Neuron, Vol. 44, 1–20, October 28, 2004, Copyright ©2004 by Cell Press

Numerical Magnitude in the Human Parietal Lobe: Tests of Representational Generality and Domain Specificity

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Summary

Behavioral evidence suggests that human adults have a single system for representing the numerical magnitude of both symbolic numbers (e.g., Arabic digits) and nonsymbolic number stimuli (e.g., dot arrays). Brain imaging studies have implicated a specific parietal region in symbolic number processing, leading to the influential hypothesis that this region is the locus of a dedicated, domain-specific number system. Here we evaluated a prediction of this hypothesis, that this region should be activated not only by symbolic but also nonsymbolic number processing. Using nonsymbolic stimuli, we tested for higher parietal activations for number than for nonnumber comparison tasks (experiment 1), fMRI adaptation for numerosity repetition (experiment 2), and greater fMRI increases with increasing task difficulty for number than nonnumber tasks (experiment 3). None of these predictions were supported by the data, posing a serious challenge to the hypothesis that a single, domain-specific parietal region underlies both symbolic and nonsymbolic number representation.

Introduction

Several converging lines of evidence support the hypothesis that animals, infants, and human adults have a biologically determined, domain-specific system for representing number (Dehaene et al., 1998). Brain imaging studies on number processing further suggest that a specific region of the parietal lobe may underlie this system (Dehaene and Cohen, 1997; Dehaene et al., 1999; Eger et al., 2003; Naccache and Dehaene, 2001; Pinel et al., 2001; Simon et al., 2002; see Dehaene et al., 2003, for a review). However, most of the relevant imaging work has used symbolic number tasks (performed on number words or digits) exclusively. Here we use fMRI to test whether the parietal regions engaged by symbolic number tasks are also engaged by nonsymbolic number tasks (performed on stimuli such as dot arrays), as is expected if these regions underlie an innate, domain-specific system for number representation.

Behavioral studies have shown that symbolic number processing in human adults is similar in important respects to the nonsymbolic number processing common to animals, infants, and human adults. For example, Moyer and Landauer (1967) demonstrated a "distance effect" for symbolic number comparison in human adults (e.g., longer response times to compare 4 and 5 versus 2 and 7) much like that observed for nonsymbolic numerosity comparison in both humans (Buckley and Gillman, 1974) and animals (Brannon and Terrace, 2000). These results, among others (see Gallistel and Gelman, 2000, for a review), support the hypothesis that a single system underlies the ability to represent the numerical magnitude of number symbols and nonsymbolic number stimuli alike.

fMRI, PET, and neuropsychological studies using symbolic number stimuli have all implicated regions of the parietal lobe in the processing and representation of number. Brain-damaged patients with focal parietal lesions can exhibit striking deficits in calculation and other aspects of number processing despite well-preserved language and semantic abilities (e.g., Cipolotti et al., 1991). Damage to other regions can also impair number processing, but double dissociations suggest that the parietal lobe may play a critical role in the representation of numerical magnitude (Dehaene and Cohen, 1997). In neuroimaging studies with symbolic number stimuli, parietal areas respond strongly during approximate addition (Dehaene et al., 1999; Stanescu-Cosson et al., 2000) and during calculation (Chochon et al., 1999; Dehaene et al., 1996; Gruber et al., 2001; Lee, 2000; Pesenti et al., 2000; Rickard et al., 2000; Simon et al., 2002; Zago et al., 2001) and show distance effects in number comparison (Pinel et al., 2001) as well as priming between Arabic numerals and number words (Naccache and Dehaene, 2001). In a series of recent studies, Dehaene and colleagues have identified the horizontal segment of the intraparietal sulcus (HIPS) as the region most specifically involved in number representation (Dehaene et al., 2003; Simon et al., 2002), and Eger et al. (2003) have shown that the response of this region is higher for Arabic numbers than for letters or colors, even when task difficulty is controlled. However, very few neuroimaging or patient studies in humans have tested whether this parietal region is also involved in processing nonsymbolic number.

If the HIPS is truly the neural instantiation of a domain-specific system for the representation and processing of numerical magnitude—the primitive number system we share with children and animals and the one engaged by symbolic and nonsymbolic number tasks alike—then two straight-forward predictions follow. First, the same brain region should be engaged not only in symbolic number tasks but also in nonsymbolic number tasks. Second, this region should be engaged more strongly by numerical cognitive tasks than by difficulty-matched tasks that do not invoke numerical processing. The studies presented here tested these two predictions.

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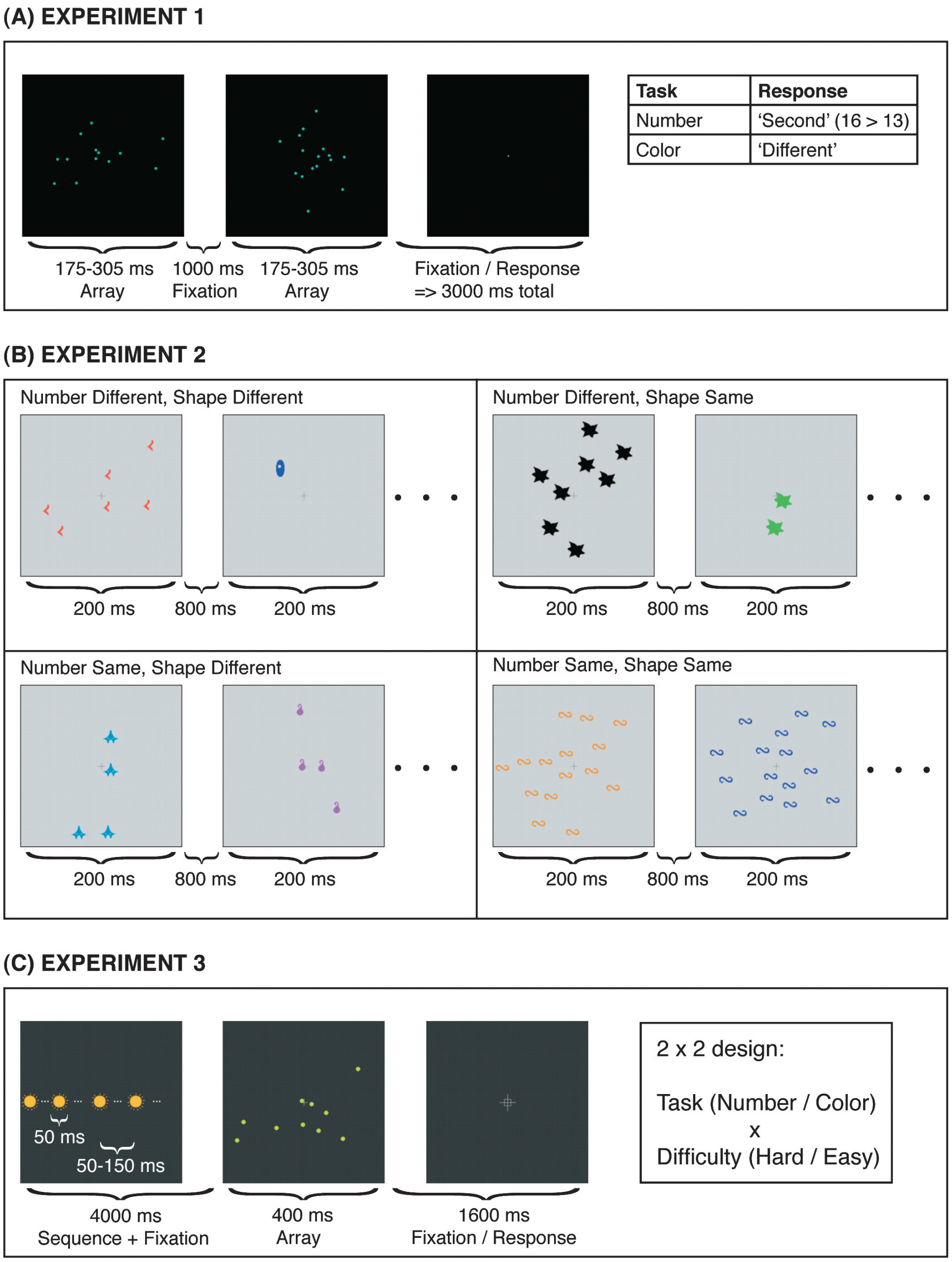

