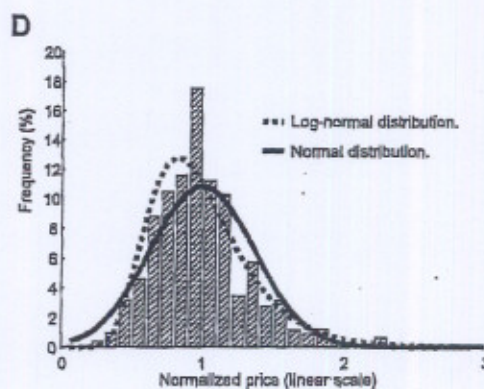
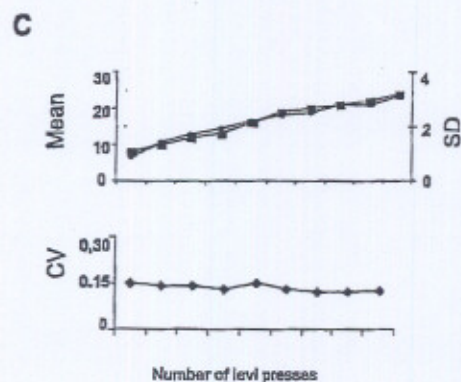
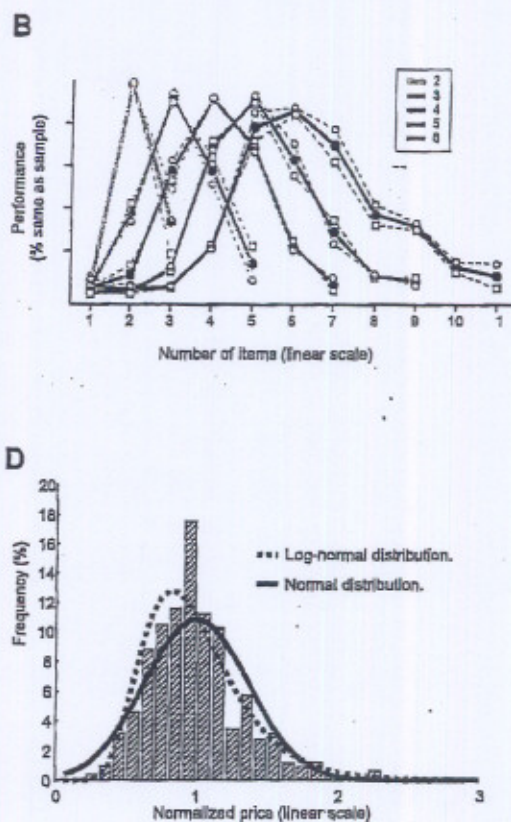
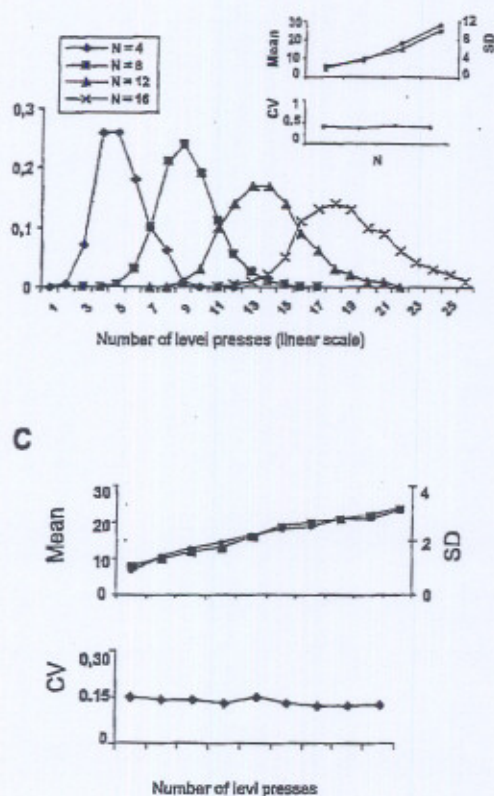


