Article

A Magnitude Code Common to Numerosities and Number Symbols in Human Intraparietal Cortex

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SUMMARY

Activation of the horizontal segment of the intraparietal sulcus (hIPS) has been observed in various number-processing tasks, whether numbers were conveyed by symbolic numerals (digits, number words) or by nonsymbolic displays (dot patterns). This suggests an abstract coding of numerical magnitude. Here, we critically tested this hypothesis using fMRI adaptation to demonstrate notation-independent coding of numerical quantity in the hIPS. Once subjects were adapted either to dot patterns or to Arabic digits, activation in the hIPS and in frontal regions recovered in a distance-dependent fashion whenever a new number was presented, irrespective of notation changes. This remained unchanged when analyzing the hIPS peaks from an independent localizer scan of mental calculation. These results suggest an abstract coding of approximate number common to dots, digits, and number words. They support the idea that symbols acquire meaning by linking neural populations coding symbol shapes to those holding nonsymbolic representations of quantities.

INTRODUCTION

Numerical quantities, like many other categories of concepts, can be expressed symbolically or analogically. The numerical quantity 3, for example, can be expressed symbolically by the digit 3 or by the spoken or written word "three." It can also be conveyed in concrete form by a set of three visual objects, a sequence of three tones, or three self-generated movements. Are the neural populations that extract and represent the cardinality of a given set (numerosity) also involved in representing the meaning of a given numerical symbol? It has been proposed that, in the course of learning to speak, read, or write, children learn to map spoken and written numerals onto a core representation of numerosity in the intraparietal sulcus (Butterworth, 1999; Dehaene, 1997). It is likely that symbolic and concrete depictions of number are linked together in the adult human brain, perhaps in the form of notation-independent assemblies of neurons coding for number at a purely conceptual level (cardinality). The goal of the present study is to put this hypothesis to a critical test using fMRI adaptation.

Recent research has suggested that concepts of number form a semantic category which dissociates from other categories of concepts (for example colors, living things, or tools). In neuropsychology, a double dissociation exists between numbers and other semantic categories. On the one hand, there are patients (with cortical atrophy mainly of temporal lobes) with heavily deteriorated semantic processing but spared calculation and number comprehension (Butterworth et al., 2001; Halpern et al., 2004; Thioux et al., 1998). On the other hand, there are patients (mainly with lesions or atrophy in the parietal cortex) that show impaired understanding of numbers but otherwise preserved knowledge of other semantic domains (Cipolotti et al., 1991; Dehaene and Cohen, 1997; Halpern et al., 2004; Zamarian et al., 2006).

Functional imaging techniques have also revealed some degree of segregation between numbers and other categories such as animals and colors (Eger et al., 2003; Thioux et al., 2002). Furthermore, they have helped clarify the organization of number-related processes in the parietal lobe. fMRI studies have suggested a crucial role of regions situated along the horizontal segment of the intraparietal sulcus (hIPS) of both hemispheres for the representation of numerical quantities (Dehaene et al., 2003). Independent lines of research have pointed to parietal cortex as crucial for coding numerical quantity both when it is conveyed by number symbols (digits, number words; Eger

et al., 2003; Pinel et al., 2001) or by nonsymbolic displays of dots patterns (Ansari et al., 2006; Cantlon et al., 2006; Piazza et al., 2004). Those results have been taken to imply that the hIPS contains a modality-independent quantity representation. However, symbolic and nonsymbolic quantities were often tested in different experimental settings and subjects; only one recent fMRI study showed common activations in the anterior IPS bilaterally, left posterior IPS, medial frontal gyrus, and left precentral gyrus for symbolic and nonsymbolic addition (Venkatraman et al., 2005). Most crucially, coactivation of the same voxels need not imply a common neural code but might simply be due to the activation of distinct neural populations intermixed at the same cortical location (Cohen Kadosh et al., 2005; Pinel et al., 2004).

Another line of research pointing to a possible convergence of symbolic and nonsymbolic representations of numbers arises from chronometric investigations. Evidence from the number comparison task has suggested that the internal metrics governing the mental representation of nonsymbolic quantities and of numerical symbols are similar. In both cases, response times and error rates show numerical distance and numerical magnitude effects: numerical judgments become more difficult when the numerical distance between two values decreases, and this effect is exacerbated as their absolute magnitude increases (Buckley & Gillman, 1974; Dehaene et al., 1990; Koechlin et al., 1999; Shepard et al., 1975). Such effects are captured by Weber's law, which states that the threshold of discrimination between two stimuli scales with their magnitude. They point to an internal coding of number by a distribution of activation on an internal compressed number "line" or "scale." These observations led some authors to the conclusion that symbolic and nonsymbolic notations converge onto a common format of representation (Buckley and Gillman, 1974; Dehaene et al., 1998; Piazza and Dehaene, 2004; Shepard et al., 1975). Once again, however, such behavioral evidence is indirect in nature and leaves open the possibility that there are two separate systems for representing symbolic and nonsymbolic numerical magnitudes that are simply governed by a similar metric. Indeed, magnitude effects are shared properties of a great variety of mental representations (e.g., size, sound intensity, etc.) that probably have little in common (Cohen Kadosh et al., 2005; Pinel et al., 2004).

To directly evaluate the presence of an abstract, notation-independent code for numerical magnitude in the hIPS, we measured brain activity with fMRI while 14 healthy volunteers passively observed both nonsymbolic (dot patterns) and symbolic (Arabic digits) numbers. Using an adaptation paradigm, we investigated whether a region in the bilateral intraparietal sulci adapts to approximate quantity and shows crossnotation recovery whenever the number changes. Previous research has shown number-related adaptation in the hIPS, both in adults and in 4-year-old subjects for numbers presented as sets of dots (Ansari et al., 2006; Cantlon et al., 2006; Piazza et al., 2004). Furthermore, Naccache and Dehaene (2001) dem-

| Adaptation values	Deviant values	
	20	50
17, 18, or 19	close	far
47, 48, or 49	far	close

Figure 1. 2 × 2 Design for Adaptation to Approximate Number
In distinct sequences, subjects adapted to numerical values close to 20 or close to 50 and were then tested with those values presented as deviants. Brain regions coding for approximate number should react more when the deviant is far from the adaptation value than when it is close to it. In the complete design, two additional factors were manipulated, as both the adaptation and the deviant numbers could be presented either in symbolic notation (Arabic digits) or nonsymbolically (as sets of dots).

onstrated subliminal fMRI repetition priming across Arabic digits and written words. The key addition of the present study is to test whether those symbolic and nonsymbolic adaptation effects occur at a shared level of parietal representation. For each subject, we also acquired a short localizer scan to identify regions active during symbolic mental calculation (subtractions of numbers presented visually or auditory). This localizer scan provided an independent definition of intraparietal regions of interest, where we investigated the presence of fMRI adaptation effects.

