Article

Deciphering Cortical Number Coding from Human Brain Activity Patterns

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Summary

Background: Neuropsychology and human functional neuroimaging have implicated human parietal cortex in numerical processing, and macaque electrophysiology has shown that intraparietal areas house neurons tuned to numerosity. Yet although the areas responding overall during numerical tasks have been well defined by neuroimaging, a direct demonstration of individual number coding by spatial patterns has thus far been elusive.
Results: We used multivariate pattern recognition on high-resolution functional imaging data to decode the information content of fine-scale signals evoked by different individual numbers. Parietal activation patterns for individual numerosities could be accurately discriminated and generalized across changes in low-level stimulus parameters. Distinct patterns were evoked by symbolic and nonsymbolic number formats, and individual digits were less accurately decoded (albeit still with significant accuracy) than numbers of dots. Interestingly, the numerosity of dot sets could be predicted above chance from the brain activation patterns evoked by digits, but not vice versa. Finally, number-evoked patterns changed in a gradual fashion as a function of numerical distance for the nonsymbolic notation, compatible with some degree of orderly layout of individual number representations.
Conclusions: Our findings demonstrate partial format invariance of individual number codes that is compatible with more numerous but more broadly tuned populations for nonsymbolic than for symbolic numbers, as postulated by recent computational models. In more general terms, our results illustrate the potential of functional magnetic resonance imaging pattern recognition to understand the detailed format of representations within a single semantic category, and beyond sensory cortical areas for which columnar architectures are well established.

Introduction

The processing and manipulation of numbers is highly developed in humans. However, although number symbols and exact arithmetic are specifically human cultural achievements, basic nonverbal comprehension of quantities is present in animals and preverbal infants [1, 2]. Numerical cognitive processes such as mental calculation rely on neuronal circuits of the frontal and parietal lobes [3, 4]. More specifically, cortical regions along the intraparietal sulcus seem to play a key role in processing numerical magnitude but also other continuous quantities or ordered entities [5–7]. Electrophysiological recordings in nonhuman primates have demonstrated numerosity tuning of single neurons in several brain regions and shown that parietal responses to number precede those in frontal cortex [8]. However, monkey neurons preferring different numbers appear to be highly intermixed between each other as well as with neurons representing other continuous quantities [9], and until now it has not been possible to directly visualize a corresponding code for individual numbers in humans.

Behavioral observations such as the distance effects in comparison tasks have led us to metaphorically think of magnitude as being represented along a "mental number line" [10–12], and neuroimaging studies have harvested evidence in accord with this concept: number-induced parietal activation during a comparison task varies with the numerical distance separating the two compared numbers [13], and release from adaptation increases with numerical distance in an approximately logarithmic fashion [11]. However, the extent to which distance effects reflect properties of neuronal representations themselves, as opposed to decision- and response-related components, remains controversial [14]. The ability to resolve response patterns evoked by different individual numbers would help to disambiguate between these alternatives, because it permits direct testing for a signature of distance on a "neural number line" while decision- or response-related effects are ruled out.

Multivariate decoding or multivoxel pattern analysis methods [15, 16] have recently shown a capacity to identify spatial patterns of functional magnetic resonance imaging (fMRI) activation discriminative of stimulus features that were long thought to be beyond the reach of functional imaging in humans, for example orientation [17, 18], motion direction [19], object exemplars of the same category [20, 21], or spoken vowels versus voices [22]. Most of this previous work, however, investigated features represented in early or midlevel sensory cortices. A recent study [23] decoded responses for individual words as a function of semantic similarity, based on the global patterns evoked across the entire brain by words with distinct sensory and motor associations. In the present study, we faced the challenge of separating representations within a single semantic category. We attempted to decode individual number signals from human intraparietal cortex, where there is no evidence thus far for a columnar or at least patchy neuronal architecture equivalent to that underpinning feature representation in sensory cortices [24, 25], while subjects made delayed numerosity comparisons in a paradigm similar to the one employed previously in the monkey [8].

Results

Experiment 1: Nonsymbolic Number Discrimination and Effects of Stimulus Parameters

Subjects were briefly presented with a sample stimulus comprising 4, 8, 16, or 32 dots that was followed after several

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A

Sample stimulus
200 ms

Delay period
3.8-6.8 s

Match stimulus
200 ms
-> response
smaller or larger number?

