

Tuning Curves for Approximate Numerosity in the Human Intraparietal Sulcus

Manuela Piazza,¹ Véronique Izard,¹
Philippe Pinel,¹ Denis Le Bihan,²
and Stanislas Dehaene^{1,*}

¹Unité INSERM 562 “Cognitive Neuroimaging”

²Unité de Neuroimagerie Anatomique-Fonctionnelle
Service Hospitalier Frédéric Joliot
CEA/DSV
91401 Orsay Cedex
France

Summary

Number, like color or movement, is a basic property of the environment. Recently, single neurons tuned to number have been observed in animals. We used both psychophysics and neuroimaging to examine whether a similar neural coding scheme is present in humans. When participants viewed sets of items with a variable number, the bilateral intraparietal sulci responded selectively to number change. Functionally, the shape of this response indicates that humans, like other animal species, encode approximate number on a compressed internal scale. Anatomically, the intraparietal site coding for number in humans is compatible with that observed in macaque monkeys. Our results therefore suggest an evolutionary basis for human elementary arithmetic.

Introduction

Whenever we engage in calculation, the left and right intraparietal regions of the brain are systematically activated (Dehaene et al., 2003, 1999; Eger et al., 2003; Lee, 2000; Naccache and Dehaene, 2001; Pesenti et al., 2000; Pinel et al., 2001, 2004; Simon et al., 2002). For instance, when we select which of two Arabic digits is larger, the intraparietal sulcus activates in direct proportion to the difficulty of the comparison, which varies with the distance between the numbers (Pinel et al., 2001, 2004). Because Arabic, spelled-out, and spoken numerals all activate this area (Eger et al., 2003; Naccache and Dehaene, 2001; Pinel et al., 2001), it is thought to be involved in cross-modal, abstract representation and manipulation of the quantity meaning of numbers, rather than any specific number notation.

How is an abstract semantic dimension such as numerical quantity encoded at the neural level? A neural network model (Dehaene and Changeux, 1993) proposes that number can be represented cortically by a population of neurons, each coarsely tuned to a preferred quantity. The coarse tuning implies that the closer two numbers are, the more similar are the coding schemes of their neuronal populations. It thus explains why numerical distance is a major determiner of number comparison performance. Furthermore, the model assumes that the preferred numbers for different neurons

are distributed on a logarithmic scale, thus permitting a wide range of quantities to be encoded with a small population of cells. This compressive property implies an increasingly coarser encoding of larger numbers. Thus, it can explain the behavioral observation that, as the numbers increase, it takes a proportionally larger difference between them for discrimination performance to remain at a constant level (Weber's law).

Recently, this model received support when neurons tuned to numerical quantity were identified in the macaque prefrontal and parietal cortex (Nieder and Miller, 2003, 2004; Sawamura et al., 2002). In macaques trained in a numerical match-to-sample task with sets of one to five visual objects, each of these quantities activated a preferred population of cells, with tuning curves that exhibited a Gaussian shape with a fixed width when plotted on a logarithmic scale. It is tempting to speculate that similar cells implement the human neural code for number. Indeed, the number sense hypothesis (Dehaene, 1997) proposes that we share with many animal species a representation of approximate number, which initially reacts only to nonsymbolic displays such as sets of objects and later becomes linked to symbols such as Arabic digits and number words. We therefore attempted to demonstrate a functional and anatomical parallel between the human and monkey codes for number, through a combination of behavioral and functional magnetic resonance imaging (fMRI) methods.

Our stimuli were sets of visual shapes varying in number, similar to those used in the monkey, but which have not yet been used in human neuroimaging. Behaviorally, we tested whether the human ability to discriminate two such sets based on their number followed Weber's law. In fMRI, we tested the hypothesis that the left and right intraparietal sulci encode the numerical quantity of sets of objects, at the same anatomical location that is known to respond during manipulation of Arabic digits. To probe the format of the human neuronal representation of numerical quantity, we used fMRI adaptation (Grill-Spector and Malach, 2001; Naccache and Dehaene, 2001), a method inspired by single-neuron electrophysiological studies in primates (Desimone, 1996; Miller et al., 1993). During an fMRI block, we repeatedly presented a specific number, n_1 , in order to habituate putative neurons tuned to this value. We reasoned that presenting an occasional deviant number, n_2 , should then lead to a recovery of fMRI responses, with an amount of activation inversely related to the n_1 – n_2 distance (see Figure 1 for examples of stimuli used). A mathematical model of this idea (presented as Supplemental Data at <http://www.neuron.org/cgi/content/full/44/3/547/DC1/>) predicted that both behavioral performance and brain activation should follow Weber's law: the detection of number change should scale with the habituation number, such that doubling its value (from 16 to 32) should result in a doubling of the change detection threshold. Equivalently, the results should depend solely on the ratio of the two numbers.