RESULTS

During short (2 min) sequences, participants were passively exposed to a fixed set of numerical quantities, all very close to a given value (e.g., 17, 18, or 19; see Figure 1). In a given sequence, these adaptation numerosities were presented in a fixed notation, either as Arabic digits or as sets of dots. Recovery from adaptation was investigated at two different temporal scales (Figure 2). First, after two minutes of adaptation with a fixed approximate quantity (hereafter called period A1), the adaptation numerosities changed abruptly (e.g., to 47, 48, or 49), with or without a concomittent change in notation, and remained approximately fixed for another 2 min period (hereafter called period A2). We examined whether this unforeseen change led to a durable rebound in the fMRI signal. Second, within each block, following a fixed adaptation part, sparse deviant stimuli were occasionally introduced. We examined whether each deviant event led to a local response dependent on the distance between the adaptation and deviant values. Crucially, all combinations of adaptation and deviant notations were used, resulting in two within-notation conditions (dots-to-dots and Arabic-to-Arabic) as well as two crossnotation conditions (dots-to-Arabic and Arabic-to-dots).
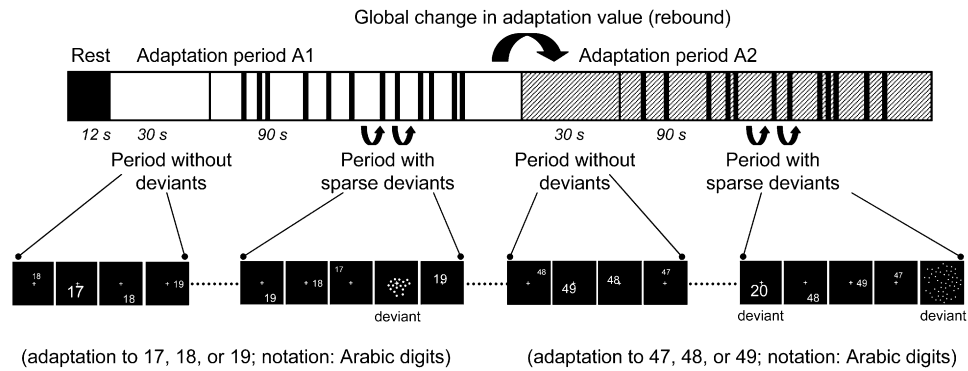
Figure 2. General Structure of Each Experimental Block and Example of Specific Stimuli

Each block comprised two successive adaptation sequences (A1 and A2). Within each sequence, the first 25 stimuli always presented the designated adaptation numbers. Deviants then occurred at pseudorandom moments (12 deviants amongst 60 adaptation stimuli). Each sequence ended with six trials with adaptation numbers only. At the transition between the sequences A1 and A2, the adaptation numbers abruptly changed without any break or warning. On half such transitions, notation also changed. The example (bottom) depicts a case in which adaptation stimuli in both A1 and A2 are Arabic numerals in the range 17–19 in A1 and in the range 47–49 in A2.

Initial Adaptation

To investigate the presence of adaptation, we searched for regions where activity decreased linearly during the first 30 s of periods A1 and A2, both after rest and after a change in number (see Figures 2 and 3). Regions showing number-related decreasing activity were mostly observed in bilateral parietal and frontal cortices, with additional effects in occipito-temporal, cerebrellar, and subcortical thalamic regions (Table 1). Given our a priori focus on parietal cortex (Piazza and Dehaene, 2004; Piazza et al., 2004), we then
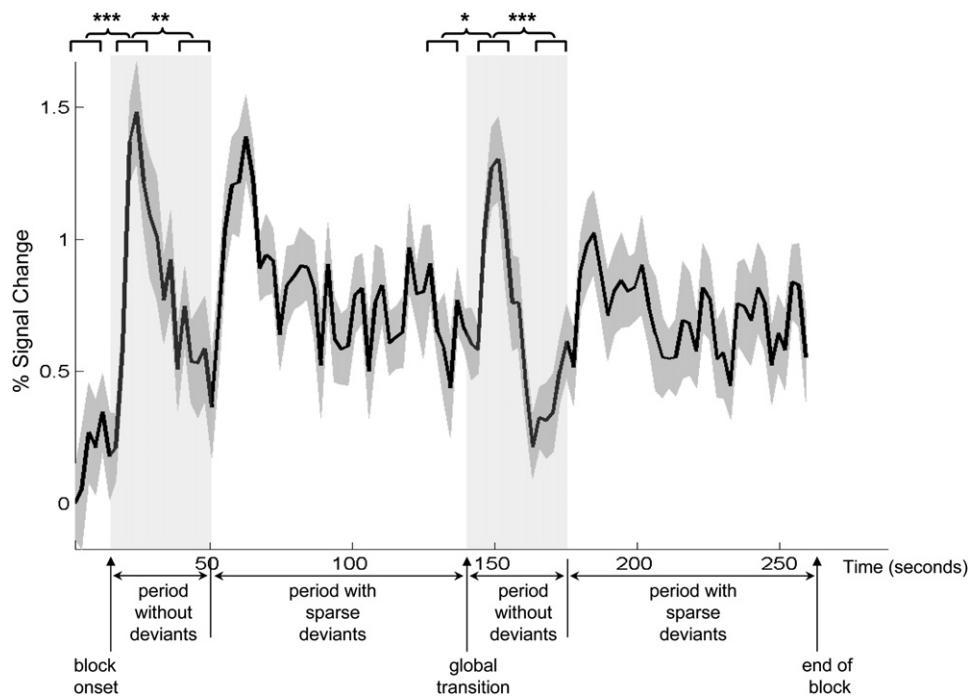
Figure 3. Time Course of Bilateral Parietal Activation during an Experimental Block (A1 Followed by A2), Averaged across Subjects and Conditions

The activation shown is the average across subjects and hemispheres of the voxels where, for each subject, the largest overall adaptation effect was observed. Error bars indicate ±1 standard error of the mean (SEM). Shaded areas represent the period in which the adaptation numbers were repeatedly presented. The signal begins to rise as soon as numbers are presented following the rest period. Following a period of adaptation, a global rebound is clearly seen, both at the transition between A1 and A2, as well as during the time periods where deviants begin to occur. *p < 0.05; **p < 0.01; ***p < 0.001.