FIGURE 62.1 Evidence for Weber's law in animal and human numerical behavior. (A) The probability of rats breaking off a sequence of lever presses as a function of the number of presses in the sequence and the number required to get the reward. The inset shows the mean number of lever presses (circles) and standard deviation (squares). The coefficient of variation (CV), which is the ratio of the mean to the standard deviation, is constant, indicating Weber's law in estimation. (Redrawn from Mechner, 1958, and modified from Gallistel and Gelman, 2000.) (B) Behavioral performance of two monkeys on a same-different task where they judged whether a test stimulus contained the same or a different number of items as the sample display. Each curve represents the percent-

age of "same" response as a function of test numerosity, for a given sample numerosity. (Modified from Nieder and Miller, 2003.) (C) Behavioral performance of human adults who were asked to produce a given number of key presses. The mean number of presses (circles), standard deviation (squares), and the CV are strikingly similar to the rats' performance shown in A. (Redrawn from Gallistel and Gelman, 2000.) (D) Distribution of human adults' estimates of prices of items, after normalization by the mean price. The distribution is consistently skewed and is better fitted by a log-normal curve than by a normal curve. (From Dehaene and Marques, 2002.)

It has been a matter of debate whether Weber's law is better described by a linear continuum with increasing variability or by a nonlinear, perhaps logarithmic scale with constant variability. Some have argued that the linear model should be preferred, because it allows a simpler calculation of sums and differences (Gallistel and Gelman, 1992). Contrarily, others have proposed a logarithmic coding because this compressive scheme avoids an explosion in the size of the internal representation as the range of represented numerosities increases (Dehaene and Changeux, 1993). In fact, both assumptions accurately predict performance, and for a long time it was thought that the linear hypothesis and the logarithmic hypothesis could not be disentangled. Recently, however, detailed analyses of the exact shape of response distributions in both humans and animals have suggested that the internal scale is not linear but logarithmic. When plotted on a linear scale, performance curves are

asymmetric and are best fitted by a log-normal distribution (see figure 62.1D). However, they become symmetric when plotted on a logarithmic scale, and are then best fitted by a simple Gaussian with fixed variability (Dehaene et al., 2003; Nieder and Miller, 2003). Thus, the behavior of both humans and monkeys can be described in a more compact way by assuming a logarithmic scale than by assuming a linear internal scale for number.

Imaging number sense in humans

Given those behavioral observations, it has been proposed that animals and humans share a common and evolutionarily ancient mechanism for representing numerical quantities, and that this mechanism serves as a foundational core of numerical knowledge, providing humans with a start-up tool that permits the acquisition of numerical symbols (Dehaene,

1997; Butterworth, 1999; but see Simon, 1999, for an opposite view). The analogical representation of number would ground our intuition of what a given numerical size means, and of the proximity relations between numbers. It would be crucial in tasks that place strong emphasis on the quantitative aspects of numbers, such as the estimation of a price (Dehaene et al., 2003; figure 62.1D), the approximation of complex arithmetical problems (Dehaene et al., 1999; Spelke and Tsivkin, 2001), or the rough estimation of the number of elements in a set (Whalen, Gallistel, and Gelman, 1999). In support of this view, recent neuroimaging data show that an area of the brain is systematically activated whenever this putative core system for numerical quantities is called for—the horizontal segment of the intraparietal sulcus (IPS) in the parietal lobes.

The first investigation of the neural correlates of human numerical abilities showed increased metabolism in both parietal and frontal regions during complex calculation, using single-photon emission computed tomography (Roland and Friberg, 1985). This result was in agreement with earlier studies of patients with brain lesions, which had shown a crucial role for the parietal lobes in number processing. Since then, many studies using more refined functional imaging techniques such as PET and fMRI have yielded evidence for the recruitment of parietal regions on different number-related tasks. On the basis of a detailed review of the recent literature, and of a meta-analysis of some of the available activation images, we proposed that

parietal activation in number-related tasks can be segregated into three distinct sites, each associated with a distinct process (Dehaene et al., 2003): the posterior superior parietal lobule, associated with visuospatial processing; the angular gyrus of the left hemisphere, associated with verbal processing of numbers; and the horizontal segment of the IPS, the most plausible candidate for a domain-specific locus where numerical quantity is represented. In this chapter we focus mostly on the last site, the horizontal segment of the IPS, or HIPS (figure 62.2A). Several features of its responsiveness to experimental conditions suggest that this region encodes the analogical representation of numerical magnitude that grounds our intuition of what a given numerical size means, and of the proximity relations between numbers.