*Correspondence: dehaene@shfj.cea.fr

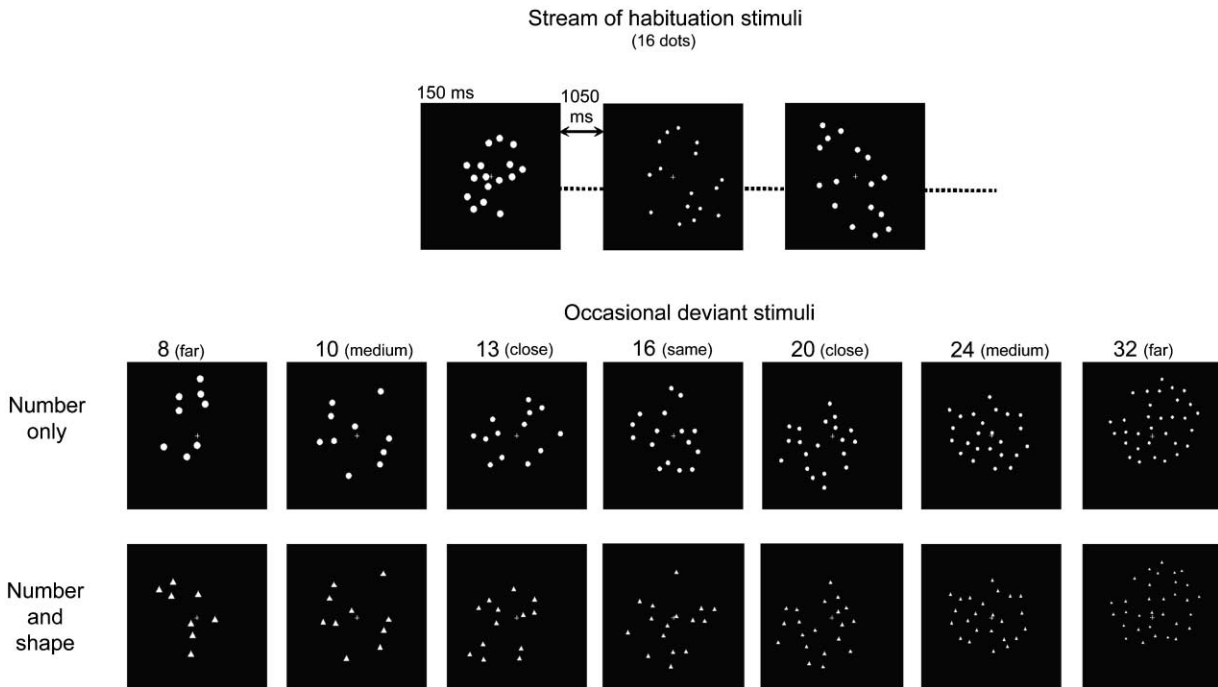


Figure 1. Experimental Design for Adaptation to Approximate Number

Twelve human participants were scanned while they were passively presented with a rapid stream of sets of dots. Unbeknownst to the participants, item shape and number occasionally changed, while all other nonnumerical visuospatial variables, such as dot density or location, were carefully controlled, so that response to number change could not be attributed to any nonnumerical visuospatial parameter. The item shape change control enabled us to rule out the possibility of a generic attentional reaction to any type of change. We predicted that number-related areas would show only a main effect of number change and that a distinct set of regions would react to item shape change.

Results and Discussion

We first examined behavior in an explicit number change detection task, where participants were asked to detect whether the last set in a series of four had a deviant number (Figures 2A–2C). Performance varied significantly with distance between the habituation and the deviant number [$F(6, 42) = 106.3$; $p < 0.0001$]. The proportion of “different” responses followed a classical U-shaped function that characterizes approximate perceptual judgments. The shape of this curve conformed precisely to the behavioral predictions of our compressed number line model. When plotted on a linear scale for number, the performance curves were asymmetrical and twice as broad for habituation number 32 than for habituation number 16 (Figure 2A). However, the curves became symmetrical and Gaussian with a fixed width when plotted on a log scale (Figure 2B). Indeed, the curves for 16 and 32 became superimposable once expressed as a function of the log ratio of the target and habituation numerosities, in agreement with Weber’s law (Figure 2C). Nonlinear fitting with either a Gaussian or a log-Gaussian function was used to compare the linear and logarithmic models quantitatively. In all participants, a better goodness of fit was obtained with the log model ($r^2 \pm 1$ SD across participants = $70.5\% \pm 11.3\%$ versus $90.9\% \pm 5.6\%$; $t(7$ d.f.) = 7.23 ; $p < 0.0001$). The data were well fitted by the maximum likelihood decision model that is described in the Supplemental Data ([http://www.neuron.org/cgi/content/full/](http://www.neuron.org/cgi/content/full/44/3/547/DC1/)

44/3/547/DC1/), which accounted for 98.8% of variance and yielded an estimate of the internal Weber fraction $w = 0.170$.

We confirmed those results in a second forced-choice task, which required subjects to decide if the fourth set was larger or smaller than the preceding ones (Figures 2E–2G). Comparison performance followed a classic sigmoid curve, with a slope twice as large for habituation 32 than for habituation 16 (Figure 2E). Although targets were now distributed regularly around the reference value, performance was again asymmetrical and better fitted by the integral of a Gaussian on a log scale than on a linear scale ($r^2 \pm 1$ SD = $88.0\% \pm 4.1\%$ versus $94.9\% \pm 2.4\%$; $t(7$ d.f.) = 6.23 ; $p = 0.0004$). The log-Gaussian model accounted for 99.7% of variance and gave a value of the internal Weber fraction that was very close to that obtained in the first task ($w = 0.174$). This value is also consistent with previous psychophysical investigations of numerosity judgments in human adults (Cordes et al., 2001; van Oeffelen and Vos, 1982; Whalen et al., 1999).

The average curves from both tasks were centered on the habituation number, suggesting that participants could extract accurate numerical information in spite of changes in item size, density, and layout between the habituation and deviant images. Changes in item shape, however, did have a modest impact on numerical performance. In the same-different task, small sets of triangles were judged to be numerically identical to the habituation displays more frequently than large sets, while no