Table 1. Regions Showing an Overall fMRI Adaptation Effect (Decreasing Activation with Repetition of the Same Approximate Quantity during the First 30 s of Periods A1 and A2)

| x	y	z	Z Score	Cortical Region
−34	−54	44	4.87	Left parietal
−20	−68	42		
−32	−64	40		
34	−64	54	4.19	Right parietal
34	−58	50		
46	−46	40		
−28	−64	−32	4.46	Left cerebellum
36	−72	−26	4.64	Right cerebellum
−34	−80	−2	3.46	Left occipital
24	−80	4	4.20	Right occipital
36	−46	−20	3.60	Right inferior temporal
−36	−60	−14	3.44	Left inferior temporal
−54	24	30	3.51	Left DLPF
38	26	20	4.50	Right DLPFC
−14	−2	2	3.43	Putamen
14	−2	0	3.35	

isolated, for each subject, within the two intraparietal regions identified by the group analysis, the voxel where the largest overall adaptation effect was observed (mean and standard deviation [SD] of coordinates = −31(6), −62(5), 48(5) in the left hemisphere and 32(4), −64(6), 47(7) in the right hemisphere). Figure 3 shows the time course of the BOLD signal in those voxels, averaged across hemispheres. The plot revealed that number-related adaptation in the parietal cortex is a slow, continuous process that takes several tens of seconds: activation continued to drop during the entire period where a given approximate numerical magnitude was repeated, both after rest and after a recovery from adaptation due to a change in number. The activation attained its peak around 10 s after the stimuli onset and then slowly decreased down to a minimum about 26 s after the peak. The adaptation effect was then tested statistically by comparing, across sub-

jects, the mean activation in three time windows of 12 s: during baseline, around the peak, and at the end of the adaptation sequence. This analysis showed a significant increase after rest (paired t test $T(13) = 5.11$, $p < 0.001$) and a significant decrease of the activation during the last adaptation period compared to activity around the peak ($T(13) = 3.02$, $p < 0.01$).

Rebound Effect

The activation profile of parietal peaks in Figure 3 suggests a rebound effect, with a sudden recovery of the fMRI signal after a change in the adaptation numbers (from A1 to A2), followed by a new period of adaptation during the subsequent repetitions of those new numbers. We compared, across subjects, the mean signal averaged over the 12 s before the change in number with the mean signal average over the first 12 s after the change in number. This analysis showed a statistically significant increase in activation ($T(13) = −2.14$, $p < 0.05$). The adaptation effect, a subsequent decrease in activation, was also highly significant (t test comparing the activity during the first and the last 12 s of the initial deviant-free period of A2, $T(13) = 4.93$, $p < 0.001$).

To further explore this rebound effect across our experimental conditions, we then isolated, for each subject, within the two IP regions identified by the group analysis, the voxel where the overall largest fMRI rebound signal was observed. The amount of rebound was quantified as the slope of a linear regression between the bold signal and a linearly decreasing vector going from 1 to −1 over the 30 s deviant-free section of period A2. An ANOVA with A1 notation and A2 notation as dependent variables, showed that rebound was invariant to notation (effect of A2 notation, left, $F(1,13) = 0.4$, $p = 0.54$; right, $F(1,13) = 0.09$, $p = 0.77$; effect of A1 notation, left, $F(1,13) = 0.05$, $p = 0.83$; right, $F(1,13) = 0.13$, $p = 0.73$) and also, crucially, invariant to *changes* in notation (A1*A2 notation interaction, left, $F(1,13) = 1.16$, $p = 0.3$; right, $F(1,13) = 0.54$, $p = 0.47$). In other words, the increased activity due to a change in number was identical with or without a concomitant change in notation (e.g., from Arabic digits to sets of dots, from sets of dots to Arabic digits, or within each notation; see Figure 4). This observation provides a first piece of evidence for an abstract coding of approximate number in the parietal cortex. At this level of analysis,
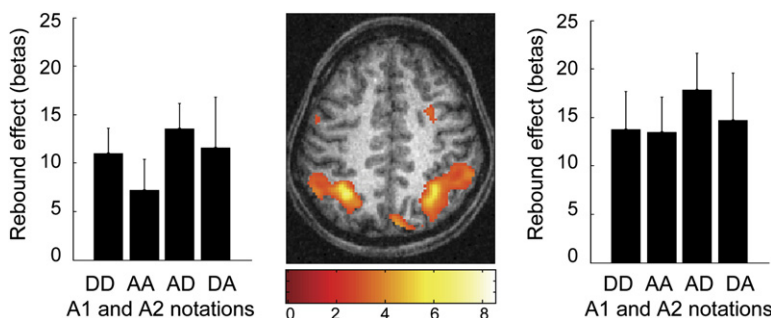
Figure 4. Left and Right Parietal Regions Showing a Significant Effect of Adaptation in the First 30 s of Periods A1 and A2
Plots show the amount of rebound activation in those regions at the beginning of period A2, as a function of the notation used for adaptation stimuli during periods A1 and A2 (A = Arabic digits, D = sets of dots). Error bars represent 1 SEM.

our design, in order to spare experimental time, did not incorporate a control condition where the transition between A1 and A2 was not accompanied by a change in number. Nevertheless, on same-notation trials, the number changed without any warning or any break in the stimulus sequence. It thus seems unlikely that the rebound would have occurred spontaneously at this precise moment in time, if it was not related specifically to the change in number.

Response to Sparse Deviants

More unambiguous evidence for an abstract numerical effect came from an analysis of the local event-related recovery from adaptation during the presentation of rare (deviant) stimuli in the second part of periods A1 and A2. Although the deviants always differed in number from the adaptation stimuli, the distance between the deviant and the adaptation numbers was either very small (a distance of an average of 2 units ±1) or large (32 ± 1 units; see Figure 1). We reasoned that presenting an occasional deviant number should lead to a local recovery of fMRI responses only if the deviant differed from the adaptation value by a sufficiently large amount. Based on our prior results with nonsymbolic stimuli, which indicate a Gaussian profile of recovery from adaptation in the hIPS, we expected little or no recovery for close deviants but a large recovery effect for far deviants. Accordingly, we looked for regions that responded more to large distances than to small ones. In a whole-brain search, this analysis revealed mostly a bilateral fronto-parietal-cerebellar network (Table 2 and Figure 5). No brain region was more active for number change than for notation change. In the converse direction, notation change yielded a supplemental increased activation in bilateral inferior and middle occipito-temporal cortex (Table 3), probably reflecting adaptation to the very different overall shapes of digits and dot patterns (Grill-Spector et al., 1999).