Figure 1. Stimuli and Design for Experiments 1 through 3

In each experiment, we scanned subjects on a different nonsymbolic number task as well as on the symbolic approximate number task of Dehaene et al. (1999). Each of the three experiments used a different method to manipulate nonsymbolic processing, allowing us to explore not only questions of localization and domain specificity but also questions pertaining to the format specificity of number processing.

In experiment 1, subjects were scanned while viewing sequentially presented pairs of dot arrays and comparing either the number or color of the dots in the two arrays (see Figure 1A), with the difficulty of the comparisons matched across tasks. If a domain-specific number system in the parietal lobe is engaged not only in symbolic (e.g., Dehaene et al., 1999) but also in nonsymbolic number processing, it should respond more strongly for the number task than the color task.

Experiment 2 was based on the fMRI adaptation effect found previously for symbolic number, in which the BOLD response was attenuated in the putative number area when the same numeral or number word was repeated (Naccache and Dehaene, 2001). We used a blocked fMRI adaptation design (Grill-Spector et al., 1999; Grill-Spector and Malach, 2001), showing subjects sequences of arrays that were either constant or randomly varied in each of two dimensions: the number of elements in the array and the shape of individual elements (see Figure 1B). We tested whether the BOLD signal in parietal regions that were implicated in number processing was lower during "constant" number blocks than during “varied” number blocks as well as whether any such adaptation was greater for repetitions of number than shape.

Experiment 3 was based on the report of higher parietal activation for comparison of close versus far digits (Pinel et al., 2001), an apparent neural correlate of Moyer and Landauer’s (Moyer and Landauer, 1967) behavioral distance effect. We asked whether an analogous neural distance effect would be found for nonsymbolic number stimuli. Subjects were presented with dot arrays followed by dot flash sequences and asked to judge either which had more elements/flashes or whether the dots in the two sets were the same or different color (see Figure 1C). Difficulty was varied on both tasks in a 2 × 2 blocked design crossing task (color versus number comparison) with difficulty (hard versus easy). We tested whether any cortical regions were more responsive to increased difficulty in the number task than in the color control task.

Results

Notes on the Analysis

We analyzed the neuroimaging data from each experiment in two different ways. The primary approach was to compare mean responses in each condition averaged across the voxels in each of several regions of interest (ROIs) reported in previous studies to be involved in approximate number representation. This is the most appropriate method for rigorously testing whether the neural response elicited by any specific task or stimulus condition generalizes to another task or stimulus condition. We also looked for significant differences in activation anywhere in the imaged brain volume using random effects group analyses; however, these should be regarded as secondary analyses, as they are less appropriate for directly testing the primary hypothesis that brain regions previously implicated in symbolic number processing should also be engaged in a domain-specific fashion by nonsymbolic number processing.

Several different ROIs were used. First, we analyzed the data in ROIs consisting of all the parietal voxels showing significant number-related activation in each of several important earlier studies: (1) Dehaene et al. (1999), (2) Simon et al. (2002), and (3) Fias et al. (2003). We also analyzed the data separately for each hemisphere for each of these ROIs. Second, we defined subject-specific ROIs by replicating the symbolic stimuli “approximate calculation” experiment of Dehaene et al. (1999) in every subject in each of our three experiments; individual ROIs were defined as regions showing significant activations in the “approximate versus letter” contrast (see Experimental Procedures). We also analyzed the data in an ROI based on our group analysis of this contrast. Finally, we analyzed the data in small spherical ROIs centered on each set of peak coordinates for number-related activations in earlier studies listed in the meta-analysis of Dehaene et al. (2003).

Replication of the Dehaene et al., 1999, “Approximate Calculation” Result

Random effects analyses (SPM 99) showed a significantly higher BOLD response in large areas along the intraparietal sulcus (IPS) for an approximate addition task compared to a letter-selection control task, replicating the findings of Dehaene et al. (1999) in each of the three experiments. A random effects analysis across all subjects ($n = 32$) yielded a similar pattern of activation (see red in Figure 2). Activation was stronger in the left hemisphere, but at lower statistical thresholds, bilateral IPS activations were clearly evident (see Supplemental Figure S1 [http://www.neuron.org/cgi/content/full/44/3/■■■/DC1/]). Analyses using published ROIs showed as expected that the approximate addition task resulted in significantly greater activation than the letter-selection control task in almost every number ROI we considered (see Table 1 for a summary of results).

Experiment 1

We carefully balanced the difficulty of the number and color tasks, resulting in nearly identical behavioral performance across tasks during scanning, both in terms of accuracy and response time. On the number comparison task, accuracy was 82.8% correct, with a mean response time (RT) for correct responses of 578 ms; on the color task, accuracy was 84.9%, with a mean RT of 583 ms. There were no significant differences in either accuracy or RT (paired Student’s t tests, $p > 0.05$.).

We observed no significantly greater BOLD fMRI response for the number comparison versus color comparison task in any ROI considered (see Table 2 for a summary of results or see Supplemental Table S2 [http://www.neuron.org/cgi/content/full/44/3/■■■/DC1/] for complete results). In fact, the average level of response in every one of these 47 ROIs was higher during the *color* comparison task than in the number comparison task, and in many, including the critical HIPS region, this difference was significant. Thus, our failure to find the predicted higher response for number than for color in the HIPS is not due to insufficient power: we found a significant effect, but it was in the wrong direction. This finding poses a challenge to the hypothesis that the previously reported parietal number area is engaged in representing numerical magnitude for both symbolic and nonsymbolic number in a domain-specific fashion.

A random effects group analysis found two regions with significantly higher activations for the number task than for the color task (see yellow in Figure 2): one in the inferior temporal gyrus (peak: $x = 57$, $y = -60$, $z = -9$) and one in the middle occipital gyrus (peak: $x = 42$, $y = -84$, $z = 21$). Neither activation was close to any area previously implicated in number cognition. Further analysis of these regions is presented at the end of the Results section.

