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# FROM NUMBER NEURONS TO MENTAL ARITHMETIC: THE COGNITIVE NEUROSCIENCE OF NUMBER SENSE

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#### **1. INTRODUCTION**

Consider a lioness in her pride in the Serengeti National park, Tanzania. One night she is all alone and hears a roar from an intruder 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 she is with four sisters, when they hear the roars of three intruder lionesses. This time it is three versus five. The lionesses peer into each others eyes and then launch the attack. But by the time they reach the expected location, they find no intruder, and that is because the sounds were actually coming 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, & Pusey, 1994). The process of "decision making" of these animals seems to be based on a multimodal comparison between the number of the number of defenders, which is perceived visually, and the number of defenders, which is perceived auditorily. This suggests hat the internal representation of number in animals can be quite abstract.

Numbers might be thought to be a very recent cultural invention in the evolution of the human species. Indeed, number words and digits arise from the specifically human and evolutionary 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 non-human species as well as in babies, and its strong adaptive value is easily seen. Such a sensitivity to numbers also seems to be 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 (Dehaene, 1998).

In this chapter we present an overview of the most relevant findings on the cognitive neuroscience of number sense, showing how data from different domains, from cognitive psychology to electrophysiology, are providing us with complementary information on how our brain represents and manipulates numbers. We first consider how behavioural data have shed light on such number sense in non-verbal 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.

# 2. BEHAVIOURAL EVIDENCE FOR ANALOGICAL REPRESENTATION OF NUMBER

The ability to make numerical judgments has been tested in many different species of animals (from pigeons to rats, racoons, dolphins and monkeys) both in the wild and in more controlled experimental settings in laboratory, with very different types of paradigms. Typically, animals are trained to respond differentially to a variety of numerically defined stimuli: the number of visual stimuli, of tones, of motor responses or of reinforcements. However, as number normally co-varies with some of the physical attributes of the stimuli (such as brightness, density, time, hedonic value) reports of numerical abilities in animals are often met with scepticism: 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 generalise to novel sequences in which auditory and visual sequences were mixed (Church & Meck, 1984). This suggests that animals possess an abstract, amodal representation of number. Second, animals are able to generalise numerically relevant behaviour to novel, non-differentially rewarded stimuli (Brannon & Terrace, 2000; Church & Meck, 1983; Sawamura, Shima, & Tanji, 2002; Nieder, Freedman, & Miller, 2002). This indicates that they are able to bring to the task more knowledge of numerical invariance than the 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 generalised their behaviour to novel, non-differentially rewarded sequences in which duration was fixed and only number varied. This suggests that the animals were representing number during the initial training phase (Church & Meck, 1983).

An ability to discriminate sets on the basis of their number is also present in pre-verbal human infants. With the classic method of habituation-recovery of looking time, both new-borns and pre-verbal infants have been shown to discriminate sets of visual objects, as well as tones or words that differed in the number of syllables, on the unique basis of their numerosity (e.g. Xu & Spelke, 2000). Again, there is suggestive evidence of cross-modal numerosity matching (Starkey, Spelke, & 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, & Chiang, 2002). Such animal and infant data, taken together, suggest that the sensitivity to the numerical aspect of the word does not depend on an acquired ability to manipulate symbols, but is based on a non-verbal amodal representation of numerosity.

This representation can also be evidenced in human adults. When prevented from using language and our counting procedures, adults can make approximate numerosity judgements 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 this without cost relative to a unimodal stimulus presentation (Barth, Kanwisher, & Spelke, 2003).

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The parallels between human and animal behavior in 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 & Gelman, 2000)(see figure 1). Number estimation performance in both humans and non-human 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 time, 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 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 & Miller, 2003)(figure 1B).

In humans, studies directly inspired by animal experiments, show exactly the same type of metric. For example, Whalen et al. (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 (Whalen, Gallistel, & Gelman, 1999; verbal counting was prevented by asking subjects to recite words while performing the task). 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 and the mean) was constant across target size (figure 1C). Very similar results are found when humans are asked to estimate prices for different items: again, the standard deviation of price estimates is directly proportional to the mean price (Dehaene & Marques, 2002)(figure 1D).

Moreover, Weber's law holds even when numerical judgements are not estimates, but exact computations made over abstract numerical symbols like digits and number words. Such symbolic numerical judgments (like, for example, choosing the larger number between 49 and 72) show magnitude effects exactly like non symbolic numerosity judgments: 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 & Landauer, 1967; Dehaene, 1992).