Hi-Res fMRI
(1.5 mm)

B

C
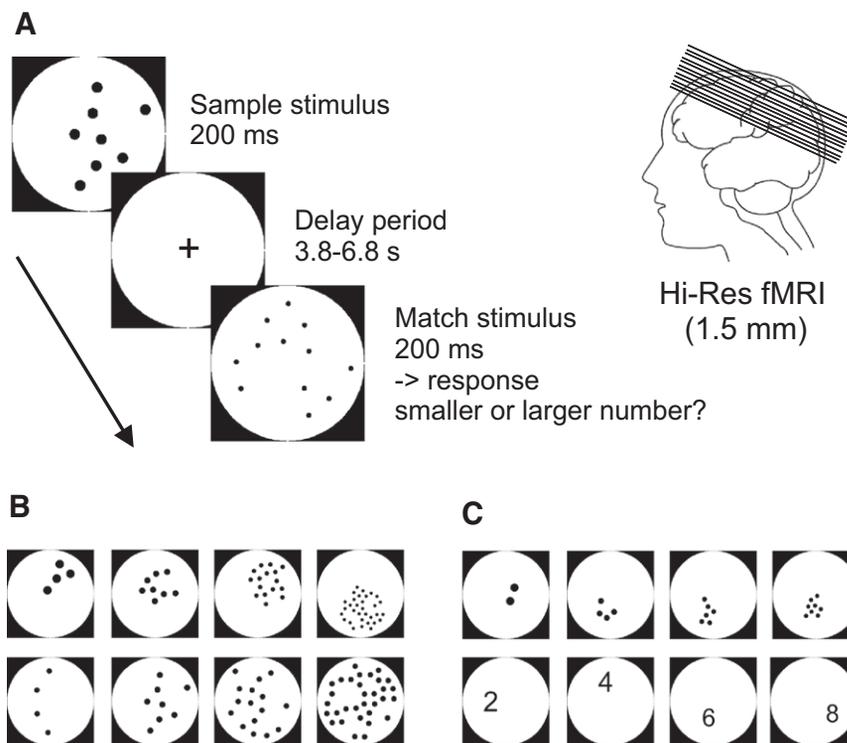
Figure 1. Overview of Experimental Design

(A) Subjects were presented briefly with a sample number stimulus (200 ms) and, after a variable delay of 3.8–6.8 s, with a match stimulus (200 ms) that differed in numerical magnitude by 50% and required a numerical smaller versus larger judgment.

(B) Two different nonsymbolic stimulus lists (equating either overall luminance or dot size between numerosities) for numerosities 4, 8, 16, and 32 were used in experiment 1. Sample and match stimuli were always from different lists to prevent subjects from solving the task by monitoring either luminance or dot size change.

(C) Dot patterns of matched luminance and single digits (numbers 2, 4, 6, and 8) were used in experiment 2, where a format change between sample and match occurred in 50% of the trials. The critical data for the fMRI analysis correspond to evoked activities for different sample stimulus conditions (four numerosities × two formats/stimulus sets).

seconds by a second set of dots requiring a smaller or larger response (see Figure 1 and Experimental Procedures). Activation patterns evoked by the sample stimulus were analyzed as a function of the numerosity presented. To unconfound number from associated low-level stimulus parameters, we used two different sample stimulus lists that equated either overall luminance change or the size of individual dots between numerosities.

We tested whether the numerosity of a given set of dots could be predicted within each sample stimulus list, as well as across low-level stimulus properties—i.e., whether a classifier trained only on data from sample numerosities of constant dot size (and therefore increasing luminance for larger numbers) could accurately discriminate data from stimuli with constant luminance, and vice versa. Successful generalization of classification performance, together with low discriminability of the two stimulus lists themselves, should indicate discrimination based on number as opposed to secondary low-level factors.

Region of Interest Analysis
On a subject-by-subject basis, we identified within a mask of parietal cortex the 1000 voxels that activated most significantly in response to all sample stimuli versus baseline. Within this region of interest (ROI), patterns for any two test numerosities could be discriminated with on average nearly 70% accuracy (chance = 50%), irrespective of whether data from the same or different sample stimulus lists served as training and test data [t(9) = 6.9, p < 0.0001 and t(9) = 8.0, p < 0.0001, respectively; see Figure 2]. Conversely, discrimination of the list from which the stimulus was drawn (for a fixed numerosity) remained nonsignificant, with only ∼54% accuracy [t(9) = 1.9, p = 0.09].

Searchlight Analysis
The above analyses indicate that activation patterns of a relatively extended parietal region of interest contain information discriminating between individual numbers. Exploratory

analyses in frontal ROIs showed a weaker but similar profile of discrimination, whereas performance for primary motor cortex was at chance (see the Supplemental Data available online). To further clarify the topographical distribution of numerosity information, we conducted a multivariate "searchlight" analysis [26], testing for the local presence of number information in a sphere with 3 voxel radius sequentially moved across all voxels (27 slices covering parietal and superior parts of the frontal lobes). The resulting maps of classification accuracy scores for each voxel and subject were submitted to a group analysis for both same and different sample stimulus lists. Number information was detected most significantly in parts of the intraparietal sulcus, although at a lower, uncorrected level of significance, additional foci appeared in medial parietal cortex and medial and lateral premotor regions (Figure 3; Table 1). This demonstrates that information discriminating individual numbers is not distributed nonspecifically across wide regions of cortex. Instead, within the limits of our imaging volume, numerical information is mainly concentrated in the intraparietal sulcus, where monkey electrophysiology has identified a high proportion of numerosity-sensitive neurons [8].