One possible explanation for the lack of a higher parietal response to number than color tasks is that number processing with nonsymbolic stimuli may be automatic. If it is, equal activation might occur in “number areas” for any number-salient stimulus, independent of attention or task, leaving a constant-stimulus task manipulation doomed from the start. Evidence that *symbolic* number *is* processed automatically comes from the Stroop-like interference observed with digits (Pavese and Umilta, 1998; Pinel et al., 2004). In addition, there is at least one report in the literature (Pansky and Algom, 2002) of nonsymbolic numerosity biasing symbolic number judgments under certain conditions. We therefore

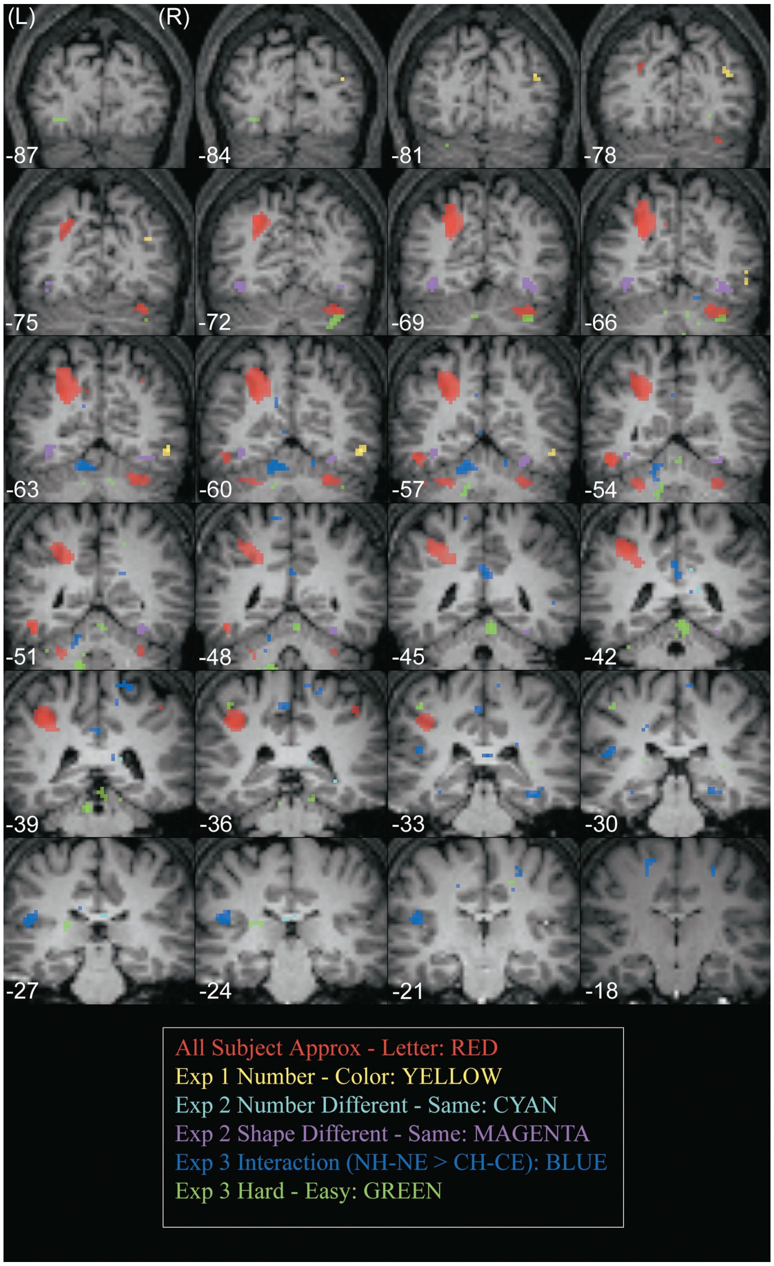

Figure 2. Random Effects Analyses

Regions showing significant activations ($T > 3.79$; $p < 0.003$–0.0003, see Experimental Procedures for details) for contrasts in all three experiments.

analyzed the behavioral data from our scans to see whether subjects performed any worse on the color task for number-inconsistent trials (in which the correct response was different from the correct response for the same stimulus in the number task) than for number-consistent trials, as predicted if automatic processing of number led to response interference. We found no significant decrement in performance for number-inconsistent versus number-consistent trials (see Supplemental Results for full analysis [http://www.neuron.org/cgi/content/full/44/3/■■■/DC1/]). Thus, if nonsymbolic number is processed automatically, such processing does not appear to have biased or interfered with response planning in this experiment. (See Supplemental Results for further analysis of the issue of automaticity and its relevance to the fMRI data.)

Experiment 2

The second experiment involved a completely different design, chosen in part for its potential to be sensitive to number processing even if it is automatic: fMRI adaptation (Grill-Spector et al., 1999; Grill-Spector and Malach, 2001). In this paradigm, the fMRI response is expected to be lower for repeated stimuli than for unrepeated stimuli in brain regions that process the relevant stimulus dimension, due to neural adaptation. Naccache and Dehaene (2001) reported significant adaptation in the IPS in an event-related fMRI design using symbolic number stimuli. We asked here whether any parietal regions would show attenuation for repeated numerosities in nonsymbolic displays, by varying whether the numerosity of shape arrays was constant within a block or varied (while orthogonally varying whether the elements in the

Table 1. ROI Analysis of Replication of Dehaene et al., 1999, “Approximate Calculation” Experiment

	Experiment 1				Experiment 2				Experiment 3				All Subjects			
Region of Interest	Data		Statistics		Data		Statistics		Data		Statistics		Data		Statistics	
	Aprx	Let	t(8)	p	Aprx	Let	t(14)	p	Aprx	Let	t(11)	p	Aprx	Let	t(31)	p
All Subjects Aprx-Let	0.17	-0.03	**3.08**	**0.02**	0.40	0.13	**5.19**	**<.01**	0.32	0.10	**3.55**	**<.01**	0.32	0.08	**>6.0**	**<.01**
Dehaene ‘99 Approx	0.12	-0.02	1.80	0.11	0.39	0.15	**4.13**	**<.01**	0.28	0.12	**2.36**	**0.04**	0.29	0.10	**4.94**	**<.01**
Simon ‘02 HIPS	0.15	-0.10	**3.49**	**0.01**	0.33	0.04	**4.86**	**<.01**	0.26	0.03	**3.53**	**<.01**	0.26	0.00	**>6.0**	**<.01**

Condition means are in units of percent signal change versus fixation. Significant values for statistical tests are show in **bold**; results consistent with the domain-specific number hypothesis are shown in blue, while results that go the “wrong way” are shown in red. Conditions: “Aprx”: Approximate Calculation; “Let”: Letter Matching Control Condition. Regions of interest: “All Subjects Aprx-Let”: ROIs defined by activation maps for random effects analysis of this experiment over all subjects. “Dehaene ’99”: The activations reported in Dehaene et al. (1999) for Approximate Calculation > Exact Calculation. “Simon ’02 HIPS”: Region activated significantly only for the Calculation condition in Simon et al. (2002), characterized as a “horizontal segment of the intraparietal sulcus” (HIPS).

arrays had constant or varied shape). These comparisons between “constant” and “varied” conditions allow rigorous control of low-level stimulus features—which would be very difficult to achieve in any other stimulus manipulation design involving nonsymbolic number.