It has been a matter of debate whether Weber's law is better described by a linear continuum with increasing variability, or by a non linear, maybe 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 & Gelman, 1992). Contrariwise, 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 & Changeux, 1993). In fact, both assumptions accurately predict performance, and for long it has been thought that the linear and the logarithmic

hypotheses could not be disentangled. However, recently, 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 asymmetrical and are best fitted by a log-normal distribution (figure 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., 2002; Nieder & Miller, 2003). Thus, the behaviour of both humans and monkeys can be described in a more compact way by assuming a logarithmic than a linear internal scale for number.

#### 3. IMAGING NUMBER SENSE IN HUMANS

Given those behavioral observations, it has been proposed that animals and humans share a common and evolutionary 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 (Butterworth, 1999; Dehaene, 1997; however, 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 put strong emphasis on the quantitative aspects of numbers, like for example the estimation of a price (Dehaene et al., 2002) (figure 1D), the approximation of complex arithmetical problems (Dehaene, Spelke, Pinel, Stanescu, & Tsivkin, 1999, Spelke & Tsivkin, 2001), or the rough estimation of the number of elements in a set (Whalen et al., 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 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 a single-photon emission (Roland & Friberg, 1985). This result was in agreement with earlier studies of brain-lesioned patients that had shown a crucial role of parietal lobes in number processing. Since then, many studies using more refined functional imaging techniques like PET or fMRI have brought converging evidence for the recruitment of parietal regions in different number-related tasks. On the basis of a

detailed review of the recent literature, and of a meta-analaysis 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, Piazza, Pinel, & Cohen, 2002): the posterior superior parietal lobule associated with visuo-spatial processing, the angular gyrus of the left hemisphere, associated with verbal processing of numbers, and the horizontal segment of the intraparietal sulcus, the most plausible candidate for a domain-specific locus where numerical quantity is represented.

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In the present review we focus mostly on the latter site, the intraparietal sulcus (hereafter HIPS) (see figure 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 subject estimate the approximate result of an addition problem than when they compute its exact solution, even when the 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 with small numbers (Dehaene et al., 1999; Stanescu-Cosson et al., 2000).

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 comparing the magnitudes of two numbers than when simply reading them. Furthermore its activation is modulated by the numerical distance separating the numbers (Pinel, Dehaene, Riviere, & LeBihan, 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 adults for numbers presented either as Arabic numerals or as sets of dots (Temple & 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 judgements, it is more active when comparing numbers than when processing other categories of objects on nonnumerical scales (such as comparing the ferocity of animals, the relative positions of body parts, or the orientation of two visually presented characters) (Pesenti, Thioux, Seron, & DeVolder, 2000; Thioux, Pesenti, Costes, De Volder, & Seron, 2002). Even in tasks that do not directly require a numerical judgement, 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, Sterzer, Russ, Giraud, & Kleinschmidt, 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 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 non-symbolic 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 the subjects attended to number, regardless of the modality of the stimuli (Piazza, Mechelli, Price, & Butterworth, 2003). In another study, the 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 colours, 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 the numerical symbols themselves.

Fifth, quantity processing and HIPS activation was demonstrated even when the subjects were not aware of having seen a numerical symbol (Naccache & Dehaene, 2001). In this experiment, subjects were asked to compare target numbers to a fixed reference of 5. Unbeknownst to them, just prior to 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 of 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": Butterworth, Cappelletti, & Kopelman, 2001; Remond-Besuchet et al., 1998). In both cases, the lesions broadly affected the left temporo-frontal 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. Dehaene & Cohen, 1998; Delazer & Benke, 1997). The majority of such cases result from parietal regions, particularly in the left hemisphere.

Developmental studies confirm that impairments of arithmetical abilities correlate with abnormalities in the functional or anatomical organization of the HIPS. Levy et al. (1999) report the case of an adult with lifelong isolated dyscalculia together with superior intelligence and reading ability, in whom the standard anatomical MRI appeared normal, yet MR spectroscopy techniques

revealed a metabolic abnormality in the left inferior parietal area. Similarly, Isaacs et al. (2001) used voxel-based morphometry to compare grey matter density in adolescents born at equally severe grades of prematurity, half of whom suffered from dyscalculia. The only brain region that showed reduced grey matter associated with dyscalculia was the left intraparietal sulcus (see figure 2C).