Experiment 2: Number Discrimination and Effects of Format
Our previous results left unresolved whether the pattern signals that permit number discrimination reflected a representation of nonsymbolic numerosity only or a more abstract code shared by symbolic numbers. Our second experiment therefore compared the discrimination of activation patterns evoked by dot patterns and by Arabic numeral (digit) stimuli (numbers 2, 4, 6, and 8). We probed discrimination of number-evoked patterns within a given format, but also when training the classifier on dot patterns and testing on digits, and vice versa.

Region of Interest Analysis
We once again tested for discrimination of pairs of numbers in a parietal region of interest comprising the 1000 parietal voxels that were most significantly activated by all sample stimuli, regardless of their notation. When comparing the patterns
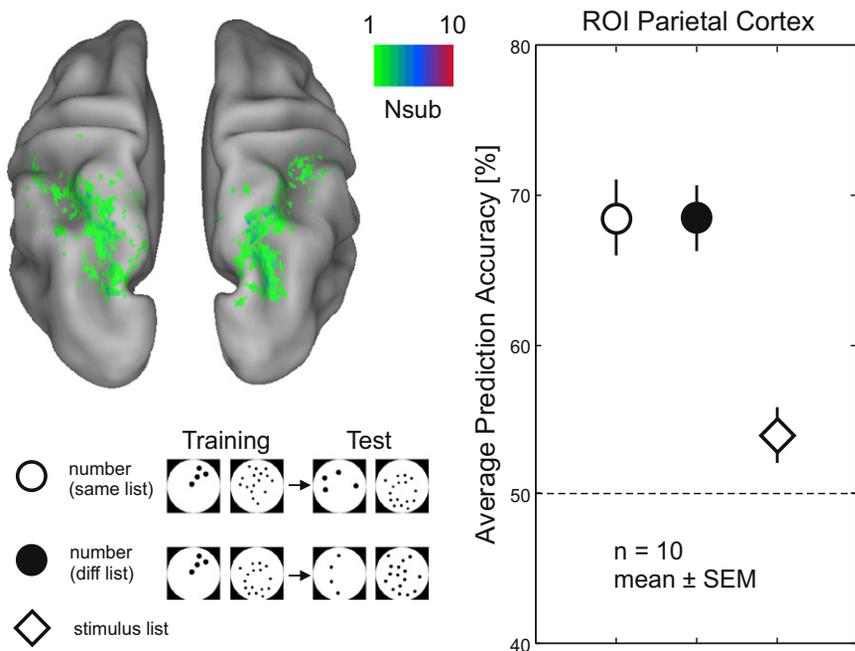
Figure 2. Experiment 1: Discrimination of Nonsymbolic Numerosity and Effects of Stimulus Parameters

Results of support vector classification for the parietal region of interest (n = 10; data show means ± standard error of the mean [SEM]). The 1000 most activated voxels across all sample stimulus conditions versus baseline within a mask of parietal cortex were chosen as a region of interest (ROI) on a subject-by-subject basis. The surface mapping (Caret PALS atlas) gives an illustration of the regions included and the across-subject overlap of voxels (color coding indicating the number of subjects activating the corresponding voxel). Pairwise discrimination of mean-corrected activation patterns for different numerosities was significant for training and test on data from the same stimulus list, as well as for training and test on data from the different stimulus list. Discrimination of the stimulus list for the same number did not reach significance.

evoked by nonsymbolic and symbolic stimuli for the same number, discrimination of formats was highly accurate, with ∼80% correct [t(9) = 14.6, p < 0.0001]. Number discrimination within the nonsymbolic format reached ∼77% correct [t(9) = 10.1, p < 0.0001], but generalization performance to symbolic numbers was at chance level (51%, t = 0.36). In the symbolic format, discrimination accuracy for individual digits was at ∼57% and hence markedly lower than dot numerosity discrimination but still significantly above chance [t(9) = 2.5, p < 0.05]. Interestingly, this level of performance of the digit-trained classifier, although relatively low, generalized completely to dot patterns [57%, t(9) = 2.3, p < 0.05] (Figure 4).