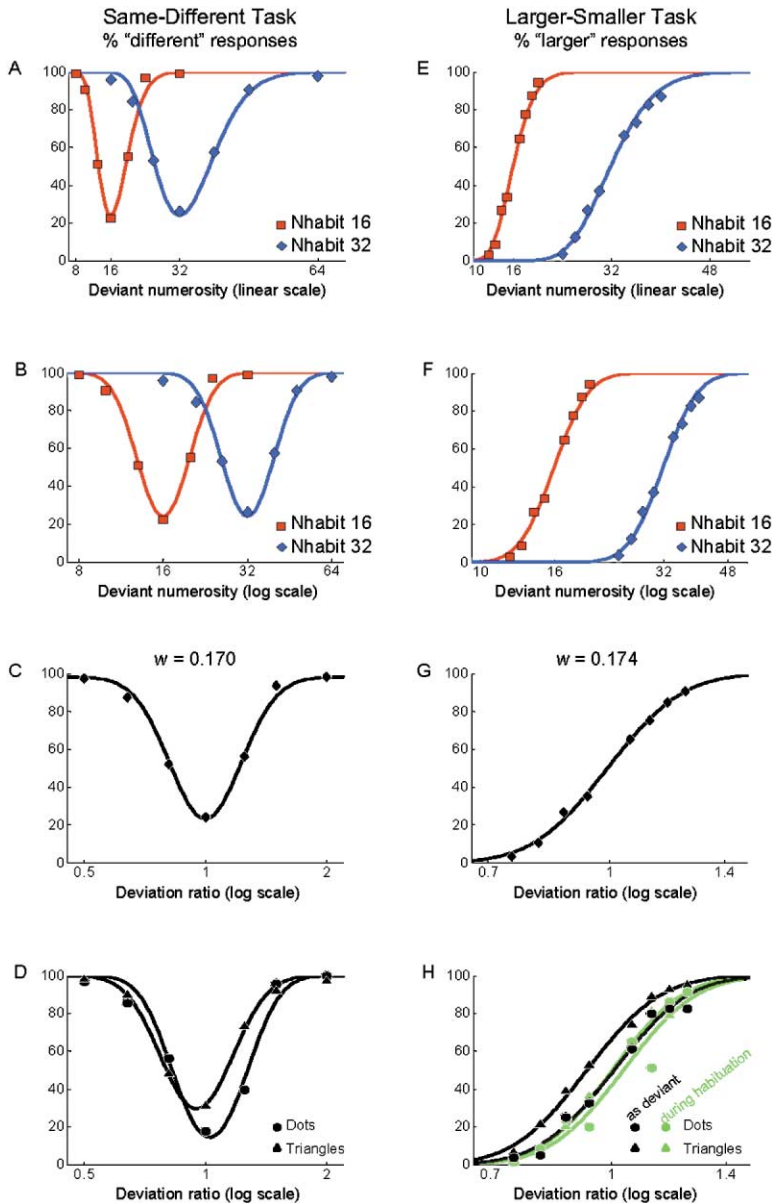


Figure 2. Behavioral Results from Same-Different and Larger-Smaller Tasks

Graphs in the left column represent the proportion of trials in which participants responded that the final set differed in number from the habituation sets. Graphs in the right column represent the proportion of trials in which participants responded that the final set was more numerous than the habituation sets. In both cases, performance is plotted as a function of the amount of numerical deviation. Performance curves assume a skewed shape when number is plotted on a linear scale (A and E) but become symmetrical on a logarithmic scale (B and F) and depend solely on the logarithm of the ratio of the two numbers (C and G). Performance was slightly affected by an irrelevant change in target shape (D and H). The fitted curves are derived from the equations that are described in the Supplemental Data at <http://www.neuron.org/cgi/content/full/44/3/547/DC1/>.

such bias was present for sets of dots (Figure 2D) [main effect of item shape, $F(1, 7) = 12.70$, $p = 0.009$; item shape by distance interaction, $F(6, 42) = 3.38$, $p = 0.008$]. In the larger-smaller task, likewise, subjects responded "larger" more often when the target set was made of triangles than when it was made of dots [item shape, $F(1, 7) = 18.81$, $p = 0.003$]. Both effects could be accounted for by a small (5%–7%) overestimation of the number of triangles compared to dots, perhaps because the triangles appeared slightly bigger. However, no such difference was found when the triangles appeared as habituation sets [$F(1, 7) = 1.60$; $p = 0.25$], even if an item shape by distance interaction was present [$F(7, 49) = 5.43$; $p = 0.0001$], presumably because the same habituation number was presented many times within a block, both as triangles and as dots. Crucially, in spite of this bias, the best-fitting Weber fraction was unchanged across conditions (range 0.162–0.175), suggesting that

subjects were estimating numerical quantity rather than any alternative physical variable.

During fMRI, participants were passively exposed to habituation and deviant sets. In a whole-brain search, the only regions that responded proportionally to numerical distance were localized in the left and right intraparietal sulci (see Table 1 and Figure 3). Importantly, there was little overlap of those number-related regions with those that responded to item shape change. Only 17 right-parietal voxels were shared, representing, respectively, 13% and 4% of the number- and shape-related activations. Item shape change activated the right and left prefrontal cortex, anterior cingulate cortex, and right parietal cortex at a site lateral to the activation evoked by number change (see Table 2 and Figure 5). The left lateral occipito-temporal cortex, which was reported in previous studies of adaptation to a single shape (Grill-Spector et al., 1998; Kourtzi and Kanwisher, 2001), also

Table 1. Regions Responding to Deviations in Number

Cortical Region	x	y	z	Corrected p (Cluster)
Left IPS	-36	-60	52	0.006
	-28	-68	48	
	-28	-56	44	
Right IPS	28	-56	52	0.008
	28	-40	40	
	16	-56	44	
	24	-58	52	

showed a marginal shape change effect (corrected $p = 0.07$).

The most anterior parietal voxels responsive to number change, especially in the right hemisphere, coincided with the horizontal intraparietal sulcus (hIPS) site common to many arithmetic tasks (Dehaene et al., 2003), including number comparison (Naccache and Dehaene, 2001; Pesenti et al., 2000; Pinel et al., 2001, 2004), subtraction (Lee, 2000; Simon et al., 2002), approximation (Dehaene et al., 1999), or mere detection of numerals (Eger et al., 2003). Here, we show that these regions respond to the nonsymbolic “numerosity” dimension of sets of physical objects. It is often argued that the parietal activation observed during number processing may result from the greater difficulty of arithmetic tasks relative to the baseline chosen. However, this argument cannot apply to the present data, which are based on a habituation protocol in which subjects did not have to explicitly respond to the stimuli and were not engaged in any effortful task. Activation related to number change also extended posteriorly in the IPS, reflecting either a sparse and distributed coding of numerosity along the IPS (Pinel et al., 2004; Nieder and Miller, 2004) or the additional engagement of attention-orientating mechanisms that might have followed the detection of numerosity changes in the display (Dehaene et al., 2003).

