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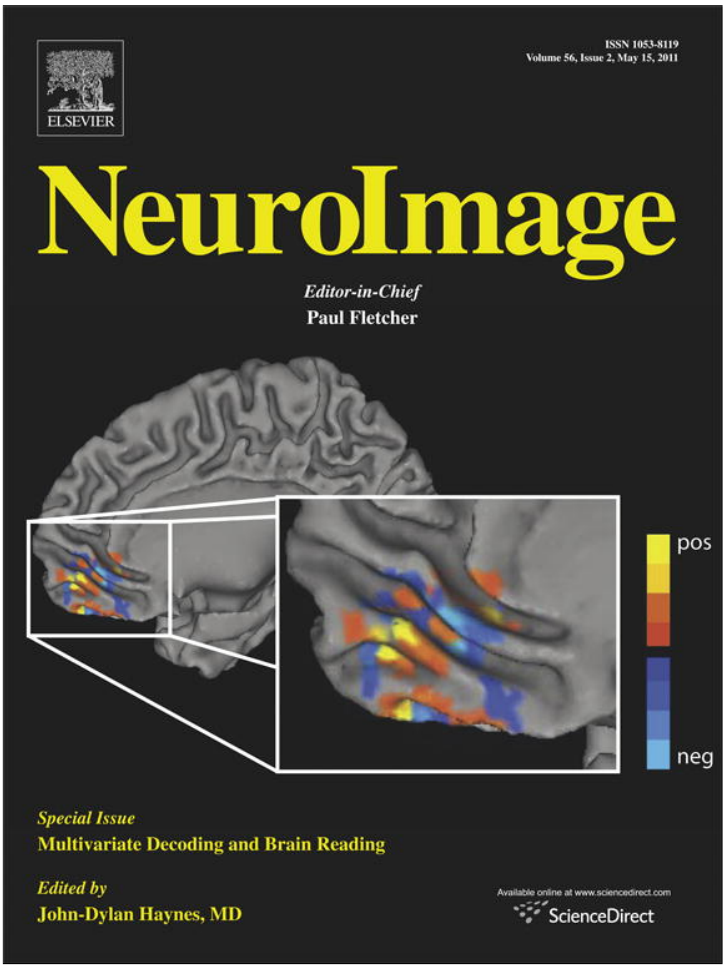

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Distinct representations of numerical and non-numerical order in the human intraparietal sulcus revealed by multivariate pattern recognition

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ABSTRACT

Neuroimaging studies of numerical cognition have pointed to the horizontal segment of the intraparietal sulcus (hIPS) as the neural correlate of numerical representations in humans. However, the specificity of hIPS for numbers remains controversial. For example, its activation during numerical comparison cannot be distinguished from activation during ordinal judgments on non-numerical sequences such as letters (Fias et al., 2007, J. Neuroscience). Based on the hypothesis that the fine-grained distinction between representations of numerical vs. letter order in hIPS might simply be invisible to conventional fMRI data analysis, we used support vector machines (SVM) to reanalyse the data of Fias et al. (2007). We show that classifiers trained on hIPS voxels can discriminate between number comparison and letter comparison, even though the two tasks produce the same metric of behaviour. Voxels discriminating between the two conditions were consistent across subjects and contribution analysis revealed maps of distinct sets of voxels implicated in the processing of numerical vs. alphabetical order in bilateral hIPS. These results reconcile the neuroimaging data with the neuropsychological evidence suggesting dissociations between numbers and other non-numerical ordered sequences, and demonstrate that multivariate analyses are fundamental to address fine-grained theoretical issues with fMRI studies.

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Introduction

The neural correlates of number representations in humans have been extensively investigated using functional neuroimaging techniques. The bilateral parietal cortex appears to be routinely involved in numerical processing and the horizontal segment of the intraparietal sulcus (hIPS) has been identified as core area for the representation of numerical quantity (Dehaene et al., 2003, for review and meta-analysis of neuroimaging data).

Ordering by magnitude (i.e., number comparison) is the most widely used number processing task because it implies explicit access to a representation of numerical quantity. Pinel et al. (2001) found that the activation of hIPS during number comparison was modulated by the numerical distance between the compared numbers, thereby mirroring the behavioural signature of the distance effect in reaction time (RT) data (e.g., Moyer and Landauer, 1967). The same modulation was found by Piazza et al. (2004) using a fMRI adaptation paradigm. A change in the quantity dimension during passive viewing of sets of dots yielded a selective activation of hIPS. Moreover, hIPS activation was found to be notation-independent in a subsequent study (Piazza et al., 2007), suggesting an abstract coding of numerical quantities. These results fit well with the properties of numerosity-selective neurons recorded in the putative monkey homolog of hIPS (Nieder and Miller, 2004).