Searchlight Analysis

Results of a searchlight analysis for the dot pattern conditions confirmed the results obtained in experiment 1. However, for discrimination of digits as well as generalization tests, we
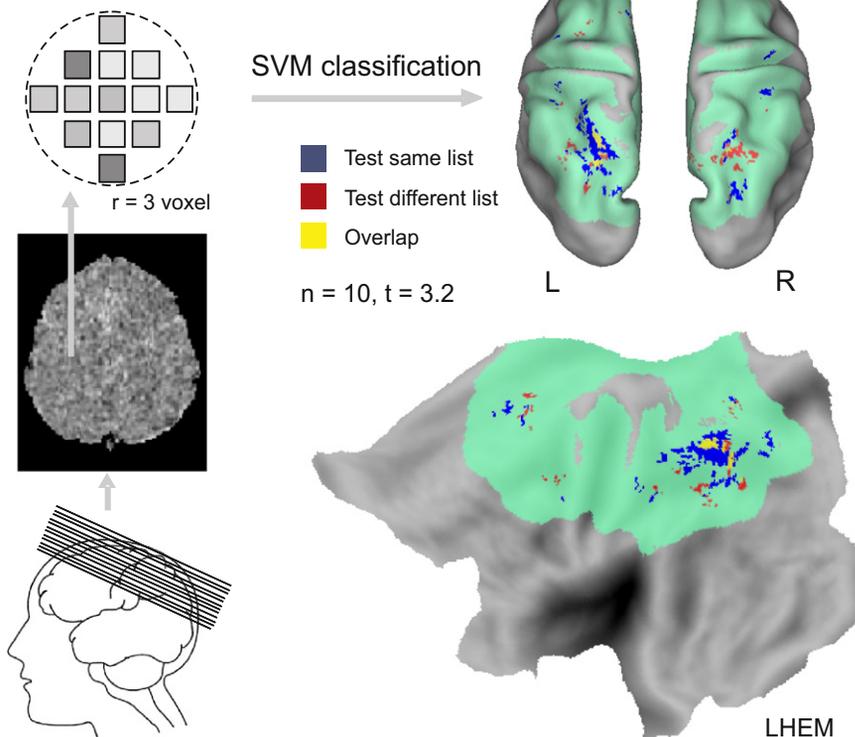
Figure 3. Experiment 1: Results from a Multivariate Searchlight Procedure

Random effects group analysis (n = 10; see Experimental Procedures for details). Accuracy maps from support vector machines (SVM) pattern classification were tested for significance across subjects with one-sample t tests (thresholded here at t = 3.2 for visualization purposes). The extent of the scanned volume (group intersection) is shown in green. See Table 1 for detailed clusters and statistical results.

Table 1. Experiment 1: Multivariate Searchlight Analysis

Comparison	Region	Stereotactic MNI Coordinates			
		x	y	z	t
Test same list	intraparietal cortex right	32	−75	36	17.4*
	intraparietal cortex left	−20	−63	57	10.0
		−39	−47	57	9.1
		−33	−42	66	7.7
	medial parietal cortex	15	−72	39	6.0
		−8	−69	47	7.0
	premotor cortex right	−48	2	51	7.4
	medial premotor cortex	−5	8	42	7.5
Test different list	intraparietal cortex right	32	−63	45	11.6*
		30	−72	50	8.9
		23	−65	53	6.0
	intraparietal cortex left	−24	−59	47	8.1
		−42	−53	54	7.8
		−17	−63	44	7.6
		−24	−62	60	6.2
	medial parietal cortex	−5	−68	56	5.8
	premotor cortex right	33	−3	65	6.7
	medial premotor cortex	6	11	57	5.8

Statistical results of a group analysis (t test, n = 10) that survive correction for multiple comparisons employing either random field theory at p < 0.05 (indicated by asterisk) or an uncorrected threshold of p < 0.001 with an extent of at least 10 voxels.

found no results at the threshold of significance employed in the previous analyses (p < 0.001, uncorrected, 10 voxel extent). This suggests that the relatively weak effect observed in the ROI analysis relies on inclusion of a large number of individually defined voxels and is no longer detectable at a relatively local scale (3 voxel radius).

Predicting Number by a Regression Approach

Understanding of numerical magnitude is not restricted to representing, for instance, 2, 4, and 6 as distinct entities but implies an ordered relation between these quantities. In

additional analyses, we used support vector regression (SVR; see Experimental Procedures and Supplemental Data) to test for gradual changes in evoked activation patterns as a function of number magnitude (e.g., reflecting that 4 is between 2 and 6). Regression requires that some sort of monotonic relationship exist between the activation patterns and the encoded quantity, which may be absent if two given numbers are coded, for instance, by unrelated tuned cells, as observed in macaques [8]. Based on the macaque research, we expected that numerical quantity should be predictable with the regression approach only if nearby numerosities are encoded by sufficiently close groups of cortical neurons. This approach would be most likely to work with experiment 2, where the tested quantities are relatively close (2, 4, 6, 8). For numerosities more distant from each other (e.g., the numerosities 4, 8, 16, 32 in experiment 1) or for symbolic numbers (in experiment 2) that are thought to be encoded by sparser and more discrete neuronal populations [27], the regression approach would be less promising.