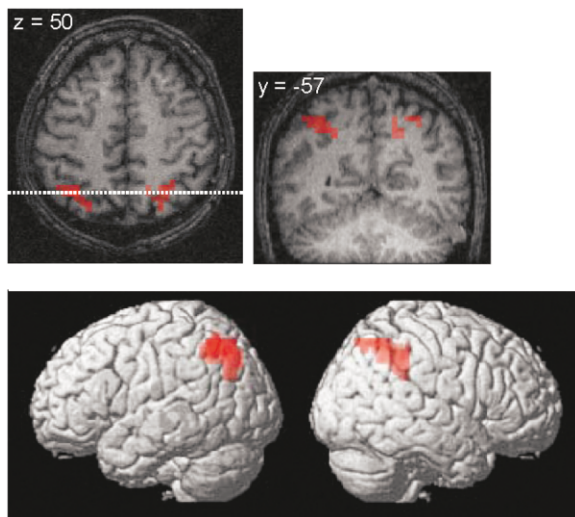


Figure 3. Brain Regions that Respond to Number Change

Brain regions that responded to number change superimposed on axial (top left) and coronal (top right) anatomical images of one subject, and on a standard 3D render of the cortex (bottom).

Table 2. Regions Responding to Deviations in Item Shape

Cortical Region	x	y	z	Corrected p (Cluster)
Left prefrontal	-48	28	12	0.003
	-28	24	28	
	-40	24	24	
Right prefrontal	48	8	36	0.000
	48	8	12	
	20	32	24	
Anterior cingulate	-8	12	56	0.004
	4	28	32	
	-4	8	44	
Right parietal	44	-52	44	0.000
	24	-48	40	
	32	-52	52	
Lateral occipital	-40	-60	-4	0.070
	-52	-60	-4	
	-60	-56	-8	

The depth of the intraparietal sulcus where number-related activation was observed occupies a reproducible location relative to other landmarks that might correspond to monkey areas LIP and AIP (Simon et al., 2002) and may constitute a putative homolog of the deep ventral intraparietal area where number-responsive neurons are found in the macaque monkey (Nieder and Miller, 2004). Interestingly, in the monkey performing a delayed match-to-sample task, number-coding neurons are also observed in prefrontal cortex. However, the parietal neurons have a shorter firing latency than the frontal ones (about 100 versus 160 ms) (Nieder and Miller, 2004). This difference is compatible with the hypothesis that numerosity is first extracted in the IPS and later transmitted to prefrontal cortex as needed for the requested task. Our experiment did not involve any explicit working memory demands, which may explain why number-related activation was not found at corrected levels of significance in prefrontal cortex, but only in the intraparietal region, where number representation is faster and more automatic. Note, however, that at a lower threshold (clusterwise $p < 0.01$ uncorrected for multiple comparisons), number-related activation was also observed in right posterior premotor (coordinates 36, 0, 32) and dorsolateral prefrontal cortex (48, 32, 16).

In the absence of further data on the geometrical and cytoarchitectonic organization of this region in both species, the proposed anatomical homology between the human and monkey parietal representations of numerosity must remain speculative. However, the present data allow us to ascertain whether detailed functional parallels in the parietal coding schemes for number are present across the two species. To study whether numerical responses in the human IPS followed the predictions of the compressive tuning curves of the macaque neurons, we isolated, for each subject, within the two IPS regions identified by the group analysis, the voxel where the largest fMRI response to numerical novelty was found. We then plotted activation in these voxels as a function of experimental conditions in the same format as the psychophysical curves (Figure 4). Although noisier than behavioral curves, the brain activation responses to habituation numerosities 16 and 32 showed the characteristic features of Weber's law. The curves had an increas-