ROI analyses (see Table 2) found no significant number adaptation effects in any region previously identified as involved in number processing. The mean percent signal change (PSC) versus fixation observed in the HIPS region (Simon et al., 2002) for the number-different condition (0.11) was actually lower than that for the number-same condition (0.14), as it was in 40 of the 47 “number” ROIs that we considered. A similar pattern of results was observed when we analyzed the response from the second half of each block alone (where adaptation effects should be strongest). Our failure to find number adaptation in the HIPS is not simply due to insufficient statistical power: the 95% confidence interval for the difference between these conditions in the HIPS [−0.071: −0.003] is entirely negative, supporting a strong inference

Table 2. ROI Analyses for Experiments 1 through 3

(A) Experiment 1	Data (Condition Means)		Statistics	
			Number-Color	
	Number	Color	T(8)	p
Individually Defined	0.09	0.20	**2.75**	**0.03**
All Subjects Approx-Letter	0.11	0.15	**2.60**	**0.03**
Dehaene ‘99 Approx	0.13	0.16	1.72	0.12
Simon ‘02 HIPS	0.08	0.15	**2.64**	**0.03**

(B) Experiment 2	Data (Condition Means)				Statistics					
					Number Different-Same		Shape Different-Same		Interaction	
	Diff Number Diff Shape	Same Number Diff Shape	Diff Number Same Shape	Same Number Same Shape	F(1,14)	p	F(1,14)	p	F(1,14)	p
Individually Defined	0.29	0.26	0.29	0.34	0.10	0.76	0.92	0.36	1.15	0.30
All Subjects Approx-Letter	0.20	0.21	0.21	0.22	0.57	0.46	0.67	0.43	0.00	0.94
Dehaene ‘99 Approx	0.25	0.25	0.24	0.25	0.22	0.65	0.02	0.90	0.08	0.77
Simon ‘02 HIPS	0.10	0.14	0.11	0.15	3.87	0.07	0.21	0.66	0.01	0.94

(C) Experiment 3	Data (Condition Means)				Statistics					
					Number-Color		Hard-Easy		Task X Difficulty	
	Hard Number	Easy Number	Hard Color	Easy Color	F(1,11)	p	F(1,11)	p	F(1,11)	p
Individually Defined	0.58	0.51	0.62	0.41	0.24	0.64	**16.87**	**<.01**	1.38	0.27
All Subjects Approx-Letter	0.18	0.14	0.26	0.15	2.07	0.18	**7.08**	**0.02**	1.74	0.21
Dehaene ‘99 Approx	0.18	0.15	0.23	0.11	0.01	0.92	**6.08**	**0.03**	1.84	0.20
Simon ‘02 HIPS	0.14	0.11	0.25	0.14	**8.24**	**0.02**	**7.48**	**0.02**	2.10	0.18

Condition means are in units of percent signal change versus fixation. Significant values for statistical tests are show in **bold**; results consistent with the domain-specific number hypothesis are shown in blue, while results that go the “wrong way” are shown in red. Regions of interest: “Individually Defined”: ROIs defined in each subject by activation maps for the Approximate Calculation replication. “All Subjects Approx-Letter”: ROIs defined by activation maps for random effects analysis of the Approximate Calculation replication over all subjects. “Dehaene ’99”: The activations reported in Dehaene et al. (1999) for Approximate Calculation > Exact Calculation. “Simon ’02 HIPS”: Region activated significantly only for the Calculation condition in Simon et al. (2002), characterized as a “horizontal segment of the intraparietal sulcus” (HIPS).

that there is no attenuation in HIPS activation for this kind of numerosity repetition. A random effects group analysis yielded several small clusters showing a higher response to varied-numerosity than constant-numerosity conditions, but none were close to previously reported parietal number areas (see cyan in Figure 2).

Nonetheless, we did observe a significant *shape* adaptation effect in a different brain region, in the same subjects, with the same stimuli. In the random effects analysis, well-defined bilateral areas in ventral occipital cortex showed a significantly attenuated BOLD response for stimulus blocks in which individual element shapes remained constant, compared to blocks in which element shapes changed with each new array presentation. These areas of significant shape adaptation (see magenta in Figure 2) are congruent with the reported locus of the shape and object processing region known as the lateral occipital complex (LOC) (Grill-Spector et al., 2001; Kanwisher et al., 1997; Malach et al., 1995). Although shape adaptation has been shown many times in this region (Grill-Spector et al., 1999; Kourtzi and Kanwisher, 2001), this experiment shows that shape adaptation can occur when only the local elements of a shape, not the global configuration, are repeated.

Table 3. Behavioral Data, Experiment 3

	Accuracy	RT		
Number hard	81%	885		
Number easy	90%	805		
Color hard	84%	841		
Color easy	96%	762		
	Accuracy		Response Time	
	t(11)	p	t(11)	p
Number hard-easy	**3.42**	**0.005**	**4.42**	**0.001**
Color hard-easy	**4.07**	**0.002**	2.57	0.026
Hard num-color	1.29	0.222	1.47	0.169
Easy num-color	1.75	0.106	1.92	0.081
	F(1,11)	p	F(1,11)	p
Hard-easy	**7.88**	**0.020**	**18.36**	**0.001**
Number-color	1.56	0.240	**5.33**	**0.041**
Interaction	0.14	0.710	0.00	0.974

Experiment 3

One possible explanation for the failure of experiments 1 and 2 to demonstrate nonsymbolic number effects is that they simply failed to elicit a number representation at all; there was no number-related *task* in the second experiment, and it is at least possible that subjects could have accomplished the numerosity comparison task in the first experiment using low-level, visual strategies based on continuous quantities confounded with number (statistically), like area. We addressed this possibility in experiment 3 using a task that should only be possible on the basis of some kind of abstract representation of numerical magnitude: comparing the numerosity of a dot array to the numerosity of a flash sequence. We also sought to explore the possibility that the putative parietal number area might be responsive to modulation of difficulty in nonsymbolic number tasks, as suggested by the "distance effect" observed both behaviorally and, with symbolic number tasks, in the fMRI experiments of Pinel et al. (2001).

Behavioral data collected during scanning confirmed that we were largely successful in matching difficulty levels for number and color comparison tasks (see Table 3 for a summary of results), as there were no significant differences in either accuracy or RT between number and color tasks at either difficulty level (paired Student's t tests, all $p > 0.05$). An ANOVA of RTs revealed significant main effects of difficulty ($F[1,11] = 18.4$; $p = 0.001$) and task (number > color; $F[1,11] = 5.3$; $p = 0.04$) but no interaction ($F[1,11] < 1$, $p > 0.5$). An ANOVA of accuracy revealed a main effect of difficulty ($F[1,11] = 7.88$, $p = 0.02$) but no main effect of task ($F[1,11] = 1.56$, $p > 0.20$) and no interaction ($F[1,11] < 1$, $p > 0.5$).

ROI analyses found no significant predicted task effect (number > color) or task × difficulty interaction (number hard − easy > color hard − easy) in any ROI we examined (see Table 2). In fact, the interaction was the reverse of that hypothesized—the difficulty effect was more pronounced for the color task than for the number task in 46 of the 47 ROIs considered, though this effect did not reach significance in any ROI. A significant main effect of difficulty (greater BOLD response for difficult number and color tasks compared to easy number and color tasks) was observed in a majority (25 of 47) of the ROIs considered. As in experiment 1, the response was actually higher during the color tasks than during the number tasks in most (33 of 47) of the "number" ROIs considered, and in many, including the critical HIPS region, the differences were significant—this despite the fact that the number tasks were, on average, slightly more difficult. Thus, again, our failure to find the predicted higher response for number than for color in the HIPS is not due to insufficient power: we found a significant effect, it was simply in the opposite direction to that predicted by the number domain-specificity hypothesis.

A random effects group analysis showed no regions with a significantly greater response to number compared to color. Several clusters showed a task × difficulty interaction (a greater difference in response for number hard − easy, compared to color hard − easy; see blue in Figure 2), but none were close to previously reported parietal number areas, and in several of them, including the lateral temporal cluster showing the strongest effect, all condition means were lower than fixation. One region in the anterior superior parietal cortex did show a significant main effect of difficulty, independent of task (see green in Figure 2), and this region is adjacent to the region of activation for approximate addition.