Given that the goals of the present study were to characterize the parietal number system, we focus here solely on the bilateral parietal clusters responding to number change. To study whether and how numerical coding in the IPS was modulated by the format of presentation of the numbers we isolated, for each subject, within the two IPS regions identified by the group analysis, the voxel where the largest fMRI response to numerical distance was found (mean and SD of the coordinates across subjects = −32(5), −57(6), 46(10) in the left hemisphere and 46(4), −42(5), 47(6) in the right hemisphere). We then plotted activation in these voxels as a function of our experimental conditions (see Figure 5). In both hemispheres, overall activation was higher when the numerical distance between deviant and adaptation values was large than when it was small (main effect of numerical distance $F(1,13) = 73.48$, $p < 0.000$ and $F(1,13) = 74.74$, $p < 0.000$ for the left and right hemispheres, respectively). Moreover, adaptation and deviant notation interacted ($F(1,13) = 37.6$, $p < 0.000$ for the left and $F(1,13) = 11.45$, $p < 0.005$ for the right hemisphere), indicating that changing notation also
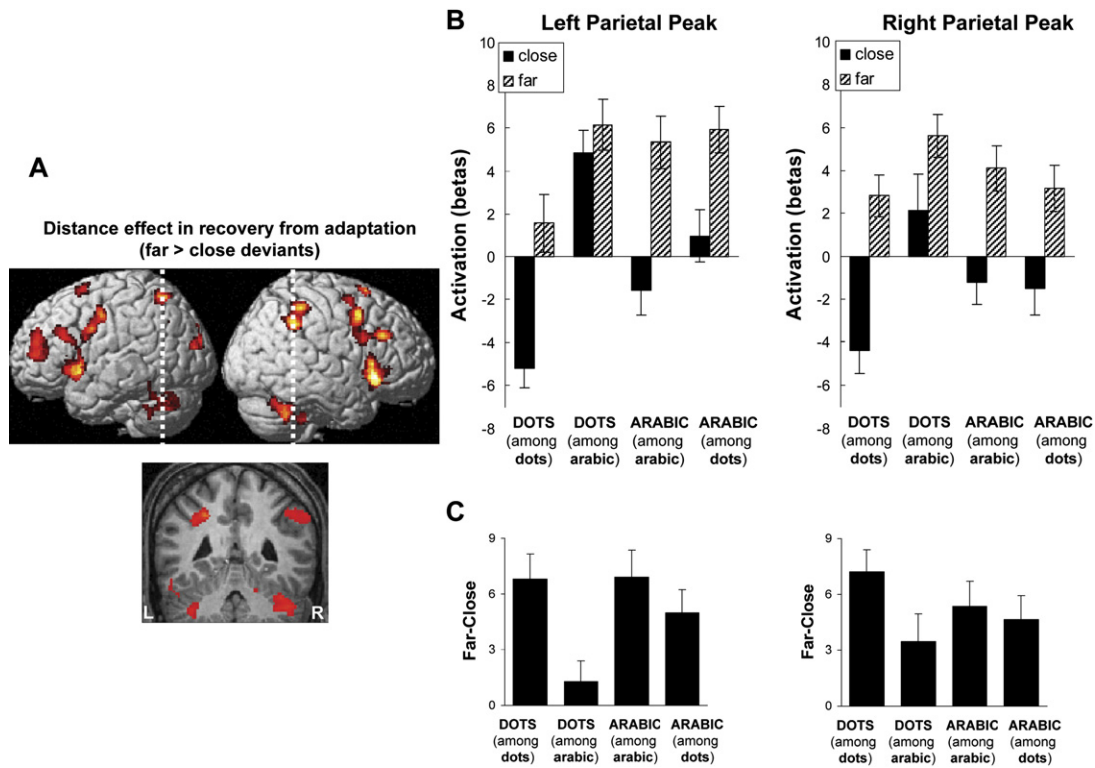
Table 2. Regions Showing a Distance-Dependent Recovery from Adaptation during Presentation of the Numerical Deviants (Far > Close)

x	y	z	Z Score	Cortical Region
−34	−62	60	3.75	Left parietal
−26	−50	40		
−24	−58	58		
48	−44	38	3.63	Right parietal
54	−40	52		
42	−44	52		
−36	22	−4	3.79	Left insula
−34	20	6		
36	22	6	5.01	Right insula
44	24	−4		
−8	12	46	4.01	Medial precentral/cingulate
4	12	30		
44	28	28	3.70	Right DLPF/precentral
40	4	42		
32	−2	60		
−30	48	18	3.44	Left anterior frontal
44	−52	−38	3.66	Left cerebellum
28	−60	−28		
−38	−66	−38	3.52	Right cerebellum
−26	−68	−28		
−4	−90	12	3.14	Primary visual cortex

had an effect on the activity of IP cortex. However, importantly, in the right hemisphere the effect of numerical distance did not interact either with deviant notation or with adaptation notation ($p > 0.1$), indicating that the effect of number change and of notation change are additive.

In the left hemisphere, a large change in number generally yielded stronger activation than a small change (see Figure 5), but there was an exception when deviant dots were presented among digits. This was reflected in a triple interaction of adaptation notation, deviant notation, and numerical distance ($F(1,13) = 8.00$, $p < 0.05$). When deviant dots were presented among digits, there was a large recovery from adaptation even for small numerical distances, contrary to the symmetrical situation where deviant digits were presented among dots for which a small numerical distance did not yield recovery from adaptation. In order to visualize this effect more easily, we calculated and plotted for each subject and hemisphere the size of the distance effect (the difference between the activation of far versus close deviants; see Figure 5C). A paired t test confirmed that in the left hemisphere the distance effect for dots amongst digits was smaller than in the right hemisphere ($T(13) = −1.87$, $p < 0.05$), where it did not differ in size from the other conditions. This effect was small but

Figure 5. Distance Effect in the Recovery from Adaptation to the Sparse Deviants
(A) Regions showing a distance-dependent response to the deviant stimuli.
(B) Amount of recovery to deviant stimuli at the peak voxels in left and right parietal cortex, as a function of adaptation notation, deviant notation, and the numerical distance between the deviant and adaptation stimuli.
(C) Distance effect (activation to far − close deviants) as a function of adaptation and deviant notation of the same peaks as in (B). (error bars represent ±1 SEM).

present in 10 out of 14 subjects (70%). It was only found by the region-of-interest method, as no other region showed a significant interaction of distance and notation in the whole-brain analysis. In the discussion, we consider a tentative interpretation of this unexpected asymmetric adaptation effect in terms of the degree of precision of the internal representations of symbolic and nonsymbolic quantities (Verguts and Fias, 2004). Most importantly, however, for the issue of notation-independent coding is the fact that distance-dependent crossnotation fMRI recovery was significant in both left and right parietal cortices when deviant digits were presented amongst dots ($t(13) = 3.99$, $p < 0.01$ and $t(13) = 3.64$, $p < 0.01$, for the left and right parietal cortices, respectively). These results show that the magnitude code of the parietal cortices is common to numerosities and numerical symbols.