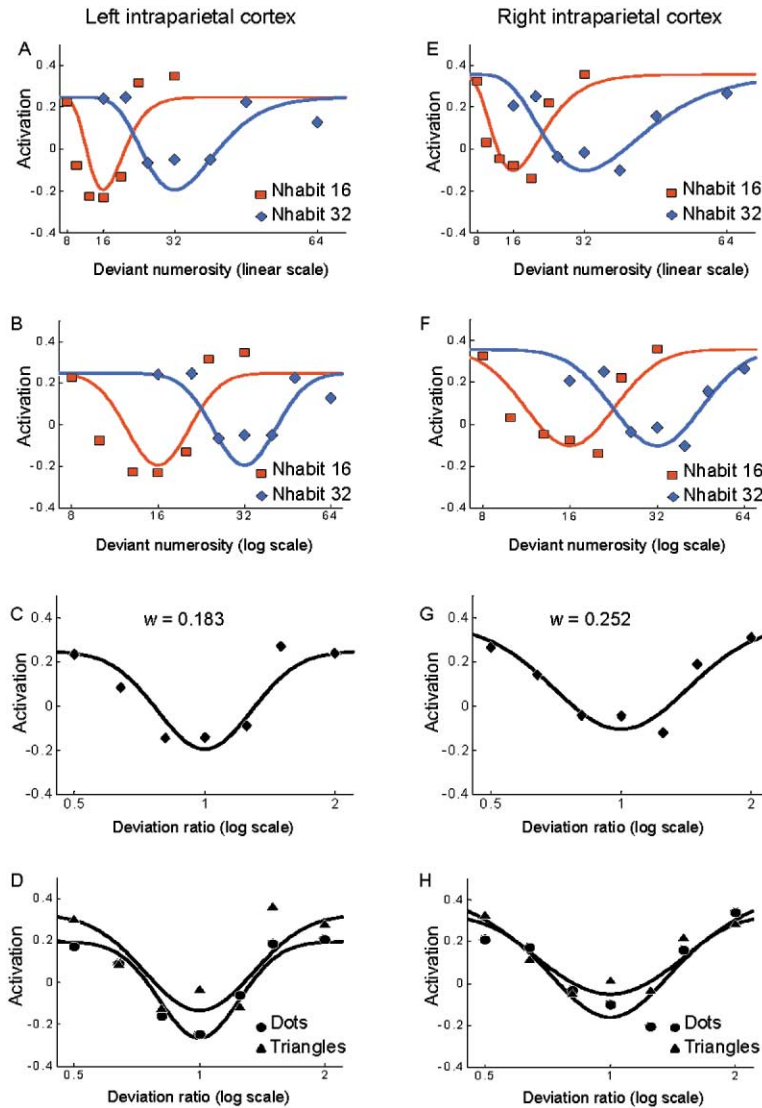


Figure 4. Parietal Responses to Number Change

Same organization as Figure 2. Deviant sets elicit an activation that increases with the amount of number change (A and B). Activation curves are a Gaussian function of the log ratio of the two numbers (C), with only minimal influence of item shape change (D). Activation is expressed as percent change in BOLD signal and is relative to the ongoing level of activation elicited by the continuous stream of habituation displays. Hence, the negative values when the deviant and habituation values match (ratio = 1) indicate continued BOLD habituation.

ing width on a linear number scale (Figure 4A), became identical in width when plotted on a log scale (Figure 3B), and could be expressed as a simple Gaussian function of log ratio (Figure 3C). However, single-subject data were too noisy for individual nonlinear curve fitting, and the group data were fitted about equally well by a log and by a linear Gaussian function of ratio (right parietal cortex, respectively, $r^2 = 0.770$ versus 0.597 ; left parietal cortex, $r^2 = 0.649$ versus 0.706).

Importantly, in those numerosity-sensitive regions, no influence of item shape change was perceptible (Figure 4D). This was confirmed statistically by submitting the data to an analysis of variance (ANOVA) with factors of habituation number (16 or 32), number deviation ratio (7 levels), and item shape change (dots, no shape change; or triangles, shape change). Only the main effect of number deviation reached significance ($p < 0.0001$), which was expected because we used it to select the fMRI peaks. To further demonstrate that number, rather than any other physical parameter, was responsible for fMRI signal recovery in the intraparietal sulcus, we performed an ANOVA on fMRI signals to the same deviant

stimuli 16 and 32, as a function of whether they were presented in blocks with habituation 16 or 32. We observed highly significant interactions of deviant number by habituation number [left parietal, $F(1, 11) = 14.390$, $p < 0.001$; right parietal, $F(1, 11) = 15.196$, $p < 0.001$]. As predicted, there was a lower fMRI signal when the deviant number matched the habituation number than when the two numbers differed. Those interactions cannot be explained by a sensitivity to item size or spacing, which were matched across the habituation sets, nor to total luminance or occupied area, which were matched across the deviant sets (see the Supplemental Data at <http://www.neuron.org/cgi/content/full/44/3/547/DC1/>). The fact that fMRI responses to deviants reached a minimum precisely at the number that was used during habituation, although very different physical parameters were used to generate the habituation and deviant stimuli, can only be explained by a genuine sensitivity to numerical change in the underlying neural population.

Activation profiles in shape-sensitive regions (left and right prefrontal, lateral occipital, anterior cingulate, and right parietal) differed radically from those of numero-

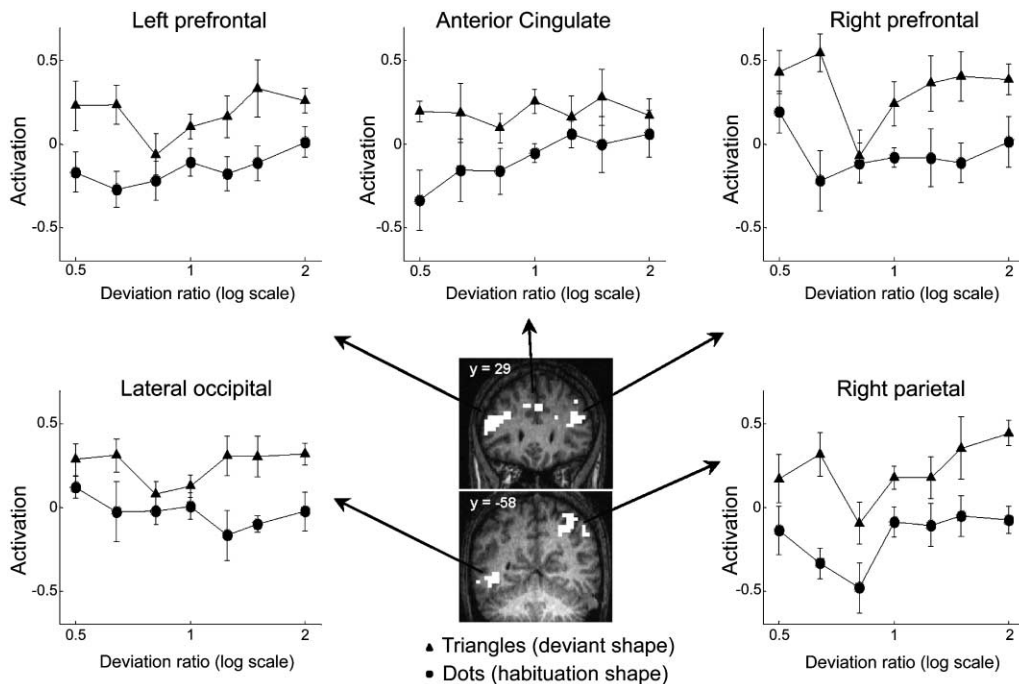


Figure 5. Responses to Item Shape Change

Activation in those regions was not significantly influenced by number change (horizontal axis) but depended solely on the presence of a change in item shape (triangles versus dots).

sity-sensitive regions (Figure 5), in that they showed a main effect of item shape change in the absence of a main effect of number change. The anterior cingulate and right parietal regions also showed a small interaction of item shape, deviation, and number ($p < 0.01$), which could be explained by a decreasing sensitivity to item shape changes for increasingly larger numbers, presumably because the individual shapes became smaller and therefore less discriminable. Previous habituation studies have revealed a coding of shape in the lateral occipital complex (Grill-Spector et al., 1998; Kourtzi and Kanwisher, 2001). The observation of additional parietal, prefrontal, and cingulate regions in our paradigm may indicate an attentional or novelty reaction to the rare changes in item shape. The absence of similar additional responses to number fitted with the participants' introspective reports that changes in item shape were obvious, while changes in numerical quantity were rare and inconspicuous.