As with experiment 1, one possible reason for the lack of a higher parietal response to number than color tasks would be automatic processing of numerosity. For the subjects in experiment 3, we indeed did find significant impairments in color judgment performance for number-inconsistent versus number-consistent trials. These results contrast with those for experiment 1 (see Supplemental Results for full analysis [http://www.neuron.org/cgi/content/full/44/3/■■■/DC1/]). However, if automatic processing influenced both behavioral performance and neural activity, resulting in the lack of an observed parietal number response, we would expect to see a negative correlation across subjects between behavioral interference and number-color activation differences in the HIPS (*less* interference → *more* number-color effect). Instead, the correlation between the interference effect for accuracy (consistent − inconsistent accuracy) and the (number − color) fMRI response in the HIPS was small and positive ($r = 0.11$); the same was true for interference effects in RT (inconsistent − consistent) and number − color fMRI response ($r = 0.11$). Both of these effects are "in the wrong direction" and undermine support for the hypothesis that automatic numerosity processing is responsible for the lack of observed parietal number activation. (See Supplemental Results for further analysis of the issue of automaticity and its relevance to the fMRI data.)

Analyses across Experiments

Although our ROI analyses found no support for the hypothesis that parietal regions such as the HIPS underlie nonsymbolic as well as symbolic number representation and processing, it is worth considering whether our data contain evidence for the involvement of any other regions in nonsymbolic number processing. For exploratory purposes, we conducted low-threshold random effects analyses (see Experimental Procedures for details) for each experiment (see Supplemental Figure S1 [http://www.neuron.org/cgi/content/full/44/3/■■■/DC1/]). At the low threshold, several candidate clusters appear. First, several lateral temporal and parietal regions show an interaction effect for experiment 3; however, upon closer examination, all of these regions show greater activation for fixation than for any of the experimental conditions, making the relevance of the effect difficult to interpret. Second, a small region in left posterior parietal cortex shows a number adaptation effect (number different > number same) in experiment 2; however, this region shows a shape adaptation effect of greater magnitude, and again, the response is stronger for fixation than for any of the experimental conditions, making the relevance of this activation hard to interpret. Finally, right anterior parietal regions show (number > color) activations for both experiment 1 (see yellow in Supplemental Figure S1) and experiment 3 (see orange in Supplemental Figure S1), although these activations do not overlap. The fact that very similar contrasts between number and color tasks are present in each of these two experiments enables us to ask whether these low-threshold activations are reliable and meaningful by testing whether they replicate in an independent dataset. Thus, we constructed ROIs based on the low-threshold activations for each experiment (1 and 3) separately and then examined the response in both datasets. The results are shown in Figure 3. In the ROI that showed higher number than color activation in experiment 1, the activation levels for number and color tasks in experiment 3 were essentially identical. Conversely, in the ROI that showed higher number than color activation in experiment 3, the activation levels for number and color tasks in experiment 1 were essentially identical. Thus, neither of these activations was replicable, even for a highly similar experimental design.

Discussion

The three experiments reported here failed to support the hypothesis that the human parietal lobe contains the neural instantiation of a domain-specific mechanism for representing abstract numerical magnitude. In experiments 1 and 3, ROI analyses showed that regions of the IPS previously implicated in numerical processing in fact respond somewhat less strongly for number tasks than for closely matched color tasks (see Figure 4). Experiment 2 found fMRI adaptation (Grill-Spector et al., 1999; Grill-Spector and Malach, 2001) for repeated shapes in the shape-processing area LOC, but no adaptation for repetitions of nonsymbolic number in any of the ROIs tested or elsewhere in the parietal lobe. In experiment 3, intraparietal regions responded more strongly to difficult than easy tasks, but did so to no greater degree for manipulations of difficulty in the number than color task. These are not "null results" and cannot be explained in terms of insufficient statistical power, because intraparietal ROIs did show significant effects—they just went in the opposite direction from that predicted by the domain-specific number hypothesis. We next consider the implications of these and previously published results for several different hypotheses about the relationship between number cognition and the parietal lobes.

First, consider the strongest hypothesis based on prior research, that the IPS contains the neural instantiation of a domain-specific mechanism for representing abstract numerical magnitude. The results listed above seriously challenge this hypothesis. Indeed, they indicate that, if this region of parietal cortex is engaged by nonsymbolic number processing, all of the following must be true: (1) there must not be domain-specific modulation of activation by task difficulty (experiment 3), (2) number representations for nonsymbolic stimuli must be activated in a task-independent fashion (experiment 1) yet (3) not consistently cause response interference (behavioral results from experiment 1), and (4) not show adaptation for repeated numerosities (experiment 2). This new set of constraints seems possible—though perhaps unlikely—when considered alone. However, the existing literature claims that *symbolic* number processing *does* elicit activations modulated by difficulty (Pinel et al., 2001), *does* respond in a domain-specific fashion to numbers and display task-dependent localization of activation (Eger et al., 2003), *does* cause response interference (Pavese and Umilta, 1998), and *does* display adaptation effects (Naccache and Dehaene, 2001). In light of these opposite characteristics, the theory that a single representational system with its locus in this region of parietal cortex underlies both symbolic and nonsymbolic processing seems unparsimonious at best.

What kind of theory might better account for the full set of results we now have before us? One possibility is that only symbolic number is represented and pro-

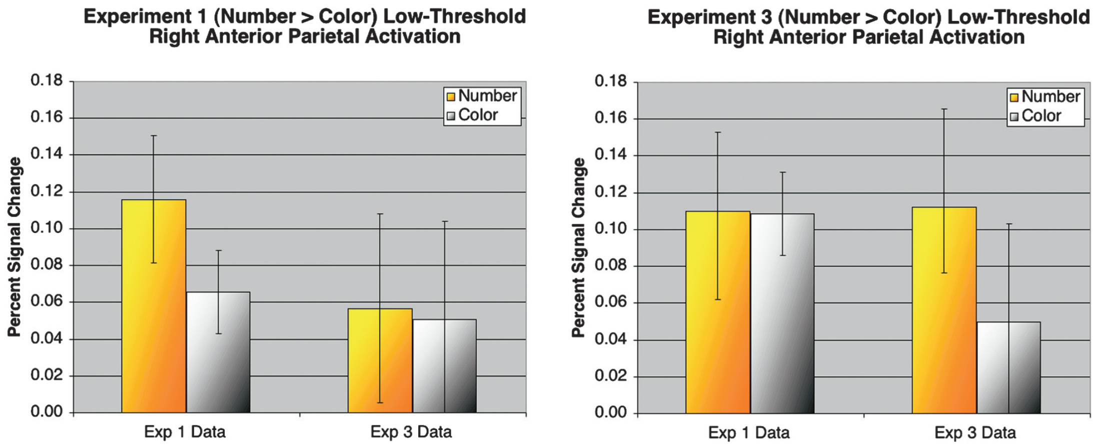

Figure 3. Activation in the HIPS

Replication of the Dehaene et al. (1999) task yielded strong activations for approximate addition versus letter matching in the horizontal segment of the intraparietal sulcus (HIPS; Simon et al., 2002) in each of the three sets of subjects. In contrast, tasks designed to elicit nonsymbolic number processing actually yielded lower levels of activation than controls in each of the three experiments. A main effect of difficulty was observed in experiment 3.

cessed in the putative parietal number area. This would mean that recent findings of localized parietal activations for nonnumerical magnitude tasks like comparing orientation differences (Fias et al., 2002) or lines and angles (Fias et al., 2003) are coincidental rather than illustrative of an important generalization of numerical processing to the processing of continuous magnitude. While fitting the data reasonably well, this hypothesis does not fit well into the broader theoretical framework. Behavioral evidence has strongly linked nonsymbolic and symbolic number processing, so it would be surprising for these to be neurally dissociated. This hypothesis would also probably require a theoretical retreat on the claim of innateness (Dehaene et al., 1998), as a biologically determined neural module specific for number *symbol* processing is unlikely given the evolutionarily recent development of such symbol systems.