First, in calculation, the HIPS is more active when subjects estimate the approximate result of an addition problem than when they compute its exact solution, even when task difficulty is strictly controlled (Dehaene et al., 1999). This fits well with the approximate nature of the representation of numerical quantities. Within exact calculation, this region is also more active for operations that require a genuine manipulation of numerical quantities, such as subtraction, than for those that can be stored in rote verbal memory, such as multiplication (Lee, 2000). Moreover, its activation is modulated by semantic parameters such as the absolute magnitude of the numbers. It is larger and lasts longer during operations with large numbers than during operations with small numbers (Dehaene et al., 1999).

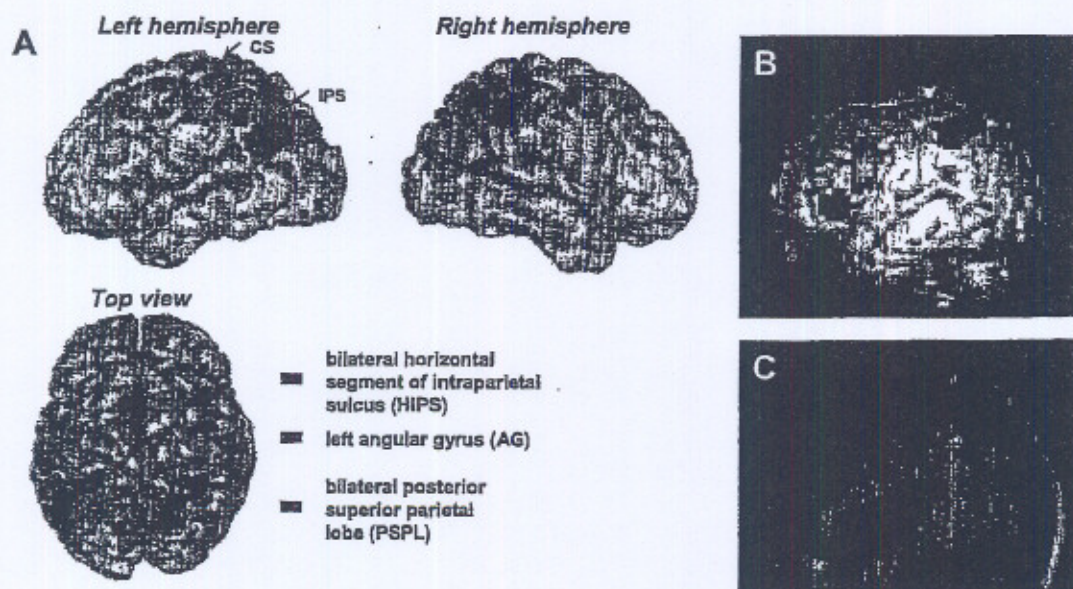


FIGURE 62.2 Brain imaging of number sense. (A) Three-dimensional representation of the three parietal sites of major activation in number processing individuated by a recent meta-analysis of fMRI studies of number processing. Abbreviations: CS, central sulcus; IPS, intraparietal sulcus. (From Dehaene et al., 2003.) (B) Regions whose activation increases with number size

during calculation, including left HIPS, left premotor, and left inferior prefrontal areas. (From Stanescu et al., 2000.) (C) Region of reduced gray matter in a population of subjects with developmental dyscalculia. The location of impairment coincides with the left HIPS. (From Isaacs et al., 2001.)

Second, the HIPS is also active whenever a comparative operation that needs access to a numerical scale is called for. For instance, its activation is higher when subjects compare the magnitudes of two numbers than when subjects simply read them. Furthermore, its activation is modulated by the numerical distance separating the numbers (Pinel et al., 2001). The systematic contribution of this region to number comparison processes has also been replicated using scalp recordings of event-related potentials (Dehaene, 1996). The typical scalp signature of a numerical distance effect, moreover, has been observed in 5-year-old children, with a topography similar to that in adults for numbers presented either as arabic numerals or as sets of dots (Temple and Posner, 1998).

Third, the HIPS shows relatively robust category specificity for numbers when directly contrasted with different categories of objects or concepts. For example, in comparative judgments, it is more active when subjects are comparing numbers than when subjects are processing other categories of objects on non-numerical scales (such as the ferocity of animals, the relative positions of body parts, or the orientation of two visually presented characters; Pesenti et al., 2000; Thioux et al., 2002). Even on tasks that do not directly require a numerical judgment, such as simple detection tasks, the HIPS is the only region that shows higher activation when processing numbers than when processing letters of the alphabet or colors (Eger et al., 2003). Both control continua (letters and colors) were chosen because, like numbers, they show a distance effect (e.g., when detecting the letter *M*, it takes longer for a subject to reject the letter *L* than the letter *C*). Moreover, the alphabet also shares with numbers a strong serial component. However, both letters and colors lack quantitative meaning. Therefore, this experiment suggests that the HIPS activation for numbers relates to the processing of their quantitative meaning.