While the above analysis focused on the peak of overall recovery from adaptation, very similar results were observed when we selected the parietal regions of interest on the basis of a completely independent data set. All but one subject performed an additional final 5 min long event-related fMRI scan during which they were asked to perform mental calculations with visually or auditory presented number words ("*Subtract five from eleven*") or

to simply attend to visually or auditory presented short sentences ("*The sailors threw the anchor into the bay*"). The contrast between mental calculation and sentence comprehension is a reproducible localizer of parietal activations (P. Pinel et al., 2006, poster presented to NUMBRA/ESCOP Summer School "Neuroscience of number processing"). We used this localizer to isolate, for each subject, within the parietal cluster from the random-effect group analysis of the localizer contrast, the peak voxel that best responded to mental calculation across modalities (see Table 4 for the parietal coordinates from the random effect analysis and Figure 6 for a picture of the whole

Table 3. Notation Change > Number Change

x	y	z	Z Score	Region
28	−42	−8	4.18	Right fusiform gyrus
32	−56	−10		
−32	−48	−8	4.02	Left fusiform gyrus
−26	−36	−16		
−14	−60	10	3.52	Left lingual gyrus
−16	−52	2		

Table 4. Mental Arithmetic > Sentence Comprehension (Parietal Clusters)

x	y	z	Z Score	Region
−45	−48	−48	4.88	Left parietal
−30	−72	−39		
−21	−60	54		
45	−45	45	3.95	Right parietal
33	−54	45		
30	−72	42		

circuit for the contrast calculation > sentence comprehension across modalities). The mean and standard deviation of the coordinates across subjects were of −37(8), −54(10), 46(7) in the left hemisphere, and 40(8), −49(14), 45(5) in the right hemisphere (for the one subject for whom we did not have the localizer scan we used the maxima from the group analysis). Those coordinates fell quite close to those isolated by the effect of numerical distance in the main adaptation experiment (indeed, 72% of the voxels responding to a distance effect in left hemisphere and 53% in the right hemisphere were also active in the calculation-sentence contrast), and the profile of activation across conditions was very similar (compare Figures 5 and 6). An ANOVA confirmed that in both hemispheres the activation increased with the numerical distance between deviant and adaptation values ($F_{(1,13)}$ = 5.6, p < 0.05 and $F_{(1,13)}$ = 10.37, p < 0.01 for the left and right hemispheres, respectively). Adaptation and deviant notation interacted ($F_{(1,13)}$ = 13.9, p < 0.05 and $F_{(1.13)}$ = 14.4, p < 0.05 for the left and right hemispheres, respectively), indicating that changing notation has also an effect on the activity of IP cortex. Finally, numerical distance did

not interact with deviant notation or with adaptation notation, indicating that the code for number is notation invariant. The triple interaction, however, approached significance, again only in the left hemisphere ($F_{(1,13)}$ = 3.76, p = 0.07), in line with the previous analysis.

DISCUSSION

Our results indicate an important role for parietal cortex in the coding of symbolic and nonsymbolic quantities. We investigated adaptation to number as well as recovery from adaptation in the parietal cortex at two different temporal scales. We now successively discuss those phenomena and their implications for issues of semantic-level representation and domain specificity in the number domain.

Adaptation

We showed that adaptation of IPS activity to a fixed approximate quantity is a slow, continuous process that takes several tens of seconds: activation continued to drop during the entire 30 s period where a given approximate numerical magnitude was repeated. Although our experiment was not designed to separate adaptation effects specifically related to number from those associated with low-level visual repetition effects, the fact that activity eventually decreased following repetition of the same approximate numbers is not trivial, given the large variability in the visual properties of the stimuli during the repetition phase. For digits, we randomized across trials not only the identity of the stimuli (17-18-19 or 47-48-49), but also their size and position. For nonsymbolic stimuli, the number, size, and position of the dots also varied from trial to trial. Given such variability, it might not be surprising that activation takes a long time to adapt and stabilize.
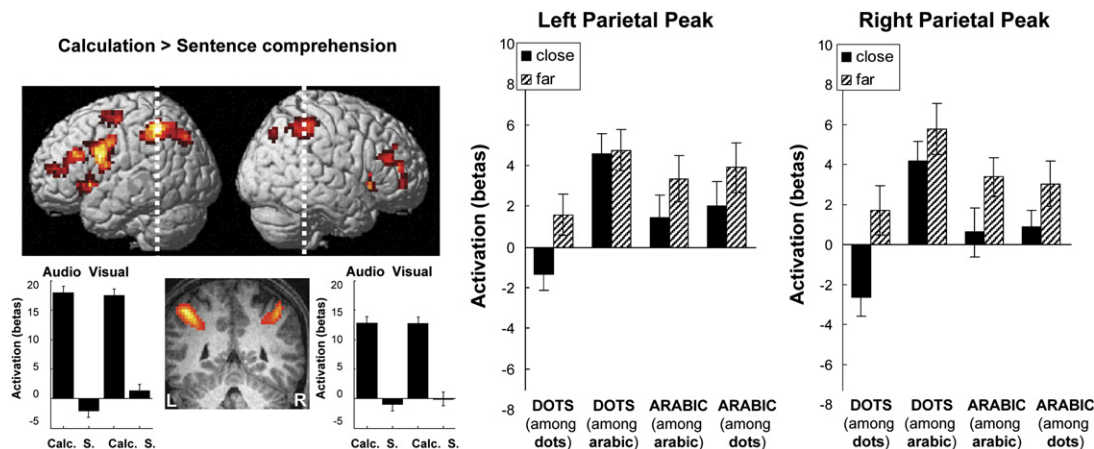
Figure 6. Localization and Response Profile of Parietal Regions Involved in Calculation
Left, brain regions with greater activity during mental calculation than during sentence comprehension. Insets show the activation of the peak voxels in parietal cortex for calculation (Calc.) and sentence comprehension (S.), showing identical responsivity whether the stimuli were presented in the visual or auditory modalities. Right, amount of recovery to deviant stimuli in the same parietal voxels as a function of adaptation notation, deviant notation, and numerical distance between the deviant and adaptation stimuli (error bars represent ±1 SEM).

The slow adaptation dynamics may shed some light on a recent controversy surrounding numerical adaptation. Our group previously used fMRI adaptation to demonstrate approximate coding of numerosity in the parietal cortex (Piazza et al., 2004), and this was later replicated by another group (Cantlon et al., 2006), but others reported the absence of such an effect (Shuman and Kanwisher, 2004). Crucially, the paradigms differed. In their adaptation experiment (experiment 2), Shuman and Kanwisher (2004) used a block design with blocks of 16 s during which they either repeatedly presented the same number or very different numbers of objects. Piazza et al. (2004), however, used an event-related design and analyzed activity triggered by rare deviant numbers within long blocks of several minutes with a fixed numerosity (Cantlon et al. [2006] then adopted this design). According to present results, the activation after 16 s of repetition of the same number (the length of a block in Shuman and Kanwisher's study) is still about 85% of its peak height. The maximal reduction of the signal, down to 40% of the initial peak height, is seen only 36 s after the onset of stimulation. Thus, the short adaptation period used by Shuman and Kanwisher (2004) might explain why they failed to observe an adaptation effect. Furthermore, Shuman and Kanwisher (2004) examined only the mean activity averaged over a whole block of 16 s, which might have further reduced the chances to detect a small adaptation effect. According to the present results, this effect presumably might have become barely visible at the end of the 16 s block.