Our design enabled a direct comparison of behavioral and fMRI responses to the same changes in numerical quantity. Interestingly, parietal activation profiles as a function of log numerical ratio tended to be broader than behavioral profiles (compare Figures 2C, 3C, and 3G). This observation was expected in our mathematical model, because the fMRI habituation signals reflect the combined influence of the habituated neural population and the activity evoked by the deviant target. Mathematically, this effect is equivalent to a convolution operation. Hence, the fMRI curves should have a width scaled up by $\sqrt{2}$ relative to the actual neuronal Weber fraction. With this simple correction, the fMRI curves yielded a Weber fraction $w = 0.18$ for the left intraparietal region,

in excellent agreement with our behavioral results ($w = 0.17$). Interestingly, the Weber fraction tended to be larger for the right intraparietal region ($w = 0.25$), although this difference did not reach significance. Further research should probe whether there is a differential precision of number coding in the two hemispheres, perhaps due to interactions with an exact verbal code for number within the language-dominant left hemisphere (Dehaene, 1997).

Other mechanisms may also contribute to the observed finer sensitivity in behavior than in fMRI. For instance, participants attended to numerical quantity in the behavioral experiments but not during fMRI. Behavioral performance might also achieve a higher sensitivity than single neurons through averaging over independent neurons, or through selection of a small neuronal subpopulation with high sensitivity (Parker and Newsome, 1998). Eventually, experiments with awake monkeys will be needed to test more directly the proposed link between neuronal tuning curves and fMRI adaptation.

While the important gap between human fMRI and monkey electrophysiological recordings must be kept in mind, the present results exhibit important parallels with the physiological recordings of number neurons in the monkey parietal and frontal regions (Nieder et al., 2002; Nieder and Miller, 2003, 2004). Both human and monkey data yield tuning profiles that (1) depend only on number independently of other parameters such as shape, density, or spatial arrangement; (2) are smooth and monotonic in response to increasing degrees of deviation in number; (3) are increasingly broader when plotted on a linear scale (Weber's law); (4) can be ex-

pressed as a simple Gaussian function of log number ratio. This functional homology, together with the compatible anatomical localization, suggests that humans and macaque monkeys have similar populations of intraparietal number-sensitive neurons. It provides important support for the notion that all humans start in life with a nonverbal representation of approximate number inherited from our evolutionary history, as also supported by studies in human adults (Barth et al., 2003; Cordes et al., 2001; Whalen et al., 1999), infants (Lipton and Spelke, 2003), nonhuman primates (Brannon and Terrace, 1998; Hauser et al., 2003), and human genetic diseases (Molko et al., 2003). Our work leaves open the exact biological mechanisms by which numerical quantity is extracted. In our experiments, strict controls over nonnumerical parameters ensured that neither the behavioral nor the parietal responses to numerical deviation could be explained by any simple physical factor other than number. Still, it is possible that participants were using combinations of physical parameters to estimate number, for instance by estimating the ratio of total luminance by individual item luminance or of total occupied area by the square of the average interitem spacing (Allik and Tuulmets, 1991). Parietal maps for object location, once normalized for object size and identity, can also be summed to yield an estimate of number (Dehaene and Changeux, 1993).

Finally, while humans and macaques may share a principle of compressed number coding, there may be interesting species differences in the precision of this code. At the neural level, our results are not incompatible with monkey physiology, since we found Weber fractions of 0.18 in left parietal and 0.24 in right parietal cortex, while Nieder and Miller (2003) observed a value of 0.24 in macaque neurons. Behaviorally, however, we observed a Weber fraction of about 0.17, in line with other psychophysical studies of human numerosity judgments (Cordes et al., 2001; Whalen et al., 1999) but about twice better than the value of 0.35 reported by Nieder and Miller (2003) for numerosity discrimination in macaque monkeys (for compatible data, see also Brannon and Terrace, 1998; Hauser et al., 2003). Such comparisons must be made cautiously, because the Weber fractions are measured using different experimental methods. Nevertheless, they consistently suggest a higher precision in humans than in other primates. The Weber fraction is also known to vary considerably in humans within the first year of life: 6-month-old infants discriminate numbers in a 2:1 ratio (e.g., 8 versus 16), but only 9-month-olds are able to discriminate numbers in a 3:2 ratio (e.g., 8 versus 12) (Lipton and Spelke, 2003). Prolonged brain maturation, greater experience with numerical quantity, and training with symbolic codes may account for the increased precision of numerical coding in humans. The present work provides a set of methods with which to track ontogenetic and phylogenetic changes in this important parameter of numerical cognition.

Experimental Procedures

fMRI Experiment

Participants

Twelve healthy human adults (mean age 23) participated in the fMRI study after giving written informed consent. All were right handed

(Edinburgh Inventory) and had normal or corrected-to-normal vision. The study was approved by the regional ethical committee (Hopital de Bicêtre, France).

Procedure

Stimuli were presented for 150 ms, white against a black background, at a constant rate of one every 1200 ms. The majority were sets of dots with a fixed number. Occasionally, a deviant set occurred randomly, with the constraint that two successive deviants were separated by at least 3 and at most 11 habituation stimuli. Stimuli could deviate by a variable ratio (1.25, 1.5, or 2) from the habituation number, in both the larger or smaller direction, or they could be equinumerous to the habituation number. Furthermore, items in the deviant sets could be of the same shape (circles) or different shape (triangles) than the habituation sets, thus defining orthogonal shape change and number change factors (see Figure 1).