Fourth, the activation of the HIPS is independent of the particular modality of input used to present numbers. Arabic numerals, spelled-out number words, and even nonsymbolic stimuli like sets of dots or tones can activate this region if subjects attend to the corresponding number. In one study, subjects attended either to the numerosity or to the physical characteristics (color, pitch) of series of auditory and visual events. The right HIPS was active whenever subjects attended to number, regardless of the modality of the stimuli (Piazza, Mechelli, et al., 2003). In another study, activation of the bilateral HIPS was found to correlate directly with the numerical distance between two numbers in a comparison task, and this effect was observed whether the numbers were presented as words or as digits (Pinel et al., 2001). Finally, in a simple detection task, the HIPS was activated for numbers relative to letters and colors, irrespective of the visual or auditory modality of presentation (Eger et al., 2003). These results are consistent with the hypothesis

that the HIPS encodes the abstract quantity meaning of numbers rather than the numerical symbols themselves.

Fifth, quantity processing and HIPS activation were demonstrated even when subjects were not aware of having seen a numerical symbol (Naccache and Dehaene, 2001). In this experiment, subjects were asked to compare target numbers to a fixed reference of 5. Unbeknownst to them, just prior to presentation of the target, another number, the prime, was briefly present in a subliminal manner. fMRI revealed that the left and right intraparietal regions were sensitive to the unconscious repetition of the same number. When the prime and target corresponded to the same quantity (possibly in two different notations, such as ONE and 1), less parietal activation was observed than when the prime and target corresponded to two distinct quantities (e.g., FOUR and 1). This result suggests that this region comprises distinct neural assemblies for different numerical quantities, so that more activation can be observed when two such neural assemblies are activated than when only one is. It also indicates that this region can contribute to number processing in a subliminal fashion.

Finally, convincing evidence for the crucial role of the HIPS in numerical quantity representation comes from neuropsychological studies of impairments in number processing and calculation in adults, as well as in developmental cases. Several single-case studies indicate that numbers doubly dissociate from other categories of concepts at the semantic level. On the one hand, spared calculation and number comprehension abilities have been described in patients with grossly deteriorated semantic processing ("semantic dementia"; Remond-Besuchet et al., 1998; Butterworth, Cappelletti, and Kopelman, 2001). In both cases, the lesions broadly affected the left temporofrontal cortices while sparing the intraparietal regions. On the other hand, several cases demonstrate that the understanding of numbers and their relations can be specifically impaired in the context of otherwise preserved language and semantics (e.g., Delazer and Benke, 1997; Dehaene and Cohen, 1998). The majority of such cases result from lesions in the parietal regions, particularly in the left hemisphere.

Developmental studies confirm that impairments in arithmetic abilities correlate with abnormalities in the functional or anatomical organization of the HIPS. Levy, Reis, and Grafman (1999) reported the case of an adult with lifelong isolated dyscalculia but superior intelligence and reading ability, in whom the standard anatomical MRI appeared normal yet MR spectroscopy revealed a metabolic abnormality in the left inferior parietal area. Similarly, Isaacs and colleagues (2001) used voxel-based morphometry to compare gray matter density in adolescents born at equally severe grades of prematurity, half of whom suffered from dyscalculia. The only brain region that showed reduced gray matter associated with dyscalculia was the left IPS.

More recently, Molko and colleagues studied a population of females affected by Turner's syndrome, a syndrome characterized by a congenital abnormality of the X chromosome and often associated with defective development of number skills in the context of a normal general intelligence (Molko et al., 2003). They used voxel-based morphometry to compare the gray matter density of this dyscalculic Turner population with an age-, education-, and sex-matched group of controls. Results showed a region of reduced gray matter in the depth of the right HIPS. Morphometric analysis restricted to the cortical sulci showed that the length and depth of the right IPS were reduced in the patients with Turner's syndrome. Finally, the fMRI activation of this region differed significantly from activation in the control group for number-related tasks such as simple additions.