Rebound Effect

When the adaptation numerosities changed abruptly (e.g., from 17, 18, 19 to 47, 48, 49), we observed a durable rebound in the fMRI signal. Since this rebound was identical whether there was a concomitant change in notation or not, it is already suggestive of a notation-invariant code in the IPS.

Response to Close and Far Deviants

In the critical trials, we measured the presence of a local recovery from adaptation when rare deviant stimuli were presented among adaptation stimuli. Furthermore, we compared close deviants, which fell when within the known coarseness of numerosity coding in the IPS and where we therefore expected continuing adaptation, with far deviants, for which we expected recovery from adaptation. The results confirmed to this prediction. In the dots-to-dots condition (deviant dots presented among dots), they reproduced earlier findings of numerical adaptation and distance-related recovery for nonsymbolic sets of dots (Piazza et al., 2004; Cantlon et al., 2006). The present activation extended further laterally and anteriorily in parietal cortex, a difference which may merely be due to interindividual difference between subjects participating in the two experiments (P. Pinel et al., 2006, poster presented to NUMBRA/ESCOP Summer School "Neuroscience of number processing"). However, beyond parietal cortex, the present study also revealed extended distance-related activation of bilateral prefrontal and inferior frontal cortices, whereas only two small parietal clusters were observed in our previous study (Piazza et al., 2004). A possible explanation for this difference across studies might be that number changes were much more evident in the present study, due both to the use of a large distance and to their presentation in digital format. The detection of a large (semantic) difference might have amplified the activation of a prefrontal cingulate attentional-arousal system. In our previous study, by contrast, number changes were not mentioned in the instructions and remained undetected by most subjects. Differences in conscious awareness of changes may thus explain the difference in the extent of the distance related activation across studies. It is possible, however, that beyond parietal cortex, other regions contain populations of neurons that also code for number, as observed in the prefrontal cortex of macaque monkeys (Nieder et al., 2002).

The results in the Arabic-to-Arabic condition also extended earlier work from our laboratory on subliminal repetition priming for Arabic digits and number words (Naccache and Dehaene, 2001). In a number comparison task where each target was preceded by a subliminal prime, Naccache and Dehaene (2001) showed reduced activation (repetition suppression) confined to bilateral parietal regions during repetition priming (e.g., prime 1 followed by target 1) compared to nonrepetition trials (e.g., prime 4, target 1). Response time measures indicate that such priming varies continuously with the distance between the prime and target (Koechlin et al., 1999; Reynvoet et al., 2002). The present results are the first to show such numerical distance-based priming in fMRI. Note that we carefully selected the adaptation and deviant sets so that, on both close and far deviant trials, there was an equal amount of change in the physical properties of the stimuli for the two distance conditions (e.g., adaptation to 17, 18, 19, deviants 20 versus 50). Thus, the observed recovery of adaptation in parietal cortex can only be attributed to semantic proximity, not to visual resemblance or to generic attentional mechanisms.

Third, and crucially, we observed crossnotation adaptation and recovery, particularly in the right parietal cortex, supporting the idea that shared neural populations encode nonsymbolic quantities and symbolic stimuli (Dehaene et al., 2003; Verguts and Fias, 2004). Converging evidence for a notation-independent code for number in the parietal cortex comes from a study showing overlapping activation of the IPS when participants performed mental arithmetic on both digits and dice dot patterns (Venkatraman et al., 2005). In principle, however, overlap of activation need not necessarily imply shared neural substrates. fMRI adaptation by contrast, implies that the neural populations that were adapted to one notation generalized their responses to the other notation, thus providing a more valid inference for a shared notation-invariant mechanism.

Note that due to the limitation of the present fMRI resolution we cannot exclude that within the region individuated in the present study there might be separate subassemblies of neurons that each code for a given input format but are highly interconnected. According to this scenario, under the present experimental circumstances, where notations were mixed in the same runs, activation of one given population (say, for example, coding for dots) would quickly spread to the other population (say, for example, coding for digits), thus leading to crossnotation adaptation. With the present experiment we cannot disentangle between these two possibilities, which, de facto, do not differ substantially at the population level. This issue might be ultimately be resolved only by means of higher-resolution fMRI (Grill-Spector et al., 2006) or by single-unit recordings. Interestingly, preliminary results on single-unit recordings in macaque monkeys show that, after the animal has undergone extensive training associating sets of dots with Arabic digits, there are neurons in the IPS that code for the preferred numerical value irrespective of whether it was presented by dot displays or numerals (I. Diester and A. Nieder, 2006, FENS Abstr., abstract). These results suggest that even the macaque brain can integrate numerical information across symbolic and nonsymbolic notations at the level of the single neuron.

Asymmetry in Recovery from Adaptation

We unexpectedly observed an asymmetry in fMRI responses to deviant stimuli in the left parietal lobe; there was a normal recovery when a distant digit was presented amongst dots, but there was an abnormal recovery independent of numerical distance whenever deviant dots, whether numerically close or far, were presented among digits. Although this effect was small and is therefore in need of replication, an interesting tentative interpretation is in terms of the precision of numerical coding. Dehaene (1997) suggested and Verguts and Fias (2004) demonstrated in a neural network simulation that the neural code for symbolic stimuli might be more precise than the neural code for nonsymbolic stimuli. Crucially, in Verguts and Fias's network, each number neuron has a preferred numerosity which is identical for symbolic and nonsymbolic numerical displays. However, the neuron has a broad tuning curve over numerosities when those are presented as dot patterns (reproducing the electrophysiological findings of Nieder et al. [2002]), and a very sharp, though still distance-dependent tuning curve when numbers are presented in symbolic format. How would such a population code explain the observed asymmetrical priming? During adaptation to dots, given the neuron's broad tuning curves, a large population of number neurons would adapt. The adapted population, being broadly tuned, would clearly include the narrow population of neurons responsive to the close symbolic numerals presented as deviants, hence the transfer of adaptation to close symbolic numerals. In the converse direction, however, adaptation to digits would not lead to the adaptation of the population code for dots. Only a relatively narrow

population of neurons would be adapted. Its breadth might be sufficient for a transfer of adaptation to nearby Arabic numerals, especially given that a range of adaptation values were used (e.g., 17, 18, 19, followed by deviant 20). However, most of the broad population code for the corresponding dot patterns would not have been adapted, thus resulting in a large recovery in the digits-to-dots condition on both close and far trials. Hence, our unexpected finding can in fact be seen as a natural prediction of the independently motivated Verguts and Fias (2004) model.