More recently, Molko and colleagues studied a population of females affected by Turner syndrome, a syndrome characterised 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., submitted). They used voxel-based morphometry to compare the grey matter density of such dyscalculic Turner population with an age, education, and sex matched group of controls. Results showed a region of reduced grey matter in the depth of the right HIPS. Morphometric analysis restricted to the cortical sulci showed that the length and depth of the right intraparietal sulcus was reduced in Turner patients. Finally, the fMRI activation of this region differed significantly with respect to the control group in number-related tasks such as simple additions.

#### Other parietal regions involved in number processing

These data, taken together suggest that the HIPS is the most crucial cortical region for the correct development of numerical skills. Clearly, however, 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 et al., 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 & 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 which are often involved in numerical tasks, even if their primary functions is not specific to numbers. We isolated a language-related region in the left angular gyrus, associated with verbal processing of numbers, and a visuo-spatial region in the posterior superior parietal lobe, presumably associated with spatial and non-spatial attention. In 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 behavioural data which indicate that exact arithmetic facts are stored in a language-specific format in bilinguals, while approximate knowledge is language-independent (Spelke et al., 2001). Moreover, within exact calculation, the left angular gyrus shows greater activation for operations that require access to a rote verbal memory of arithmetic facts, such as multiplication, than for operations that are not stored and require some form of quantity manipulation like subtraction.

The posterior superior parietal regions is also frequently active, usually in synergy with the HIPS, for instance in number processing during number comparison (Pinel et al., 2001; Pesenti et al., 2000), approximation (Dehaene et al., 1999), some subtraction tasks (Lee, 2000), and counting (Piazza, Mechelli, Butterworth, & Price, 2002; Piazza, Giacomini, Le Bihan, & Dehaene, 2003). However, this region is clearly not specific to the number domain as it plays a central role in attentional selection in space and time (Wojciulik & 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 on which numbers are organized by their proximity (Moyer et al., 1967; Dehaene, Bossini, & 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 to the HIPS should affect all tasks requiring a genuine manipulation of both symbolic and non-symbolic 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 arithmetical facts which are stored in verbal format, such as multiplication facts. Finally, lesions extending to the most posterior portion of the intraparietal sulcus and/or the superior parietal lobe should impair tasks that put strong

emphasis on the visuo-spatial layout of number, like, for example, bisection tasks (e.g. what number lies between 11 and 19?). Indeed such dissociations have been reported in the literature. For example, some patients are much more impaired in subtraction than in multiplication (Dehaene & Cohen, 1997; Delazer et al., 1997; van Harskamp & Cipolotti, 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, Dehaene, Spelke, & Cohen, 2003). Lesions are often reported around the left intraparietal sulcus. Other patients show the reverse dissociation, being more severely impaired in multiplication than in subtraction. They almost always have associated aphasia (Cohen & Dehaene, 2000; Dehaene & Cohen, 1997; Sandrini, Miozzo, Cotelli, & Cappa, 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 parieto-temporal 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 another with semantic dementia with predominantly left temporal hypometabolism. As predicted by a numerical quantity deficit, the first patient was more impaired in subtraction than in multiplication, showed a severe slowness in approximation of calculation, and exhibited associated impairments in estimation and numerical comparison tasks, both with Arabic digits and with sets of dots. As predicted by a verbal deficit, the second patient was more impaired in multiplication than in subtraction, had intact approximation abilities, and showed preserved processing of non-symbolic numerosities (Lemer et al., 2003).

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, & Umilta, 2002). It is a well-known, indeed almost a defining feature of those patients that they perform poorly in 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 et al. tested their performance in a *numerical* bisection task, where they were asked to find the middle of two orally presented numbers. Strikingly, the patients erred systematically, often selecting a number far larger than the correct answer (e.g. what number falls in

between 11 and 19? 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 in 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 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 visuo-spatial circuit (supporting number bisection and other tasks where 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, like estimating the number of dots in briefly presented arrays of elements (Warrington & James, 1967). Such a right-hemisphere superiority in non-symbolic numerical tasks was replicated in an imaging study of numerosity estimation, where parietal activation was indeed restricted to the right hemisphere (Piazza 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 non-symbolic tasks in the right hemisphere. Such speculation, however, awaits confirmation.