OTHER PARIETAL REGIONS INVOLVED IN NUMBER PROCESSING

Taken together, these data suggest that the HIPS is the most crucial cortical region for the correct development of numerical skills. Clearly, it is not the only system involved in number processing. Mental arithmetic relies on a highly composite set of processes, many of which are probably not specific to the number domain. For instance, studies of language interference in normal subjects suggest that language-based processes play an important role in exact but not approximate calculation (Spelke and Tsivkin, 2001). Likewise, concurrent performance of a spatial task interferes with subtraction but not multiplication, while concurrent performance of a language task interferes with multiplication but not subtraction (Lee and Kang, 2002). Such behavioral dissociations suggest that the neural bases of calculation must be heterogeneous.

A recent re-analysis of brain activation studies allowed us to individuate two satellite parietal systems that are often involved in numerical tasks, even if their primary function is not specific to numbers. We isolated a language-related region in the left angular gyrus associated with verbal processing of numbers and a visuospatial region in the posterior superior parietal lobe, presumably associated with spatial and nonspatial attention. On arithmetic tests, the left angular gyrus shows increasingly greater activation as the task puts greater requirement on verbal processing. For example, this region is more active in exact calculation than in approximation (Dehaene et al., 1999). This fits with behavioral data that indicate that exact arithmetic facts are stored in a language-specific format in bilinguals, while approximate knowledge is language independent (Spelke and Tsivkin, 2001). Moreover, within exact calculation, the left angular gyrus shows greater activation during operations that require access to a rote verbal memory of arithmetic facts, such as multiplication, than during operations that are not stored and require some form of quantity manipulation, such as subtraction.

The posterior superior parietal region is also frequently active, usually in synergy with the HIPS, for instance, in number processing during number comparison (Pesenti et al., 2000; Pinel et al., 2001), approximation (Dehaene et al., 1999), some subtraction tasks (Lee, 2000), and counting (Piazza et al., 2002; Piazza, Giacomini, et al., 2003). However, this region is clearly not specific to the number domain, because it plays a central role in attentional selection in space and time (Wojciulik and Kanwisher, 1999). Psychological experiments indicate that numbers have a strong serial and therefore spatial component, to the point that it has been metaphorically proposed that numbers are represented internally on a "number line," a quasi-spatial representation in which numbers are organized by their proximity (Moyer and Landauer, 1967; Dehaene, Bossini, and Giraux, 1993). It is therefore conceivable that the same process of covert attention that operates to select locations in space can also be engaged when attending to specific quantities on the number line.

According to the proposed tripartite organization of parietal activation during arithmetic suggested by our meta-analysis of existing neuroimaging studies, dissociations are expected between the types of arithmetic tasks that patients should or should not be able to perform according to the lesion site. For example, a lesion of the HIPS should affect all tasks requiring genuine manipulation of both symbolic and nonsymbolic numerical quantities, including approximation, subtraction, comparison, or estimation of numerosity. Lesions of the angular gyrus or other language-related regions of the left hemisphere should result in an impairment in retrieving arithmetic facts that are stored in verbal format, such as multiplication facts. Finally, lesions extending to the most posterior portion of the IPS or the superior parietal lobe should impair tasks that put strong emphasis on the visuospatial layout of number, such as bisection tasks (e.g., what number lies in the middle of 11 and 19?). Indeed, such dissociations have been reported in the literature. For example, some patients are much more impaired on subtraction than on multiplication (Dehaene and Cohen, 1997; Delazer and Benke, 1997; van Harskamp and Cipolletti, 2001). Such patients typically do not show language impairments but, in the rare case in which this has been investigated, may show difficulties in estimating the numerosity of arrays (Lemer et al., in press). Lesions are often reported around the left IPS. Other patients show the reverse dissociation, being more severely impaired on multiplication than on subtraction. They almost always have associated aphasia (Dehaene and Cohen, 1997; Cohen and Dehaene, 2000; Sandrini et al., 2003). Furthermore, the lesions in such patients often spare the intraparietal cortex and can affect multiple regions known to be engaged in language processing, such as the left perisylvian cortices, including the inferior angular gyrus,

the left parietotemporal carrefour, or the left basal ganglia.