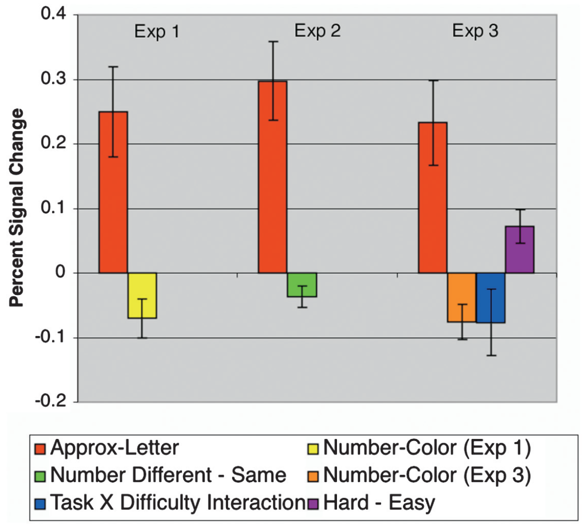

Figure 4. Validation Analyses for Low-Threshold Activations

At low statistical thresholds, both experiment 1 and experiment 3 yielded right anterior parietal regions with a stronger response to number than color. However, neither activation replicated across the two experiments.

Another possibility is that activations previously ascribed to the representation and processing of number are due only to general difficulty differences or attentional demands, not to any kind of number processing per se. Indeed, the parietal lobes in general and the IPS in particular are notorious for their indiscriminate activation in almost any difficult or attention-requiring task (Culham et al., 1998; Culham and Kanwisher, 2001; Jiang and Kanwisher, 2003; Wojciulik and Kanwisher, 1999). Several prominent studies of the neural localization of number representation have used the "distance-effect" paradigm (Dehaene, 1996; Pinel et al., 2001; Temple and Posner, 1998), which contains an inherent difficulty confound (but see Pinel et al., 2001, for an argument that such difficulty alone cannot explain their distance effects). Other studies have contrasted "number" conditions with control conditions that are much less difficult (Simon et al., 2002) or simply with fixation (Dehaene et al., 1996). Many studies of calculation (e.g., contrasting multiplication and subtraction tasks) have not controlled for behavioral difficulty (Rickard et al., 2000; Zago et al., 2001) or have not reported behavioral data (Dehaene et al., 1996; Kazui et al., 2000; Lee, 2000). However, several studies have carefully controlled for difficulty and still shown activations localized in intraparietal regions for approximate calculation versus exact calculation (Dehaene et al., 1999) and for viewing Arabic numerals versus letters and colors (Eger et al., 2003). The repetition suppression effect reported for Arabic numerals and number words (Naccache and Dehaene, 2001) might be partially explained by a difficulty-confound account, but in that study, simple response priming had an effect on difficulty comparable to that of exact quantity priming yet had no impact on brain activations. Thus, it seems unlikely that all reported parietal number activations can be attributed to nonnumerical processing associated with any difficult task; instead, this region appears to play a genuine role in some aspect of symbolic number processing, even when difficulty is controlled.

A final hypothesis, and the one we believe is best supported by the available data, is that the IPS *is* involved in number representation and processing but that it is also involved in many other processes that do not involve number or even continuous magnitude—including those processes elicited by the control conditions in our experiments. In other words, number processing may be localized to some degree in the IPS, but the IPS is not domain specific for number. What can we make of prior claims about the domain specificity of the IPS (Dehaene et al., 1998, 2003; Simon et al., 2002)? Some of these claims have rested on nonoverlap analyses, in which IPS activation is shown to be significant for number tasks compared to control, but not significant for non-number tasks compared to control (Pinel et al., 2004; Simon et al., 2002). This is a weak argument, as activations in the non-number comparisons could be just below threshold and not significantly different from the activations in the number comparisons. A strong version of this argument requires not just a difference in significances (between number and non-number contrasts), but a significant difference between the two contrasts (in this case, a significant interaction between number/non-number × test/control). One study does provide support for the claim that the IPS activation is domain specific, at least for symbolic number: Eger and colleagues (Eger et al., 2003) found that Arabic numerals produced significantly higher IPS activation than either letters or colors in an event-related fMRI experiment that tightly controlled for difficulty. Yet strong domain specificity arguments entail, not merely a failure of the mechanism in question to be engaged by *some* processes outside the domain, but its failure to be engaged by *any* processes outside the domain. The results we present here showing that the IPS is more responsive to color than to numerosity thus pose a serious challenge to the strong domain specificity view.

Further investigation will undoubtedly improve our understanding of the full range of cognitive processes that this region of cortex is involved in as well as our understanding of where and how number and continuous magnitude are represented and processed. It is possible, for instance, that distinct neural populations in the IPS are engaged in numerical and nonnumerical processing but that they are physically interleaved. This would make it difficult to find evidence for domain specificity with fMRI due to its limited spatial resolution. Suggestive evidence for this number-neuron subpopulation hypothesis comes from the recent discovery of numerosity-selective neurons concentrated in the IPS in monkeys (Nieder and Miller, 2004). However, if similar neural populations exist in the human brain and constitute the dedicated "number system" hypothesized to underlie symbolic-number fMRI activations in the IPS, we would expect to find similar fMRI results for both symbolic and nonsymbolic number experiments. Instead, major differences are apparent in (1) fMRI adaptation (observed in the IPS for symbolic number repetition [Naccache and Dehaene, 2001] but not for numerosity repetition [present study]); (2) the domain specificity of activation (symbolic number versus color shows IPS activation [Eger et al., 2003] but numerosity versus color does not [present study]); and (3) the parametric variation of activation with task difficulty (symbolic number shows an fMRI distance effect in the IPS [Pinel et al., 2001], but we find no IPS "task × difficulty" effect with numerosity comparison. Another possibility is that there is some functional subspecialization within the parietal lobe, with the processing of symbolic number, nonsymbolic numerosity, and other continuous magnitude dimensions each engaging distinct or only partially overlapping cortical regions, with varying degrees of domain specificity (Kleinschmidt, 2004; Pinel et al., 2004). While this hypothesis must, as yet, be regarded as somewhat speculative, our findings are not inconsistent with it. Specifying this hypothesis in sufficient detail for it to produce testable predictions is a worthwhile avenue for future research.