#### 4. 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 for the existence of such neurons. As we shall see below, the fine-grained analysis of those neurons' responses has proven extremely valuable for understanding the nature of the numerical representation underlying animal behaviour.

The first, pioneer study that investigated elementary numerosity discrimination abilities in animals at the neuronal level dates back to the work of Thompson and colleagues (Thompson, Mayers, Robertson, & Patterson, 1970). They recorded from cells in the posterior association cortex of the anaesthetised 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" (Sawamura et al., 2002; Nieder 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 intraparietal sulcus, responded selectively to numerical information. While some of these cells responded specifically to a single number (which varied from 1 to 5), for most cells the activity dropped off progressively with the numerical distance. Hence, a neuron coding preferentially for number 3 fired a little less for 2 and 4, and even lesser for 1 or 5.

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 perform 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.

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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 & Miller, 2003). Macaque monkeys were trained to perform a match-to-sample task on successively presented visual displays containing between 1 and 5 randomly arranged items (see figure 3A). During training, certain visual features inevitably co-varied with numerosity. However, after training, the monkeys spontaneously generalised to novel displays in which all of the relevant non-numerical variables were controlled, suggesting that they were attending to number.

Neurons were then recorded, initially mainly in the dorsolateral prefrontal cortex (Nieder et al., 2002). About one-third of the neurons there were tuned to a specific numerosity between 1 and 5 (the maximal numerosity that was tested). This finding was very similar to the Sawamura et al. study, but because the stimulation was visual it was possible to extensively vary the stimulus and verify to what extent it 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 required to assess 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 study. However, human data suggested the intraparietal cortex, not the prefrontal cortex, as a crucial site for number processing (see session 2 and 4). While Sawamura et al. (2002) reported many number-tuned neurons in the superior parietal lobule, Nieder et al.(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 intraparietal sulcus, at a location that might correspond to area VIP, Nieder and Miller observed a much higher proportion of neurons tuned to numerosity (Andreas Nieder and Earl Miller, personal communication)(see figure 3B). Crucially, those neurons showed differential firing as a function of numerosity at a latency of about 80 ms, which is shorter than the value of 120 ms 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 & Changeux, 1993). Furthermore, their localization in the depth of the IPS is a plausible monkey homolog 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 visuo-motor 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 (see figure 3C). This result is not compatible with models that postulate a serial accumulator mechanism, and which would therefore an linear increase in firing latency with numerosity (Gallistel & 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 & Miller 2003)(see figure 3D). Exactly like behavioural data, this suggests a compressive logarithmic neural encoding of numerical quantity.

#### 5. CONCLUSION

Altogether, these neurophysiological results 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 naïve 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 non-symbolic 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 also non-invasively using the "priming method" in fMRI (Naccache et al., 2001).

The number domain represents one of the very few domains of cognitive neuroscience where 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 and 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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## FIGURE LEGENDS

#### FIGURE 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), standard deviation (squares). The coefficient of variation (CV), which is the ratio between the mean and the standard deviation, is constant, indicating Weber's law (redrawn from Mechner, 1958 and from Gallistel & Gelman, 2000). (B) Behavioral performance of two monkeys in 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 percentage of "same" response as a function of test numerosity, for a given sample numerosity (modified from Nieder, 2003). (C) Behavioral performance of human adults that were asked to produce a given number of key presses. The mean number of presses (circles), standard deviation (squares), and the coefficient of variation are striking similar to the rats' performance drawn above (redrawn from Gallistel & 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 than by a normal curve (from Dehaene & Marques, 2002).

#### FIGURE 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. CS, central sulcus; IPS, intraparietal sulcus. (from Dehaene et al., 2003). (B) Regions whose activation increases with number size during calculation (from Stanescu et al., 2001), including left HIPS, left premotor, and left inferior prefrontal areas. (C) Region of reduced grey matter in a population of subjects with developmental dyscalculia (from Isaacs et al., 2000). The location of impairment coincides with the left HIPS.

**FIGURE 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 from 1 to 5 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 3 and the other to 4 items. Each colored line shows the time course of activity for the five tested numbers. Grey 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 (1 to 5 from top to bottom)(Modified from Nieder et al., 2002 and Nieder & Miller, 2003). This population code for number coincides with the theoretical code proposed in Dehaene and Changeux's (1993) neuronal network model.



### FIGURE 1. Evidence for Weber's law in animal and human numerical behavior

# FIGURE 2. Brain imaging of number sense



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