Figure 5 shows the percentage of variance explained by SVR on the logarithm of numerical magnitude for the two experiments. Because the regression fit was tested on independent data (cross-validation), the theoretically expected performance in noninformative data corresponds to 0%. In experiment 1, the variance explained by SVR for the parietal ROI also used for classification was low and not significantly different from 0% [t(9) = 0.3 for set 1; t(9) = 1.7 for set 2]. (Although in the first experiment using dot patterns within a larger number range, no significant regression result was obtained in the analysis using all voxels in the ROI, the explained variance could be increased with additional preprocessing (removal of session effects, restriction to 500 maximally discriminative voxels in training data) for set 1 to ∼18% [t(9) = 2.17, p = 0.06] and for set 2 to ∼20% [t(9) = 3.96, p < 0.05]. This suggests that a similar gradual dependence on numerosity also exists for evoked patterns in the larger number range but is less pronounced. For consistency with the rest of the
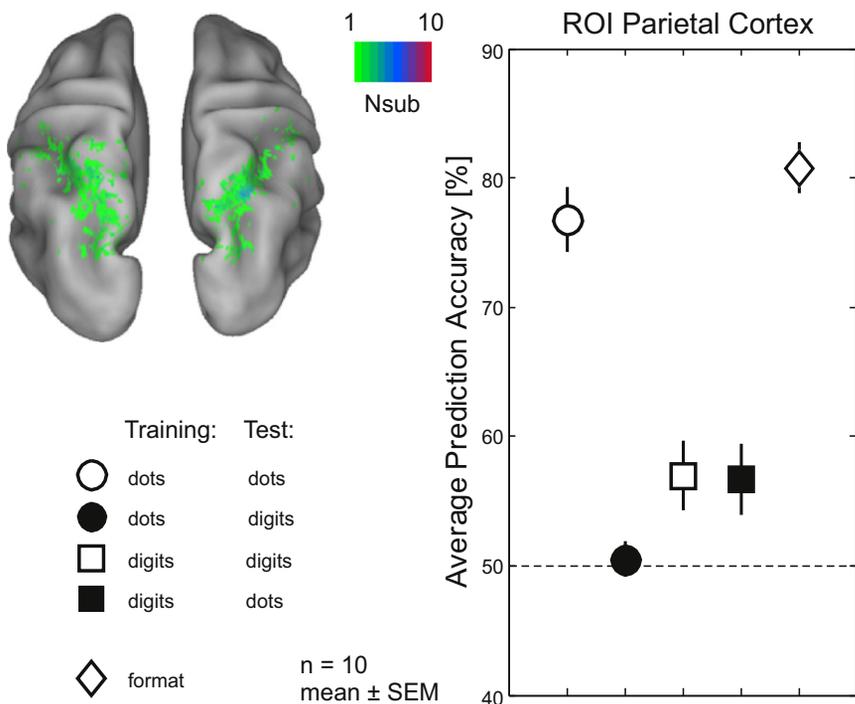
Figure 4. Experiment 2: Discrimination of Individual Nonsymbolic and Symbolic Numbers and of Format

Results of support vector classification for the parietal ROI (n = 10; data show means ± SEM). The surface mapping (Caret PALS atlas) gives an illustration of the regions included and the across-subject overlap of voxels (color coding indicating the number of subjects activating the corresponding voxel). Pairwise discrimination of mean-corrected activation patterns for different numerosities was significant for training and test on data from dot pattern stimuli, but not for training on data from dot pattern stimuli and test on data from digits. Training and test on data from digits was significantly above chance but less accurate than for dot patterns, as was generalization from digits to dot patterns. Discrimination of the stimulus format (symbolic versus nonsymbolic) for the same number was also significant and highly accurate.

Support vector regression
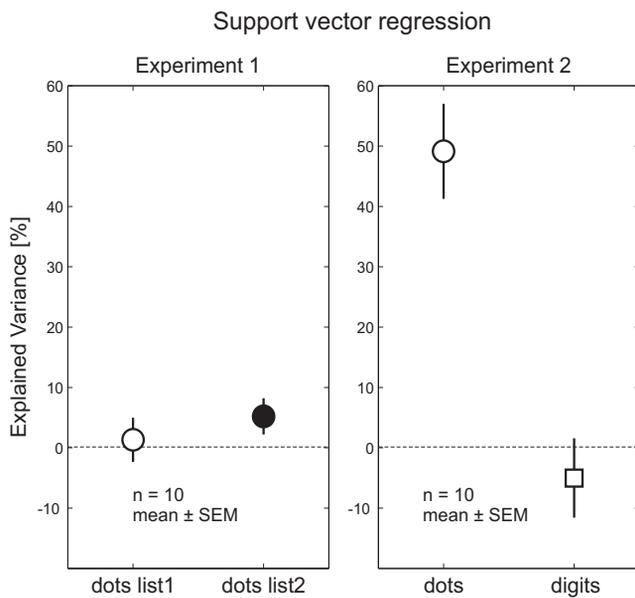
Figure 5. Result of Support Vector Regression on Parietal Region of Interest