Processing of Continuous Magnitude

Several studies have linked the processing of continuous magnitudes and number. In one study, posterior parietal cortex was found to be significantly more active when subjects judged whether the difference in orientation between two gratings was "large" or "small" compared to when they simply judged whether the orientations of the gratings were the same or different; the peak of the activation was relatively close (8–20 mm) to peaks found for a range of number processing studies (Fias et al., 2002). In a later study, magnitude comparisons for lines, angles, and numbers all yielded similar parietal activations when contrasted with dimming judgment control tasks performed on the same stimuli (Fias et al., 2003). Another study found "considerable overlap" between activations for size, luminance, and numerical magnitude comparisons with Arabic numeral stimuli (Pinel et al., 2004). In line with these findings and their theoretical motivations and implications, Walsh has proposed a "theory of magnitude" in which time, space, and quantity are all processed by a single parietal "magnitude" system (Walsh, 2003). While these studies link symbolic number processing with the processing of a variety of continuous magnitudes, the processing of nonsymbolic discrete magnitude—numerosity—is not assessed. Our results indicate that nonsymbolic numerosity processing does *not* activate the putative parietal magnitude region any more than the same region is activated by a same-different color discrimination task that does not involve magnitude. It is difficult to imagine a coherent theory of magnitude processing that includes symbolic number and the magnitudes of lines, angles, and luminances but does not include assessment of the number of elements in a set.

Other Studies

Several other imaging studies *have* involved numerosity judgment tasks and/or nonsymbolic stimuli. Some have contrasted subitizing and counting (Piazza et al., 2002, 2003; Sathian et al., 1999); this is of little help in identifying brain regions involved in the estimation of approximate numerical magnitude, since the process of explicit counting should engage symbolic number processing even in the absence of symbolic number stimuli. One study (Fink et al., 2001) contrasted numerosity judgment ("is the number of dots equal to four?") and shape judgment ("do the dots form a square?") on arrays of three to five dots. Greater activations for the numerosity judgment task were found in striate and extrastriate visual areas and in the inferior frontal gyrus, but no activations were found in parietal cortex. This result may be regarded as complementary to the results we present here, but the fact that it only involved numerosities of up to five makes it very different and possibly incomparable, as substantial evidence in the developmental and animal behavior literature suggests that small sets are processed by a different system from that used for larger sets (Feigenson et al., 2002; Hauser and Carey, 2003). Finally, one study found similar parietal evoked potentials for numerical magnitude comparisons with both Arabic numeral and dot array stimuli (Temple and Posner, 1998). This result was a motivation for the experiments we describe here, and it does contrast notably with our failure to find parietal activation for dot-array numerosity comparison. One difference between this study and ours is that Temple and Posner used regular, rectangular arrays of dots, which might have been more easily identified and labeled with symbolic number "tags" than our random arrays of generally larger numbers of dots. The spatial resolution of ERP is also extremely limited compared to that of fMRI, so results are not entirely comparable.

Neural Localization versus Cognitive Representation

It is important to note that while we believe the results presented here constitute a serious challenge to claims about the cortical localization and domain specificity of analog number representation and processing in the HIPS or other areas in the parietal lobe they are not inconsistent with the more restricted, strictly cognitive claim that an analog representation for number exists and plays an important role in both symbolic and nonsymbolic number processing. This latter claim has strong support from a long history of behavioral work, and cognitive questions about the representation are to some degree orthogonal to questions about *where* in the brain number is represented and processed, or indeed, whether it is localized at all.

Conclusion

In conclusion, despite the substantial evidence that human adults, infants, and several other animal species have similar abilities to represent the numerosity of nonsymbolic stimuli, that human adults encode symbolic number in a similar system, that symbolic number selectively activates a specific region of parietal cortex, and that this region displays some degree of domain specificity for symbolic number, we find no evidence in these three experiments to support the hypothesis that a single *domain-specific* cortical region, with its locus in the IPS, underlies both symbolic and nonsymbolic number processing.

Experimental Procedures

Subjects

Nine healthy adult subjects, (seven males and two females) participated in experiment 1. Fifteen subjects (eight males and seven females) participated in experiment 2. Twelve subjects (six males and six females) participated in experiment 3. One subject (included in the above counts) participated in all three experiments, and one other subject participated in experiments 1 and 2.

MRI Acquisition

All scans were done on 3T scanners at the Massachusetts General Hospital Nuclear Magnetic Resonance Center in Charlestown, MA. A head coil and a Gradient Echo pulse sequence with TR, 2; TE, 30 ms; flip angle, 90° were used. In all experiments, data were collected from 20 4 mm thick near-coronal slices oriented parallel to the brainstem, covering the occipital and parietal lobes and the posterior portion of the temporal lobe. Several subjects were exceptions to this rule and were scanned with 20 5 mm thick slices covering a similar relative brain volume. For the "approximate" experiment (for establishing ROIs), 168 functional images were collected for each slice in each scan. For experiment 1, either 121 or 146 functional images (depending on the length of fixation periods) were collected for each slice in each scan. For experiment 2, 136 functional images were collected for each slice in each scan. For experiment 3, 145 functional images were collected for each slice in each scan.

MRI Data Analysis

The data were processed and analyzed with SPM99 (Wellcome Department of Cognitive Neurology, London, UK). Data were motion corrected, normalized to the MNI template, and smoothed with a Gaussian filter (FWHM = 8 mm) prior to analysis. For random effects analyses, we chose a constant T threshold in order to facilitate the comparison of activations across experiments with different numbers of subjects; the analyses described in the text and shown in Figure 2 used a voxel-wise threshold of $T > 3.79$, corresponding to p value thresholds of 0.003, 0.001, and 0.002 (uncorrected) for experiments 1 through 3, respectively, and 0.0003 for the "all subject approx-letter" analysis; a constant T threshold was chosen to facilitate the comparison of activations across experiments with different numbers of subjects. The lower threshold analyses shown in Supplemental Figure S1 (http://www.neuron.org/cgi/content/full/44/3/■■■/DC1/) used a voxel-wise threshold of $T > 2.62$, corresponding to p value thresholds of 0.015, 0.010, and 0.012 (uncorrected) for experiments 1 through 3, respectively, and 0.007 for the "all subject approx-letter" analysis. For the ROI analyses, in-house software was used to repack and average across runs for each subject, extract average response levels in each condition in each voxel, and finally to average across the voxels in each ROI. The percent signal change (PSC) versus fixation was calculated for each condition and entered into an ANOVA (experiments 2 and 3) or Student's t test (experiment 1 and the Dehaene et al. [1999] replication) across subjects.

Replication of the Dehaene et al., 1999, "Approximate Calculation" Experiment

Full details of the stimuli and design for this experiment can be found in the original publication (Dehaene et al., 1999). In brief, there were two conditions: (1) approximate addition and (2) letter matching. In approximate addition trials, subjects saw a pair of digits between 1 and 9 on either side of a "+" symbol at fixation, followed by a pair of "answers" between 3 and 17; the task was to choose the answer that was approximately equal to the sum of the first two digits shown (the correct exact sum was never shown). Subjects were specifically instructed not to calculate the exact sum, but rather to "just pick the answer that seems about right." Subjects in experiments 2 and 3 were given two sessions of practice with this task prior to scanning; many subjects reported difficulty suppressing exact calculation at first but found that with practice they were able to complete the task as instructed, and indeed, practice seemed to improve the consistency of brain activations across subjects. In the letter-matching task, subjects saw one pair of uppercase letters followed by another pair; on each trial, the letter would remain the same on one side while changing on the other side, and the task was simply to indicate on which side the letter stayed the same.