A recent study directly compared two acalculic patients, one with a focal lesion of the left parietal lobe and Gerstmann's syndrome and the other with semantic dementia with predominantly left temporal hypometabolism. As predicted by a numerical quantity deficit, the first patient was more impaired on subtraction than on multiplication, showed a severe slowness in approximation of calculation, and exhibited associated impairments in estimation and numerical comparison tasks, both with arabic numerals and with sets of dots. As predicted by a verbal deficit, the second patient was more impaired on multiplication than on subtraction, had intact approximation abilities, and showed preserved processing of nonsymbolic numerosities (Lerner et al., in press).

Support for the dissociation between quantity representation and the spatial scanning of the mental number line is provided by a study with unilateral neglect patients (Zorzi, Priftis, and Umiltà, 2002). It is a well-known, indeed, almost a defining feature of those patients that they perform poorly on spatial bisection tests. When asked to locate the middle of a line segment, neglect patients with right parietal lesions tend to indicate a location further to the right, consistent with their failure to attend to the left side of space. Zorzi and colleagues tested their performance on a numerical bisection task, where they were asked to find the middle of two numbers presented orally. Strikingly, the patients erred systematically, often selecting a number far larger than the correct answer (e.g., what number falls in the middle of 11 and 19? Patient's answer: 17). This suggests that spatial attention can be oriented on the left-to-right oriented number line, and that this attention-orienting process contributes to the resolution of simple arithmetic problems such as the bisection test. Interestingly, these patients were not acalculic and did not show deficits on other numerical tasks, such as simple arithmetic fact retrieval.

In summary, a review of neuropsychological dissociations between numerical operations indicates that most if not all cases so far described can be accommodated by the postulated dissociation between a quantity circuit (supporting subtraction and other quantity-manipulation operations), a verbal circuit (supporting multiplication and other rote memory-based operations), and a visuospatial circuit (supporting number bisection and other tasks on which the spatial sense of numbers is particularly relevant).

One intriguing discrepancy between the lesion and imaging studies relates to the lateralization of the core quantity circuit. In quantity-related dyscalculia, lesions are often restricted to the left hemisphere. However, imaging studies show bilateral parietal activation in quantity tasks. The exact role of the right hemisphere in number processing is therefore still unclear. Some neuropsychological studies have

suggested a superiority of the right hemisphere, and in particular of the parietal region, in numerosity estimation tasks, such as estimating the number of dots in briefly presented arrays of elements (Warrington and James, 1967). Such a right hemisphere superiority in nonsymbolic numerical tasks was replicated in an imaging study of numerosity estimation, where parietal activation was indeed restricted to the right hemisphere (Piazza, Mechelli, et al., 2003). One possibility is that our core numerical system is initially bilateral and progressively becomes biased for symbolic manipulations of numbers in the left hemisphere and for nonsymbolic tasks in the right hemisphere. Such speculation, however, awaits confirmation.

The neural coding of numerosity

Recent electrophysiological studies have considerably improved our understanding of the neural bases of number sense. In 1993, Dehaene and Changeux presented a theoretical model of how numerical quantity could be represented at the single-neuron level. They proposed the existence of "numerosity detectors," neurons coarsely tuned to an approximate quantity. In 2002, two electrophysiological studies reported the first clear evidence of the existence of such neurons. The fine-grained analysis of those neurons' responses has proved extremely valuable for understanding the nature of the numerical representation underlying animal behavior.

The first pioneering study that investigated elementary numerosity discrimination abilities in animals at the neuronal level dates back to the work of Thompson and colleagues (1970). They recorded from cells in the posterior association cortex of the anesthetized cat (in an area that might be homologous to posterior parietal cortex in monkeys and humans) and found a handful of neurons that preferentially responded to a given numerosity, for instance, a sequence of three sounds or three light flashes. For many years, this finding stood alone. Very recently, however, two independent groups confirmed the existence of such "numerosity detectors" (Nieder, Freedman, and Miller, 2002; Sawamura et al., 2002). Sawamura and colleagues trained monkeys to push a lever five times in a row, then turn it five times, and so on. To prevent the monkeys from using time instead of number in deciding when to switch their actions, the time spent in a block of consecutive trials was varied between 20 and 46 s and decorrelated from the number of movements performed. Neurons located in the superior parietal lobule, relatively superficially on the anterior bank of the IPS, responded selectively to numerical information. Although some of these cells responded specifically to a single number (which varied from one to five), for most cells the activity dropped off progressively with the numerical distance. Hence, a neuron coding preferentially

for number three fired a little less for two and four, and even lesser for one or five.