The experiment was divided in four blocks. Each block consisted of 384 stimuli, of which one-eighth were deviant. Two different habituation numbers were presented in counterbalanced blocks: 16 (with deviants 8, 10, 13, 16, 20, 24, and 32) and 32 (with deviants 16, 21, 26, 32, 40, 48, and 64). Each block started with the presentation of a small centered yellow fixation cross, which remained visible throughout. Accurate fixation was controlled using a MR-compatible eye tracker (ASL 5000 LRO system; Applied Science Laboratories, Bedford, MA).

To avoid decision and response confounds, fMRI participants were simply instructed to fixate and to pay attention to the stimuli. They were not informed of the aim of the experiment or told to focus on any specific dimension of the stimuli but were told that the experimenter would later ask them questions about the displays. During informal questioning at the end, all participants spontaneously reported noticing the changes in objects' shape as well as details of their size, spacing, and configuration. The changes in number tended to be less conspicuous, as they were mostly reported only after explicit questioning.

Stimuli

Stimuli were designed so that, aside from the number change, all deviant stimuli were equally novel with respect to all physical parameters. Total luminance and total occupied area (extensive parameters) were equated across the deviant stimuli (see Supplemental Figure S1 at <http://www.neuron.org/cgi/content/full/44/3/547/DC1/>). This means that larger deviant numbers had on average smaller individual item sizes and smaller interitem spacing. However, the latter parameters (intensive parameters) were varied randomly and equated on average across the habituation stimuli: habituation stimuli were generated randomly, with item size and interitem spacing values drawn randomly from fixed distributions that spanned all the range of values used for the deviant stimuli. As a result, all of the parameter values that occurred in the deviants had already been presented equally often during habituation and were equally non-novel. Therefore, the only novel aspect of the deviant stimuli was number. An automated program generated random configurations within those constraints, so that stimuli were never repeated identically during the experiment. The use of large numbers further prevented any possibility of using pattern recognition as a cue.

fMRI Parameters

The experiment was performed on a 3T fMRI system (Bruker, Germany). Functional images sensitive to blood oxygen level-dependent contrast were obtained with a T2*-weighted gradient echo-planar imaging sequence (repetition time [TR] = 2.4 s; echo time [TE] = 40 ms; angle = 90°; field of vision [FOV] = 192 × 256 mm; matrix = 64 × 64). The whole brain was acquired in 26 slices with a slice thickness of 4.5 mm. High-resolution images (3D gradient echo inversion-recovery sequence; inversion time [TI] = 700 ms; TR = 2400 ms; FOV = 192 × 256 × 256 mm; matrix = 256 × 128 × 256; slice thickness = 1 mm) were also acquired.

Image Processing and Statistical Analysis

Data were analyzed with SPM99 (<http://www.fil.ion.ucl.ac.uk/spm/>). The first 4 volumes were discarded. All other volumes were realigned using the first volume as reference, then normalized to the standard template of the Montreal Neurological Institute using an affine transformation, spatially smoothed (6 mm), and low-pass (4 s) and high-pass (140 s) filtered. Activations were modeled by a linear combination of eight functions derived by convolution of the standard hemodynamic function with the known onsets of the different types

of deviants. Time derivatives were added to capture variance in activation timing. Random effect analyses were then applied to two contrasts: main effect of item shape change and linear effect of deviation ratio. Data are reported at $p < 0.05$ corrected for multiple comparisons at the cluster level, $p < 0.01$ at the voxel level.

Psychophysical Experiments

Same-Different Judgment

Eight healthy human adults participated (mean age 29). After a fixation cross appeared for 1050 ms, stimuli were presented at the same rate as in fMRI, but now in short series of four. The first three were habituation stimuli containing either 16 or 32 dots (in different blocks) and were taken randomly from the set of habituation stimuli used in the fMRI experiment. The fourth stimulus was a deviant identical to those used in the fMRI experiment. Immediately after, a question mark appeared and remained on the screen until the subject had pressed one of two keys to decide whether the number of items had changed. Visual feedback was provided for 1500 ms (the word "correct" or "incorrect"). The participants were told that in 75% of trials the number would be different and that they had to disregard changes in item shape. The experiment comprised four counterbalanced blocks of 48 trials each.

Larger-Smaller Judgment

Eight healthy human adults participated (mean age 26). On each trial, a series of four sets was presented, three with the same number of items (16 or 32, fixed in a given block) and a fourth with a different number of items. Participants judged whether the last set had a larger or smaller number of items than the preceding ones. This forced-choice task presented the advantage of eliminating the response criterion inherent in the same-different task and allowing a fit of the data with a single free parameter w (the internal Weber fraction). Because performance was predicted to be better than that for same-different judgments (see the mathematical model in the Supplemental Data at <http://www.neuron.org/cgi/content/full/44/3/547/DC1/>), we selected target numbers closer to the reference value, namely 12, 13, 14, 15, 17, 18, 19, and 20 when the reference was 16 and twice those amounts when the reference was 32. The distribution of targets was symmetrical around the reference, thus responding to a possible criticism of the previous experiment, in which performance asymmetries might conceivably have been induced by the logarithmic distribution of targets.

The experiment comprised 8 blocks of 40 trials each (four with reference 16 and four with reference 32, in counterbalanced order). Timing, stimulus generation, and feedback were identical to the same-different task. On half the trials, the first three displays were generated using the parameters of fMRI habituation displays, and the fourth was generated using the parameters of fMRI deviant displays. On the other half, this order was reversed. This manipulation allowed the examination of the effect of nonnumerical variables on performance, since target number was correlated with different variables in the two sets (item size and interitem spacing in the first set, total luminance and total occupied area in the second set). The similarity of performance and Weber fraction estimates in the two sets (Figure 2H), at least for dot patterns, supports our hypothesis that participants attended to number rather than to other physical parameters.