This method includes only half of the full experimental design in the original article (Dehaene et al., 1999); the "approximate" activations presented there were for the double subtraction (approximate addition − letter matching) − (exact addition − letter matching). While a full replication of the original design in each subject would have been ideal, this was not technically feasible, as the scan time required would have sharply limited the power attainable in our main experiments. However, preliminary studies that we completed suggested that there is no qualitative difference in the regions activated for the double subtraction versus the simpler approx-letter contrast, so we chose the simple design as the most efficient method for establishing ROIs. The effect was sufficiently strong and robust for significant and characteristic IPS activation maps to be obtained in all but four individual subjects, allowing analysis using individual functionally defined ROIs in each experiment. Further, ROI analyses based on the full reported set of approx-exact activation coordinates (Dehaene et al., 1999) validated this approach, yielding a similar pattern of results as ROI analyses based on our replication (see Table 2).

Experiment 1

Visual Stimuli

Stimuli consisted of arrays of blue-green dots on a black background (see Figure 1A). Dots were either 5 or 7 pixels in diameter (0.17° or 0.23° of visual angle), with size constant within any given array, and arrays consisted of between 8 and 22 dots placed randomly (with a constraint to prevent overlap) within a circular envelope of between 186 and 236 pixel diameter (6.20° to 7.87° of visual angle).

Procedure and Design

A task-manipulation blocked design was used, with identical stimuli across tasks (over the course of the experiment). There were four tasks: number ("which has more dots?") and color ("are the two arrays the same color or different?") along with two other tasks designed to test other hypotheses. Ratios for each dimension were set to match difficulty across tasks, based on the results of preliminary behavioral testing. For magnitude dimensions, subjects made comparisons for a range of eight different ratios, across a range of eight different base values; for the color same/different task, subjects made judgments on four distinct "different" ratios, across a range of eight different base values (in "green" values for RGB color codes; "red" and "blue" values were held constant).

Each scan consisted of four blocks, 48 s each, with fixation intervals interleaved. Each block consisted of 16 stimulus array pairs: each array was presented for between 175 and 305 ms (duration judgment was one of the additional tasks, so in each pair, one array was presented for longer than the other) with a 1 s fixation in between, followed by a fixation/response period of the correct duration to bring the total elapsed time for presentation of the pair up to 3 s. In each four-block scan, a subject completed one block of each task, with order counterbalanced across runs. There were two full "sets" of stimulus pairs with $16 \times 4 = 64$ pairs in each set, for 128 total. Each individual stimulus pair appeared exactly once under each task condition (i.e., four times total) over the course of the experiment, which consisted of eight runs per subject.

Experiment 2

Visual Stimuli

Stimuli consisted of arrays of colored shapes on a gray background (see Figure 1B). Arrays consisted of between 1 and 15 elements (from the set [1, 2, 3, 4, 6, 8, 11, 15], which consists of the first eight "discriminable" numbers, assuming a Weber discriminability ratio of between 0.75 and 0.80) of one of eight different shapes. Elements were placed randomly (with a constraint to prevent overlap) within a 265 pixel diameter (8.83° of visual angle) circular envelope.

Procedure and Design

There were four conditions (see Figure 1B), constructed by crossing number (same versus different) and shape (same versus different): (1) number same, shape same (SS), (2) number same, shape different (SD), (3) number different, shape same (DS), and (4) number different, shape different (DD). Each scan consisted of eight blocks, 16 s each, with fixation intervals of 16 s interleaved. Each of the four conditions occurred twice in a scan, with counterbalancing for order across scans. Each block consisted of 16 shape-array stimuli, each presented for 200 ms, followed by 800 ms of fixation. In "same" conditions, all 16 stimuli would be identical on the dimension (e.g., all 16 would consist of four elements, in a particular "number same" block). In "different" conditions, each of the eight different shapes or numbers would occur twice, ordered pseudorandomly, barring repeats. Importantly, the configuration of elements always varied through the course of a block—the subject never saw exactly the same images repeated. Even in shape-different blocks, elements within a given array were all the same.

For the sake of continuous quantity control (area, density) the "colored pixel" counts were varied across the eight shapes in the same way that number varied—that is, the number of non-gray pixels in single exemplars of the eight shapes were $N \times [1, 2, 3, 4, 6, 8, 11, 15]$ (where N happens to have been 35). Thus, the total "colored pixel area" of stimulus arrays varied in the same way for (SD) blocks as it did in (DS) blocks. Number-shape pairings for arrays in (DD) blocks were selected such that colored pixel area also varied in the same way for these blocks. This kind of area obviously did not vary at all in (SS) blocks. All this simply means that area variation (and density variation) was orthogonal to number variation versus shape variation.

Each subject completed a total of eight scans. On four of these scans ("passive"), the subject simply maintained fixation on a central point while attending to the stimuli. On the other four scans ("one-back"), the subjects attended to the color of the arrays (a dimension orthogonal to both number and shape) and pressed a response key whenever the same color appeared twice in a row. To prevent task confusion, on "passive" scans, the color of the elements was held constant across all blocks within a run. Because fMRI data were very similar, all analyses we present collapse across the two task conditions.

Experiment 3

Visual Stimuli

"Array" stimuli consisted of arrays of yellow-orange or blue-green dots on a black background (see Figure 1C). Dots were 9 pixels in diameter (0.3° of visual angle), and arrays consisted of between 5 and 16 dots placed randomly (with a constraint to prevent overlap) within a circular envelope. "Sequence" stimuli consisted of a single 23 pixel diameter (0.77° of visual angle) yellow-orange or blue-green dot flashed on a black background in a sequence as described below.

Procedure and Design

As in experiment 1, a task-manipulation blocked design was used, with constant stimuli across tasks (over the course of the experiment). There were four task conditions, constructed by crossing task (number versus color) and difficulty (hard versus easy): hard number (HN), Easy Number [EN], Hard Color [HC], and Easy Color [EC]. Each scan consisted of four blocks, 48 s each, with 20 s fixation intervals interleaved. Each block consisted of eight stimulus pairs, each consisting of a flash sequence and an array. Each flash sequence consisted of N "on" flashes of 50 ms each, with "off" periods of 50–150 ms interleaved. Durations of "off" periods were randomly selected from the distribution [50, 50, 50, 50, 100, 100, 150 ms] so that total duration of the sequence did not determine the number of elements (as would be the case with a constant frequency sequence). It should be noted that a constant duration sequence, making duration orthogonal to number, would make frequency perfectly anticorrelated with number. This variable-duration sequence scheme was chosen as a compromise—it does leave a large degree of correlation between duration and number, but it's very difficult if not impossible to perfectly unconfound these dimensions. Sequences were followed by a fixation and then by presentation of the array 4 s after sequence onset. The array was presented for 400 ms, followed by a fixation/response period of 1600 ms, bringing the total elapsed time for presentation of the pair up to 6 s. In each four-block scan, a subject completed one block of each task, with order counterbalanced across runs.

Acknowledgments

The authors thank Elizabeth Spelke and Stanislas Dehaene for valuable suggestions, particularly in the design of experiment 3; Neil Brenner, Nicholas Knouf, and Jorge Jovicich for assistance with data analysis; Stanislas Dehaene and Wim Fias for providing full coordinate sets for ROI analysis; and Hilary Barth and Yuhong Jiang for helpful comments on the manuscript. This research was supported by National Science Foundation ROLE grant REC-0087721 and the Human Frontiers Science Program.

Received: March 19, 2004
Revised: July 8, 2004
Accepted: October 5, 2004
Published: October 27, 2004

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