This study represented an elegant effort to “read” the neural code supporting the representation of number in the monkey brain. However, some aspects of the task used made the interpretations of the results slightly problematic. First, the numerical information relevant to performing the task was related to the numerical position in a sequence (ordinal number) and not to the numerical quantity itself (cardinal number). Second, many of the neurons fired only for one of the two actions, thus showing both action and number tuning. It is not known whether these neurons would generalize to other numerical tasks.

A more recent study, however, reported neurons tuned to cardinal number, and performed fine-grained analysis of the neurons’ tuning curves in parallel with a thorough analysis of the monkeys’ behavior (Nieder et al., 2002; Nieder and Miller, 2003). Macaque monkeys were trained to perform a match-to-sample task on successively presented visual displays containing between one and five randomly arranged

items. During training, certain visual features inevitably covaried with numerosity. However, after training, the monkeys spontaneously generalized to novel displays in which all of the relevant non-numerical variables were controlled, suggesting that they were attending to number (figure 62.3).

Neurons were then recorded, initially only in the dorso-lateral prefrontal cortex (Nieder, Freedman, and Miller, 2002). About one-third of the neurons there were tuned to a specific numerosity between one and five (the maximal numerosity that was tested). This finding was very similar to the findings of Sawamura, Shima, and Tanji (2002), but because the stimulation was visual it was possible to vary the stimulus extensively and verify to what extent neuronal response could be explained by other non-numerical parameters. The results indicated a remarkable degree of invariance to non-numerical parameters: a given neuron remained tuned to the same number across a broad variation of stimuli that controlled for object size, density, spacing, and spatial layout. Nevertheless, further tests will be necessary to assess

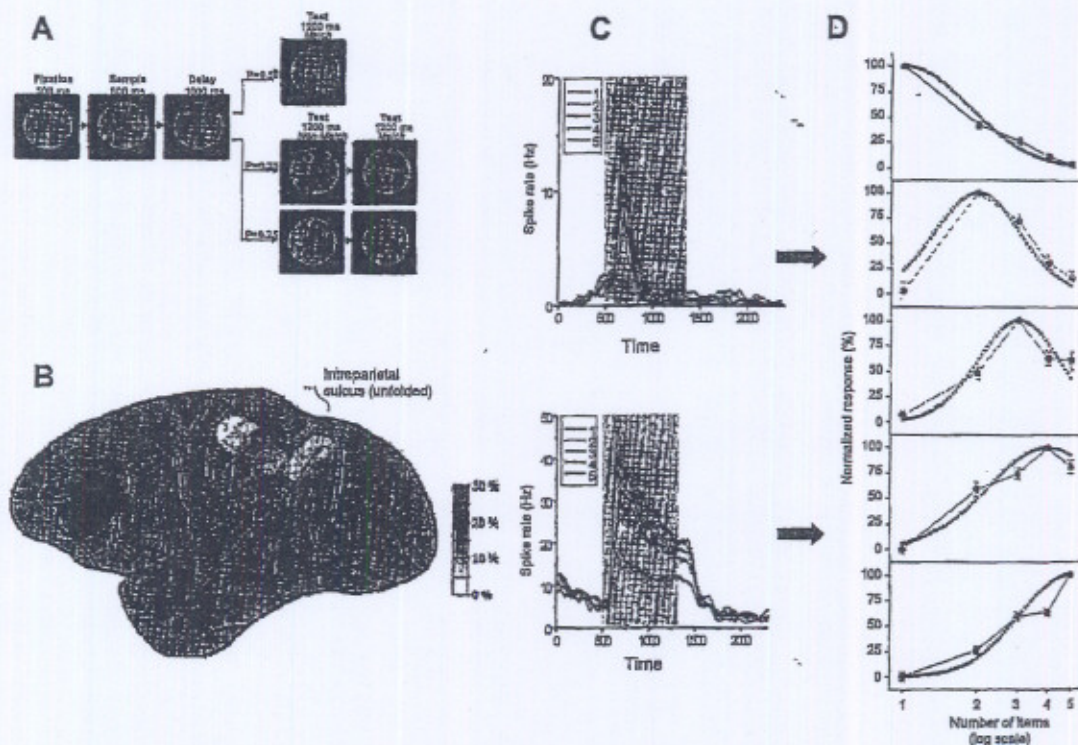


FIGURE 62.3 Evidence for Weber's law in neural coding. (Courtesy of Andreas Nieder and Earl Miller.) (A) Example of stimuli presented to monkeys instructed to perform a delayed match-to-sample number task on visual displays containing one to five items. (B) Recording sites in parietal and prefrontal cortex, with the percentage of numerosity-sensitive neurons observed in each subregion. (C) Responses (spike density functions) of two sample neurons, one preferentially responding to three and the other to four items. Each colored line shows the time course of activity for the five