An alternative scenario which could also lead to the present observations supposes that what differs between symbolic and nonsymbolic representations of numbers in the left hemisphere is the relative number of neurons that code for each notation. In order to account for our observations, one would need to assume that, for any given number, there are more neurons coding for dots arrays than for Arabic digits. The present experiment does not allow distinguishing between the two alternatives. For the time being, given that fMRI can only observe activity pooled across large number of neurons, we should refrain from further speculation on this point and note simply that our results point to a population code invariant to the notation used for number presentation.

Hemispheric Asymmetry

Existing models of number processing do not explicitly address the question of the hemispheric asymmetry in the precision of the neural code for number. Interestingly, the asymmetry in crossnotation priming was only found in the left hemisphere, which may suggest, according to the Verguts and Fias (2004) model, that only the left parietal representation has been affected by the acquisition of number symbols and has acquired a refined precision, while the right parietal representation has kept a coarse representation for both symbolic and nonsymbolic notations. Several previous results bring some support to this hypothesis. In a developmental fMRI study, Rivera et al. (2005) found that activation during a calculation task with symbolic digits increased with age in the left parietal and left occipito-temporal cortices, but not in the right parietal lobe. Along this same line, Cantlon et al. (2006) reported that the only region showing overlapping activation in preschool children and adults during processing of numerosity was the right IPS. Both results together suggest that the right IPS is predominant for nonsymbolic numerosity coding in childhood and that the left IPS develops as a function of experience with numerical symbols. In adults, Piazza et al. (2004) also observed that although numerical adaptation was present in both left and right IPS, the precision of the representation, as measured by the Gaussian tuning curve for recovery of adaptation, tended to be higher in the left than in the right IPS. Finally, the two hemispheres seems to be differentially involved in approximate and exact numerical judgments: approximate judgments (in both the visual and auditory domain) correlate with stronger activation in the

right than in the left IPS, while exact judgments correlate with more activation in the left versus right IPS (Piazza et al., 2006). Along the same line, neuropsychologically, a superiority for the left hemisphere in exact calculation and for the right hemisphere in approximate calculation has been reported (Cohen and Dehaene, 1996; Dehaene and Cohen, 1991). Moreover, transcranial magnetic stimulation suggests that it is sufficient to stimulate the left parietal cortex to produce deficits for precisely coding numbers, while it is necessary to stimulate bilaterally to disrupt approximate numerical judgments (Andres et al., 2005). Imaging studies also tend to show right-lateralized parietal activation in tasks that involve comparisons and left lateralized activation when retrieving of exact arithmetical facts (Chochon et al., 1999; Dehaene, 1996; Pinel et al., 2001; Rickard et al., 2000). Outside the number domain, a similar hemispheric asymmetry has been proposed, whereby the left hemisphere would be superior for exact or categorical judgments, and the right for approximate, continuous or coordinate-based judgments (Kimura, 1996; Kosslyn et al., 1989; McGlone and Davidson, 1973; Pasini and Tessari, 2001; Piazza et al., 2004; Warrington and James, 1967; Young and Bion, 1979).

While there is thus tentative support for a difference in the precision of left and right hemisphere number codes, further work will be needed to directly establish the tuning curves for Arabic digits and for dot patterns. The fMRI adaptation method could again be used for that purpose. While we used here only two levels of distance (close and far deviants), a more continuous variation of deviancy, as in our previous work (Piazza et al., 2006), would allow one to trace the precision of the metric of proximity between numbers, separately for symbolic and nonsymbolic stimuli, and for the left and right hemispheres, thus directly testing the tuning curves predicted by Verguts and Fias (2004).

Criteria for Semantic-Level Representation

The present experiment used two independent criteria, both of which associate intraparietal cortex with a semantic level of representation: semantic metric (activation varies with proximity of meaning, here defined by numerical distance) and notation independence (activation is identical across major changes in input notation). We propose that those two criteria could be used to define semantic-level representation in domains other that numerical cognition (Maess et al., 2002). The IPS voxels isolated in the independent mental calculation localizer were also activated by both visual and auditory presented stimuli (see insets in Figure 6). This is further evidence for convergence toward a representation of numerical quantity that is independent from the task (mental calculation or passive viewing), from the modality of stimuli presentation (auditory or visual), and from the notation (symbolic or nonsymbolic). In this respect, our findings parallel those on the representation of object categories such as animals or tools in the occipito-temporal cortex, where activation (in the cases of brain imaging studies) and impairment

(in the cases of brain lesions studies) has been found consistent across modalities, notations (pictures and words), and tasks (naming, matching, reading; Caramazza and Shelton, 1998; Gorno-Tempini et al., 1998; Perani et al., 1999).

The Issue of Domain Specificity

Shuman and Kanwisher (2004) analyzed several ROIs from a mental calculation localizer similar to the one used in the present study and failed to observe a stronger response for number tasks than for closely matched color tasks. However, this logic supposes that an entire patch of intraparietal cortex is specialized for numerical processing, a hypothesis that we find unnecessary. The present results indicate a response to number change, with appropriate controls to suggest that this response can only come from neural populations coding for an abstract representation of numbers. They are, however, completely neutral relative to the issue of whether, within the same voxels, there might be other neural populations coding e.g., for color, size, space, time, or other such parameters. Indeed, previous work has reported an important overlap in the neural coding of number and object size (Cohen Kadosh et al., 2005; Pinel et al., 2004). In theory, deciding whether a given region is "specific" for any given category would require a systematic comparison of the target category (e.g., number) against a potentially infinite list of alternatives. Moreover, it is not clear which level of spatial precision is needed in order to test claims for specificity (voxels, columns, or single neurons; see Grill-Spector et al. [2006]). Even at the level of individual neurons, recent electrophysiological data shows that a subset of number-coding neurons in the macaque parietal cortex also responded to flow field stimuli in a direction selective fashion (I. Diester and A. Nieder, 2006, FENS Abstr., abstract). These results suggest that the question of domain specificity might be an ill-posed question or, at the very least, one very difficult to answer with fMRI alone.