Acknowledgments

Supported by INSERM; CEA; a Marie Curie fellowship of the European Community (QLK6-CT-2002-51635) (M.P.); and a McDonnell Foundation centennial fellowship (S.D.).

Received: July 9, 2004

Revised: September 1, 2004

Accepted: September 27, 2004

Published: October 27, 2004

References

Allik, J., and Tuulmets, T. (1991). Occupancy model of perceived numerosity. *Percept. Psychophys.* 49, 303–314.

Barth, H., Kanwisher, N., and Spelke, E. (2003). The construction of large number representations in adults. *Cognition* 86, 201–221.

Brannon, E.M., and Terrace, H.S. (1998). Ordering of the numerosities 1 to 9 by monkeys. *Science* 282, 746–749.

Cordes, S., Gelman, R., Gallistel, C.R., and Whalen, J. (2001). Variability signatures distinguish verbal from nonverbal counting for both large and small numbers. *Psychon. Bull. Rev.* 8, 698–707.

Dehaene, S. (1997). *The Number Sense* (New York: Oxford University Press).

Dehaene, S., and Changeux, J.P. (1993). Development of elementary numerical abilities: A neuronal model. *J. Cogn. Neurosci.* 5, 390–407.

Dehaene, S., Spelke, E., Pinel, P., Stanescu, R., and Tsivkin, S. (1999). Sources of mathematical thinking: behavioral and brain-imaging evidence. *Science* 284, 970–974.

Dehaene, S., Piazza, M., Pinel, P., and Cohen, L. (2003). Three parietal circuits for number processing. *Cogn. Neuropsychol.* 20, 487–506.

Desimone, R. (1996). Neural mechanisms for visual memory and their role in attention. *Proc. Natl. Acad. Sci. USA* 93, 13494–13499.

Eger, E., Sterzer, P., Russ, M.O., Giraudo, A.L., and Kleinschmidt, A. (2003). A supramodal number representation in human intraparietal cortex. *Neuron* 37, 719–725.

Grill-Spector, K., and Malach, R. (2001). fMR-adaptation: a tool for studying the functional properties of human cortical neurons. *Acta Psychol. (Amst.)* 107, 293–321.

Grill-Spector, K., Kushnir, T., Edelman, S., Itzhack, Y., and Malach, R. (1998). Cue-invariant activation in object-related areas of the human occipital lobe. *Neuron* 21, 191–202.

Hauser, M.D., Tsao, F., Garcia, P., and Spelke, E. (2003). Evolutionary foundations of number: spontaneous representation of numerical magnitudes by cotton-top tamarins. *Proc. R. Soc. Lond. B Biol. Sci.* 270, 1441–1446.

Kourtzi, Z., and Kanwisher, N. (2001). Representation of perceived object shape by the human lateral occipital complex. *Science* 293, 1506–1509.

Lee, K.M. (2000). Cortical areas differentially involved in multiplication and subtraction: A functional magnetic resonance imaging study and correlation with a case of selective acalculia. *Ann. Neurol.* 48, 657–661.

Lipton, J., and Spelke, E. (2003). Origins of number sense: Large number discrimination in human infants. *Psychol. Sci.* 14, 396–401.

Miller, E.K., Li, L., and Desimone, R. (1993). Activity of neurons in anterior inferior temporal cortex during a short-term memory task. *J. Neurosci.* 13, 1460–1478.

Molko, N., Cachia, A., Riviere, D., Mangin, J.F., Bruandet, M., Le Bihan, D., Cohen, L., and Dehaene, S. (2003). Functional and structural alterations of the intraparietal sulcus in a developmental dyscalculia of genetic origin. *Neuron* 40, 847–858.

Naccache, L., and Dehaene, S. (2001). The priming method: Imaging unconscious repetition priming reveals an abstract representation of number in the parietal lobes. *Cereb. Cortex* 11, 966–974.

Nieder, A., and Miller, E.K. (2003). Coding of cognitive magnitude. Compressed scaling of numerical information in the primate prefrontal cortex. *Neuron* 37, 149–157.

Nieder, A., and Miller, E.K. (2004). A parieto-frontal network for visual numerical information in the monkey. *Proc. Natl. Acad. Sci. USA* 101, 7457–7462.

Nieder, A., Freedman, D.J., and Miller, E.K. (2002). Representation of the quantity of visual items in the primate prefrontal cortex. *Science* 297, 1708–1711.

Parker, A.J., and Newsome, W.T. (1998). Sense and the single neuron: Probing the physiology of perception. *Annu. Rev. Neurosci.* 21, 227–277.

Pesenti, M., Thioux, M., Seron, X., and De Volder, A. (2000). Neuroanatomical substrates of Arabic number processing, numerical comparison, and simple addition: A PET study. *J. Cogn. Neurosci.* 12, 461–479.

Pinel, P., Dehaene, S., Riviere, D., and LeBihan, D. (2001). Modulation

of parietal activation by semantic distance in a number comparison task. *Neuroimage* 14, 1013–1026.

Pinel, P., Piazza, M., Le Bihan, D., and Dehaene, S. (2004). Distributed and overlapping cerebral representations of number, size, and luminance during comparative judgments. *Neuron* 41, 983–993.

Sawamura, H., Shima, K., and Tanji, J. (2002). Numerical representation for action in the parietal cortex of the monkey. *Nature* 415, 918–922.

Simon, O., Mangin, J.F., Cohen, L., Le Bihan, D., and Dehaene, S. (2002). Topographical layout of hand, eye, calculation, and language-related areas in the human parietal lobe. *Neuron* 33, 475–487.

van Oeffelen, M.P., and Vos, P.G. (1982). A probabilistic model for the discrimination of visual number. *Percept. Psychophys.* 32, 163–170.

Whalen, J., Gallistel, C.R., and Gelman, R. (1999). Non-verbal counting in humans: The psychophysics of number representation. *Psychol. Sci.* 10, 130–137.