tested numbers. Gray shading represents the sample period (800 ms). (D) Neural representation of number by a bank of visual numerosity detectors in the monkey prefrontal cortex. The different graphs represent the average activity of neurons tuned to different specific number (one to five from top to bottom). This population code for number coincides with the theoretical code proposed in Dehaene and Changeux's (1993) neuronal network model. (Modified from Nieder et al., 2002; Nieder and Miller, 2003; and Nieder and Miller, 2004.)

generalization to ordinal numerosity as well as to other modalities of auditory or motor stimulation.

One intriguing feature was the localization of such number-sensitive neurons in the prefrontal cortex. Intensive training may explain why many prefrontal neurons became sensitive to number in Nieder and Miller's (2003) study. However, human data suggested the intraparietal cortex, not the prefrontal cortex, as a crucial site for number processing. Although Sawamura and colleagues (2002) reported many number-tuned neurons in the superior parietal lobule, Nieder and colleagues (2002) reported finding only a small proportion of number neurons in area 7a of the inferior parietal lobule (about 7%). More recently, however, by recording in the depth of the IPS at a location that might correspond to area VIP, Nieder and Miller observed a much higher proportion of neurons tuned to numerosity (Nieder and Miller, 2004). Crucially, those neurons showed differential firing as a function of numerosity at a latency of about 80ms, which is shorter than the value of 120ms observed for prefrontal neurons. This is compatible with the hypothesis that numerosity is first extracted and represented in the IPS, and later transmitted to prefrontal circuits as needed for the requested task (Dehaene and Changeux, 1993). Furthermore, their localization in the depth of the IPS is a plausible monkey homologue to the site of activation observed in humans. Indeed, this localization was predicted by a human brain imaging study in which the activation during subtraction was found to be inserted within a network of visuomotor areas plausibly corresponding to areas AIP, MIP, V6A, and LIP in monkeys (Simon et al., 2002).

Several features of the response of those visual numerosity neurons illuminate the mechanisms of extraction and representation of number. First, their firing latency is independent of the number being represented. This result is not compatible with models that postulate a serial accumulator mechanism, which would therefore predict a linear increase in firing latency with numerosity (Gallistel and Gelman, 1992). It fits, however, with a parallel mechanism of numerosity abstraction as predicted by the Dehaene and Changeux (1993) model. A second important feature of number-coding neurons is that their tuning curves are broad, again suggesting approximate coding. Furthermore, this breadth is proportional to the neuron's preferred number. Thus, evidence for Weber's law can be observed at the single-neuron level, mirroring behavior. Finally, the neural tuning curves are asymmetrical on a linear scale but assume a Gaussian shape when plotted on a logarithmic scale (Nieder and Miller, 2003). Exactly like behavioral data, this suggests a compressive logarithmic neural encoding of numerical quantity.

Conclusion

The neurophysiological results reviewed in this chapter indicate that, down to a rather minute level of detail, the visual numerosity neurons observed by Nieder and Miller (2003) provide a plausible neuronal basis for the sense of number that is known to be present in animals and humans. Nevertheless, several experimental steps will be needed to confirm this hypothesis. More extensive studies in animals are needed to evaluate the abstractness and invariance of the neurons to multimodal stimuli. Investigating a greater range of numerosities, and examining the presence of those neurons in naive untrained animals, is crucial. Finally, reversible lesion or microstimulation studies are necessary to demonstrate that those neuronal representations play a causal role in the monkeys' numerical abilities. In parallel, experiments in humans with both nonsymbolic and symbolic numerical stimuli should attempt to demonstrate that a similar code for number is present in the human brain. This could be done with intracranial recordings, but it could also noninvasively using the "priming method" in fMRI (Naccache and Dehaene, 2001).

The number domain is one of the very few domains of cognitive neuroscience in which experimental studies can range from recordings of single neurons in the monkey to response-time studies of verbal symbols in humans. Such parallel studies in various species, performed using a range of experimental methods, are helping making sense of the human ability for mathematics through an integrated and progressively more coherent picture of the working brain.

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