Many studies have sought to demonstrate number selectivity in IPS (e.g., Ansari et al., 2006; Cantlon et al., 2006; Chochon et al., 1999; Cohen Kadosh et al., 2005, 2007; Dehaene et al., 1996; Eger et al., 2003; Fias et al., 2003; Pinel et al., 1999; Naccache and Dehaene, 2001; Pinel et al., 2001; Shuman and Kanwisher, 2004; Thioux et al., 2005). Nonetheless, the specificity of IPS for numbers remains controversial. A first concern is that number selectivity might be indistinguishable from aspecific processes associated with RT changes in the IPS. For example, Göbel et al. (2004) found that the main effect of response times over three different tasks (number comparison, vertical line judgment on numbers and vertical line judgment on non-numbers) activated the same left IPS area as the main effect of number comparison relative to either of the other two tasks. Similarly, Cappelletti et al. (2010) reported that left parietal activation is not number selective when response times are factored out, although they observed number selectivity in the right parietal lobe (not reported by Göbel et al.). Cappelletti et al. concluded that left parietal activation during conceptual tasks reflects the extraction and comparison of learnt information irrespective of stimulus type (e.g., whether numbers or object names).

A second issue that challenges the putative specificity of hIPS is related to the fact that numbers, in addition to the cardinal meaning

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(quantity), can also express ordinal meaning (i.e., rank). The role of hIPS in number processing might be to represent ordinality rather than just quantity/cardinality (Nieder, 2005). Indeed, Fias et al. (2007) showed that the hIPS is equally responsive during comparisons of numerical magnitude and letter order. Participants in their study had to judge which of two letters came later in the alphabet and the resulting activations were compared with those obtained when the task was to judge which of two numbers was larger (a more detailed description of the experimental paradigm, including control tasks, is provided in Materials and methods). Highly similar neural networks were activated by number and letter comparisons. Crucially, the conjunction between number and letter comparisons (each contrasted with a dimming detection task on the same stimuli) showed selective activation of bilateral hIPS. Thus, hIPS activation was not related to stimulus complexity or response selection but specifically to order comparison. It is worth noting that Eger et al. (2003) found stronger activation of hIPS for number processing than for letter processing but their simple identification task did not involve processing the ordinal dimension of letters. Further support to the hypothesis that hIPS is involved in the representation and processing of non-numerical ordered sequences (Fias et al., 2007) is provided by the study of Ischebeck et al. (2008), who found no significant difference in IPS between ordered generation of months and numbers, compared to the generation of non-ordered names of animals.

Both number comparison and letter comparison tasks reveal a graded distance effect in the RTs (Hamilton and Sanford, 1978; Moyer and Landauer, 1967). The SNARC effect (Dehaene et al., 1993), which indexes faster left-hand than right-hand responses to small numbers and faster right-hand than left-hand responses for larger numbers (in Western cultures), has been extended to non-numerical ordered sequences (Gevers et al., 2003), suggesting that both numbers and the alphabet are spatially coded. Left neglect patients, who are known to misbisect numerical intervals to the right of the true midpoint (Zorzi et al., 2002), show a spatial bias in the bisection of letter intervals, although with subtle differences from number interval bisection (Zorzi et al., 2006; also see Zamarian et al., 2007).

In summary, the fact that hIPS activation during number comparison cannot be distinguished from activation during comparison of non-numerical ordered sequences can be interpreted in two ways: either hIPS is coding abstract order information, common to all ordered sequences (Fias et al., 2007; Ischebeck et al., 2008), or hIPS activation reflects a shared comparison mechanism that operates on any type of conceptual information (Cappelletti et al., 2010). However, there is a third possible interpretation. The results of Fias et al. (2007) and Ischebeck et al. (2008), though suggestive, do not necessarily imply that the same neuronal populations within hIPS are involved in processing both numerical and non-numerical ordered sequences (see Jacob and Nieder, 2008, for a similar argument). The results might be an artefact due to the limited spatial resolution of fMRI and/or the limitations imposed by the conventional univariate fMRI data analysis (general linear model). For example, single-cell recording studies in monkeys have shown that the representation of discrete and continuous quantities (numerosity vs. line length) is supported by largely distinct subpopulations of IPS neurons (Tudusciuc and Nieder, 2007). Moreover, neuropsychological evidence suggests that, even within the number domain, ordinal meaning of numbers can dissociate from cardinal meaning in single case studies (Delazer and Butterworth, 1997; Turconi and Seron, 2002).

Multivariate pattern recognition techniques provide a powerful tool for investigating fine-grained theoretical issues with fMRI. For example, multivariate analysis of fMRI data has revealed spatially distinct object categories in ventrotemporal cortex (e.g., Haxby et al., 2001; O'Toole et al., 2005) and it has been used for decoding line orientation from primary visual cortex (Haynes and Rees, 2005; Kamitani and Tong, 2005). In the number domain, multivariate pattern recognition has been used to test the hypothesis that cortical circuits for spatial attention contribute to mental arithmetic (Knops et al., 2009) and to investigate number coding in the parietal cortex (Eger et al., 2009).