The percentage of explained variance by the support vector regression (SVR) on the logarithm of number magnitude is shown for the two nonsymbolic stimulus lists in experiment 1 (left) and for nonsymbolic and symbolic numbers in experiment 2 (right). n = 10; data show means ± SEM.

analyses, we focus on reporting the results for the same ROIs as used in classification above.) In experiment 2, which studied a smaller (and closer) range of numbers, the explained variance for dot patterns reached ∼50% on average and was highly significant [t(9) = 6.0, p < 0.001]. However, the same analysis remained nonsignificant for patterns evoked by digits [t(9) = 0.7].

We further investigated whether pairwise classification accuracies varied with the numerical distance between numbers (see Supplemental Data). Both regression and distance analyses converged to demonstrate a gradual change of evoked activation patterns for small and sufficiently close nonsymbolic numbers. Arabic numerals and numerosities separated by a large ratio showed no such dependency, suggesting that they are encoded by essentially distinct and unrelated neuronal populations.

Discussion

Our studies probed the coding of information on individual numbers by distributed activity patterns in human parietal cortex, as recorded by high-resolution functional imaging. In two experiments, multivariate pattern recognition was used to decode cortical activity patterns associated with the different numerical stimuli that subjects saw and then held in mind.

Multivariate searchlight analyses showed that number information was present most significantly in the posterior and/or middle parts of the intraparietal sulcus, confirming the suggested role of this region in numerical processing [3]. Overall increases of intraparietal activity as observed previously while performing numerical tasks could be due to a range of factors, and explanations related to attention and/or working memory have been invoked by some [28]. Here, we show that the information in number-evoked fMRI activity patterns is specific

enough to predict the individual numerosity of nonsymbolic sets of dots that subjects were mentally processing with high accuracy, in spite of changes in low-level parameters of those stimuli. Furthermore, symbolic and nonsymbolic numbers evoked partially different patterns that were very accurately discriminated and led to an asymmetric generalization of classification: above-chance generalization when the classifier was trained on digits and tested on numerosities of dot patterns, but no generalization from dot patterns to digits. Finally, our experiments produced evidence that, at least for small (or sufficiently close) numerosities of dots, pattern discriminability increases with numerical distance.

The present evidence for numerosity coding by spatial patterns is orthogonal and complementary to previous indirect findings from adaptation or priming experiments where parietal activation decreased for repeated numbers and recovered when novel numbers were introduced (e.g., [11, 29, 30]). Somewhat surprising is the highly accurate format discrimination obtained by our methods, because repetition paradigms have found adaptation across number notations [29]. However, a similar scenario is present in studies on object representation in the ventral stream, where the amount of information on object size detected by pattern recognition methods [20] appears large compared with what had been suggested by adaptation or priming studies. In this context, it is important to note that although fMRI adaptation effects are commonly interpreted as being related to neuronal selectivity, the relation is probably more complex [31], and expectations, saliency, or novelty might play a role, especially if awareness of repetition is not prevented. Another possible explanation for why results from the two methods might disagree is if the spatial scale of different effects varies (e.g., if format-specific codes show a coarser spatial structure than format-invariant ones), in analogy with what has been proposed for object representation [32].

Our present findings also permit the establishment of a closer parallel to monkey neurophysiology, where selectivity to individual numerosities (initially in the range of small numerosities 1–5, but recently also in a larger range of 1–30) has been observed in intraparietal and lateral prefrontal neurons [8]. Of note, we did not cover homologous frontal regions in our scanning volume. It is possible that the frontal selectivity observed in monkeys is due to their extensive training in the delayed response task, especially because similar frontal selectivity of monkey neuronal responses has also been observed in other situations after monkeys learned to group stimuli into categories, for example to classify continuously varying morphs as either cats or dogs [33]. In a recent neurophysiological study in the macaque, neuronal activity was recorded after monkeys had been trained to associate nonsymbolic numerical stimuli with symbols [34]. After training, neurons that were selective both for a given number of dots and for the corresponding symbol were observed in lateral prefrontal, but only very rarely in intraparietal, cortex. In contrast, our study in human subjects found that individual symbolic number could be significantly decoded from parietal activity patterns, though less accurately than nonsymbolic number. It is commonly assumed that number symbols acquire meaning by being mapped onto a preexisting nonsymbolic quantity representation, creating format-independent number representations in the adult human brain [2, 35, 36]. The better discrimination that we observed for individual dot patterns than individual digits agrees well with the notion of the nonsymbolic representation being the evolutionarily older

one, probably still represented by more numerous neuronal populations.