The Symbol-Grounding Problem

A classical problem in semantics is the "symbol-grounding" problem of attaching meaning to the arbitrary shapes and sounds selected, in a given culture, to serve as written and spoken words (Harnad, 1999). Harnad proposed that symbolic representations are grounded bottom-up in nonsymbolic representations of two kinds: (1) "iconic representations," which are analogs of the proximal sensory projections of distal objects and events, and (2) "categorical representations," which are learned or innate feature-detectors that pick out the invariant features of object and event categories from their sensory projections. Elementary symbols (such for example "2" or "nine") are the names of these object and event categories, assigned on the basis of their (nonsymbolic) categorical representations. Harnad's second case may provide a solution to the symbol-grounding problem for numbers. Our results show that, at least in the adult brain, numerical symbols and nonnumerical numerosities converge onto shared

neural representations. Perhaps we attach meaning to symbols by physically linking populations of neurons sensitive to symbol shapes to preexisting neural populations holding a nonsymbolic representation of the corresponding preverbal domain (e.g., numerosity). Behavioral findings indeed suggest that the nonsymbolic numerosity representation is present in infants and adults prior to the acquisition of number words and symbols (Brannon, 2006; Feigenson et al., 2004; Pica et al., 2004) and is thus available to serve as the foundation for symbol grounding in the number domain. An unresolved difficulty, however, is that symbolic numerals do not merely refer to approximate numerosities but ultimately come to acquire exact meanings (e.g., exactly seventeen), which do not seem available in the absence of language and education. The nature of this "crystallization" of exact number concepts remains an unsolved issue, for which the present methods might ultimately turn out to be useful.

EXPERIMENTAL PROCEDURES

Participants

Fourteen healthy human adults participated in the study after giving written informed consent. All were right handed (Edimburgh Inventory) and had normal or corrected-to-normal vision. The study was approved by the regional ethical committee (Hopital de Bicêtre, France).

Stimuli and Procedure

Stimuli were dot patterns and Arabic digits. Both were presented for 150 ms at a constant rate of one every 1200 ms, white on a black background, varying in size and position within an invisible circle of 5° radius around fixation. Dot patterns were designed so that, aside from the number change, all deviant stimuli were equally novel with respect to all physical parameters. In half of the blocks, total luminance and total occupied area (extensive parameters) were equated across the deviant stimuli. This means that dots in the deviant number 50 had on average smaller individual item sizes and smaller inter-item spacing. However, the latter parameters (intensive parameters) were varied randomly and equated on average across the adaptation stimuli: adaptation stimuli were generated with item size and inter-item 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 adaptation and were therefore *equally nonnovel*. Therefore, the only novel aspect of the deviant stimuli was number. In the other half of the blocks, the parameters were controlled in a symmetric fashion (e.g., the extensive parameters were equated across the adaptation and the intensive parameters across the deviant stimuli). An automated program (freely available on our website [http://www.unicog.org/main/pages.php?page=Documentation]) generated random configurations within those constraints, so that stimuli were never repeated identically during the experiment. (see also Piazza et al. [2004]). Arabic digits were presented in Arial font and varied, from trial to trial, in size (from 16 to 33 point size) and position (within a circle of 5 degrees radius around fixation).

There were two types of periods, those where the majority of the stimuli were sets of dots and those where they were Arabic numbers, both with a fixed (though approximate) quantity. Occasionally, a deviant stimulus occurred randomly, with the constraint that two successive deviants were separated by at least three and at most seven adaptation stimuli. Adaptation numbers varied randomly between 17, 18, and 19 in half of the experiment, and between 47, 48, and 49 in the other half. Deviant stimuli always differed from the adaptation number, but there was either a small deviation (the deviant was in the same

range as the adaptation, for example 20 among 17, 18, and 19), or a large deviation (ratio of 2.4, for example 20 among 47, 48, and 49). Furthermore, items in the deviant sets could be of the same notation or of a different notation of the adaptation sets, thus defining fully orthogonal notation-change and number-change factors (see Figure 1 for examples of stimuli).

The experiment was divided into four runs. Each run consisted in 206 stimuli and started with a 12 s resting period, during which a small centered fixation cross, which remained visible throughout all the experiment, was presented on the screen. Each run consisted in two blocks separated by a 12 s rest period. Finally, each block comprised two different adaptation sequences (A1 and A2; see Figure 2). The first 25 and the last 6 stimuli of each sequence were adaptation stimuli only, while in the central part of each sequence, deviants (12 stimuli overall) appeared among the adaptation stimuli (60 overall). A2 followed A1 without a break.

To avoid decision and response confounds, participants were simply instructed to fixate and to pay attention to the quantity conveyed by the stimuli. They were informed that they would be shown quantities in different formats and that their approximate values would be ~20 and ~50. Moreover, immediately prior to the scanning session, subjects were shown approximately four exemplars of each numerosities (17:20 and 47:50 dots) and informed about their approximate range (~20 and ~50, respectively) in order to calibrate them.

Thirteen subjects (out of fourteen) performed an additional 5 min long event-related fMRI scan for isolate individual neural correlates of mental calculation. This short functional localizer sequence was routinely used to map various individual cortical networks involved in motor action, reading, language comprehension, and mental calculation. Subjects were engaged in various tasks such as left or right clicking after audio or video instruction, mental calculation (subtraction) after video or audio instruction ("*Subtract five from eleven*"), sentence comprehension from audio or visual modality ("*The sailors threw the anchor into the bay*"), and passive viewing of horizontal or a vertical checkerboards. For this paper, we only considered the calculation task and used sentence comprehension as a control. For the mental calculation task, subjects were asked to perform the operation silently ("in their head") and not to utter the result, while for the sentence comprehension they were asked to simply listen (or read) attentively.

fMRI Parameters

The experiments were 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 (TR [repetition time] = 2.4 s, TE [echo time] = 40 ms, angle = 90°, FOV [field of view] 192 × 256 mm, matrix = 64 × 64). The whole brain was acquired in 40 slices with a slice thickness of 3 mm. High-resolution images (3D gradient echo inversion-recovery sequence, TI [inversion time] = 700 mm, 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 SPM2 (http://www.fil.ion.ucl.ac.uk/spm). The first four volumes were discarded for each experiment. All other volumes were realigned using the first volume as reference, normalized to the standard template of the Montreal Neurological Institute using an affine transformation, resampled (2 × 2 × 2 mm), spatially smoothed (6 mm), and low-pass (4 s) filtered. Activations for the main experiment were modeled by a linear combination of (1) eight functions derived by convolution of the standard hemodynamic function with the known onsets of the different types of deviants (2 × 2 × 2 design with factors of distance [close, far], deviant notation [dots, digits], and adaptation notation [dots, digits]) and (2) sixteen linearly decreasing regressors, modeling the adaptation in the first part of each adaptation period (A1 and A2). Parameters of no interest were also entered, coding for the horizontal and vertical location of the dot

and digit stimuli on screen, and for the size of the digits. Random effect analyses were then applied to several contrasts: the main effects of number and notation change in deviants, and the main effect of the regressors modeling the beginning of each adaptation period.

For the additional functional localizer, activations were modeled by eight functions derived by convolution of the standard hemodynamic function with the known onsets of the different types of task and modality trials. In the present analysis, we looked for regions showing increased activation for subtraction relative to sentence comprehension, in both the visual and auditory modality (random effect analyses of the contrast looking for the main effect of calculation across modalities). Data for both experiments are reported at $p < 0.05$ corrected for multiple comparisons at the cluster level, $p < 0.01$ at the voxel level.

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