We also found clear evidence of pattern differences between formats and an asymmetric generalization of classification across formats, with above-chance generalization when the classifier was trained on digits and tested on numerosity but no generalization from dot patterns to digits. A neural network model of numerical representation that explicitly simulated the association of nonsymbolic and symbolic numerals into a common representation [27] found that a subset of neurons originally responding to nonsymbolic analog number acquired selectivity to the corresponding discrete symbol and, while preserving analog response properties, became more narrowly tuned to the specific number symbol. The asymmetric generalization that we observed here fits nicely with the predictions of this model. When fed nonsymbolic data, the classifier would be trained on the entire set of number-selective neurons that are coarsely tuned to numerosity, including many neurons that, because of their narrower tuning for symbolic number, would not be responsive when the corresponding number is presented symbolically—predicting good discrimination for nonsymbolic number but poor generalization to the symbolic format. Conversely, although the neurons used to encode symbolic numerals may be a minority, thus providing weaker fMRI activation patterns on which to form a multivariate classifier, the same neurons participate in the neuronal assembly used to encode the corresponding nonsymbolic numerosities—thus predicting lower overall discrimination power for symbolic stimuli but complete generalization to the nonsymbolic notation, as observed here.

Another aspect of the aforementioned model [27] is that nonsymbolic numbers are coded through an additional earlier stage relying on summation coding. Although previous neuroimaging studies have found processing of symbolic and nonsymbolic numerals to activate overall similar parietal regions [37, 38], our pattern analyses show that the parietal responses evoked by a given number of dots and the corresponding digit are not identical (even after having accounted for differences in overall activation by mean correction). This and the lower level of accuracy for discrimination of digits than for discrimination of dot patterns could be compatible with an additional parietal processing stage unique to nonsymbolic numerosities. Recently, response properties compatible with summation coding have been observed in human posterior parietal cortex [39] and in the monkey lateral intraparietal area [40], whereas cells tuned to numerosity are primarily found in the neighboring ventral intraparietal area [41, 42]. Future human fMRI decoding studies should therefore attempt to disentangle different numerical codes in terms of their spatial generators.

So far, studies in the monkey brain have not revealed any clustering of neurons preferring the same numerosity in the same patches or columns of cortex. However, if neurons with different numerical preferences were mixed completely randomly, it would seem unlikely for voxels as used here to exhibit biases toward one or the other number. The fact that number can be decoded from multivoxel pattern signals suggests that the layout of individual number codes is at least sufficiently nonhomogeneous for coarse spatial structure to arise in fMRI data, even if there should be no clear columnar ("numerotopic") map structure comparable to, for example, the structure of orientation coding in area V1. Although our fMRI decoding cannot directly visualize the underlying architecture, it remains possible that more detailed electrophysiological studies or optical imaging in monkeys might in the future reveal some clustering of neuronal tuning to numerosity.

Our results further show that pattern codes of numerically close numbers are more similar than those of numerically distant numbers. Previous fMRI studies reported that when comparing numbers, activation in parietal regions depended on numerical distance [6, 13], but such results could reflect representational proximity just as well as secondary effects from task demands (decisions for close numbers being more difficult). Our present results, however, speak more unambiguously for representational overlap because they were obtained while subjects were merely engaged in processing and memorizing a given quantity, but not yet in a direct comparative judgment. Although a distance effect in classification accuracy was only significant for dot pattern stimuli, the absence of distance effects for digits could reflect the lower overall sensitivity as well as the use of too distant numbers, thus leading to a saturation of numerical distance effects due to sharper tuning curves for symbolic numbers, as discussed above [27, 36]. In the future, by using a narrower range of consecutive numbers and a more specific set of arithmetic tasks, fMRI decoding studies might eventually further clarify how numerical symbols are represented cortically, how numerical codes are combined in mathematical operations, and how they are changed by education [43].

Experimental Procedures

Data Acquisition and Stimulation

Ten healthy volunteers per experiment (experiment 1, five male and five female, 22.6 ± 3.8 years old; experiment 2, six male and four female, 21.2 ± 3.0 years old) were included in the study, which had been approved by the regional ethics committee (Hôpital de Bicêtre, France). Functional images were acquired on a 3 tesla MR system (Siemens Tim Trio) with 12-channel head coil as T2*-weighted echo-planar image (EPI) volumes with 1.5 mm isotropic voxels. Twenty-seven oblique transverse slices covering parietal and superior frontal lobes were obtained in interleaved order (repetition time 2.5 s, field of view 192 mm, echo time 30 ms, flip angle 78°).

Stimuli were back projected onto a screen at the end of the scanner bore and viewed via a mirror attached to the head coil. Trials started with brief (200 ms) presentation of a sample dot pattern (experiment 1) or either a dot pattern or a digit (experiment 2) in black color within a white circle subtending ∼8° of visual angle. After a delay of 3.8–6.8 s, a match stimulus appeared for 200 ms. This stimulus was another dot pattern (experiment 1) or a dot pattern or digit (experiment 2) differing in number by a ratio of 50% (smaller or larger) relative to the sample numerosity. Subjects were instructed to keep in mind the number shown as sample and respond with one of two buttons (left or right hand) depending on whether the match number was numerically smaller or larger than the previous sample number. The assignment of hands to smaller versus larger responses was systematically changed between scanning sessions with counterbalanced order across subjects. Subjects performed eight experimental sessions of ∼6 min length, each session containing four trials for each of eight experimental conditions.

In experiment 1, numerosities 4, 8, 16, and 32 served as sample. Two stimulus lists were used that either equated the overall luminance change (list 1, resulting in decreasing dot size with increasing number) or dot size (list 2, resulting in increasing luminance change with increasing number) between numerosities (see Figure 1). Dot positions were randomly chosen for each stimulus and trial. Dot patterns further included four different density levels in list 1 and four different dot sizes in list 2 (the same individual sizes that resulted from equating overall luminance change between numerosities in list 1). Stimuli used for sample and match displays in a given trial were always drawn from different lists.

Experiment 2 used numerosities 2, 4, 6, and 8 as sample stimuli (either dot patterns of equated luminance or Arabic numerals adjusted in size so that their luminance was constant and matched to the dot stimuli). In equal proportions of trials, sample and match stimulus were of the same format (dot followed by dot, digit followed by digit) or different formats (dot followed by digit, digit followed by dot).

Data Analysis

After preprocessing including motion correction and normalization to Montreal Neurological Institute (MNI) space with SPM5 (http://www.fil.ion.ucl.ac.uk/spm/software/spm5), the unsmoothed EPI images were entered into a general linear model, including regressors for the eight sample stimulus conditions (four numerosities × two stimulus lists or formats) and eight match stimulus conditions (four numerosities × smaller versus larger match stimulus) with a standard hemodynamic response function. The resulting eight independent estimates of fMRI signal change for each sample condition (one parameter estimate image per condition for each session) were used for pattern analysis.

Regions of interest were defined subject by subject as the 1000 (not necessarily contiguous) voxels most significantly activated across all sample stimulus conditions within a mask of the parietal lobe in MNI space (Wake Forest University PickAtlas, http://fmri.wfubmc.edu/cms/software). In additional analyses, a multivariate searchlight with a 3 voxel radius (encompassing $\leq$ 93 voxels) was used as a moving ROI centered in an iterative procedure on each voxel of the volume. (A relatively small radius was chosen to avoid disproportionally increased computation time.)

Pattern recognition analysis in both ROI and whole-brain searchlight analyses was performed on parameter estimate images mean corrected across voxels with linear support vector machines (SVM) [44] applied either for classification or regression. All analyses were based on leave-one-session-out cross-validation (with one pattern per condition for each of the eight sessions). Classification on predefined ROIs used SVM in the implementation of Gunn (http://www.isis.ecs.soton.ac.uk) for MATLAB; searchlight analysis and regression used in-house software based on a Python binding of LIBSVM (http://www.csie.ntu.edu.tw/~cjlin/libsvm/).

Classification for all pairwise comparisons between conditions used a fixed regularization parameter C = 1, and accuracies were subsequently averaged over different comparisons of interest (e.g., all dots, all digits, all comparisons between format for a given number). Generalization of classification performance was tested training on a given pairwise number comparison involving stimulus list 1 and testing the same comparison on stimulus list 2 and vice versa in experiment 1, and analogously for the two formats in experiment 2. Classification performance for ROI data was tested for significance across the group of subjects by pairwise t tests with respect to chance level (50%). For searchlight analysis, starting with voxel-wise values reflecting discrimination accuracies for a given pair of conditions within the sphere centered on that voxel, images were adjusted with respect to chance level by subtracting 50%, averaged over all comparisons of interest, and subsequently tested for significance across subjects in one-sample t tests, applying correction for multiple comparisons by random field theory in SPM5. Display of statistical results (and regions of interest) used the PALS atlas [45] of Caret 5.51 (http://www.nitrc.org/projects/caret/).

Multivariate support vector regression [44] was used to test for gradual changes in activity pattern as a function of magnitude. Patterns evoked by the four numerosities (separately for stimulus lists and formats) were fitted by a four-step function corresponding to the logarithm of the four numerosities after mean correction. The percentage of variance explained by this fit was evaluated in session-wise leave-one-out cross-validation (see Technical Appendix in Supplemental Experimental Procedures).

Supplemental Data

Supplemental Data include Supplemental Results, Supplemental Experimental Procedures, and nine figures and can be found with this article online at http://www.cell.com/current-biology/supplemental/S0960-9822(09)01623-6.

Acknowledgments

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