The question of whether the cardinal and ordinal dimensions can be dissociated at the level of hIPS seems an excellent test case for multivariate analysis. In the present study we reanalysed the fMRI data of Fias et al. (2007) using support vector machines (SVM) as multivariate classifiers. Our aim was to i) establish whether the parietal activation induced by number comparison and letter comparison, indistinguishable in conventional univariate analyses, would contain sufficient information to allow reliable classification in a multivariate approach; ii) compare linear and nonlinear classifiers; iii) obtain maps of the discriminating voxels to establish whether activation related to number and letter comparison can be spatially resolved within hIPS and, if so, whether the locations are consistent across subjects.

Materials and methods

In this section we briefly describe the fMRI data acquired by Fias et al. (2007). We then provide a detailed description of our multivariate analysis of the fMRI data. In particular, we illustrate the methodological aspects related to two pattern recognition techniques employed here (linear SVM vs. nonlinear SVM), the statistical analyses applied to the classifier results, and the activation maps obtained from the classifiers.

Experimental setting

Fias et al. (2007) investigated whether hIPS is selectively involved in processing numerical information in its cardinal dimension (i.e., numerical quantity) or it is also recruited in processing the ordinal dimension, which is typical of other non-numerical sequences like the alphabet. In the following section we summarise stimuli, procedure, and fMRI data acquisition. Full details can be found in Fias et al. (2007).

Participants

Seventeen volunteers (9 female, 13 right-handed; age, 20–37 years) participated in the study. All gave written informed consent as approved by the ethics committee of the Medical Department of Ghent University. None of the subjects had a history of neurological or psychiatric illness.

Stimuli

There were three types of stimuli: numbers and letters presented in white, and coloured squares. In each trial, two stimuli of the same type were presented on both sides of a central fixation cross. Participants had to perform two different tasks: a comparison task and a dimming detection task. Thus, the resulting experimental conditions were: number comparison, letter comparison, or saturation comparison, and dimming detection on numbers, letters, or squares. For both tasks, the first item of the presented pair was randomly chosen from a set of 24 letters (B–Y), or 89 numbers (10–98), or any combination of hue and saturation values in the hue–saturation–brightness (HSB) colour space. The second item of the pair was chosen in a way that it differed by a certain distance from the first one. This distance was determined, for each subject, examining the accuracy performance of each subject during a training session executed before the scanning sessions. In both tasks, the brightness of one randomly selected item of the pair was reduced for a period of 75 ms. Fias et al. determined the magnitude of the luminance reduction in the initial practice session, on the basis of the accuracy reached by each participant in the dimming detection task.

Procedure

The experiment was structured into five sessions (runs). All the runs were composed of 12 blocks (2 blocks per condition) of 16 trials. In each block, before the presentation of the trials, there was a period of fixation (5.6 s), followed by a period of 2.8 s during which the

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instructions of that block were visualised. In the number comparison task, participants were asked to select which one of the presented numbers was the larger. In the same task with letters, participants had to select which letter came later in the alphabet, whereas when stimuli were coloured squares they had to select the most saturated one. In the dimming detection task, participants had to select the dimmed stimulus. In all the tasks the response was performed by pressing a key on the same side of the chosen stimulus.

fMRI data acquisition

For each participant, a T1 anatomical image (176 slices; slice thickness, 0.90 mm; in-plane resolution, 0.9 x 0.9 mm; repetition time (TR), 1550 ms; echo time (TE), 2.89 ms) was acquired for co-registration with the functional images using a Siemens 3 T Trio scanner. Functional volumes were acquired using a multiple slice $T2^*$-weighted echo planar imaging (EPI), with TR = 2800 ms, TE = 33 ms, flip angle = 90°; in-plane resolution = 3 × 3 mm; matrix dimension = 64 × 64, field of view = 192 × 192 mm; slice thickness = 2 mm. For each run, 40 slices per volume and a total of 132 volumes were acquired, resulting in 660 functional volumes.

Multivariate analysis

A number of important technical issues must be considered before running multivariate analyses of fMRI data. First, pre-processing steps (i.e., realignment, co-registration, normalization, spatial and temporal smoothing) can have a considerable impact on the final results. Spatial smoothing is the most critical step, because it introduces a certain degree of intervoxel correlation and it also increases the normality of data, which is a pre-requisite for many statistical tests. However, spatial filters can also reduce the signal to noise ratio (SNR) and may cause the loss of information useful for separating adjacent but functionally different brain areas. Thus, even if it produces some advantages for voxelwise analysis, it has little effect or is even dangerous in multivariate brain analysis. We therefore applied our analyses on the functional images without spatial smoothing. Second, fMRI data are affected by a problem known as the curse of dimensionality, which refers to the fact that the higher the dimensionality of the input space, the more data may be needed to find out what is important and what is not in the classification. Therefore, the number of samples (i.e., volumes) has to increase exponentially with the number of variables (i.e., voxels) in order to maintain a given level of accuracy. This problem is generally faced by using different approaches (e.g., univariate, wrapper or embedded methods) for feature (i.e., voxel) selection, or by performing hypothesis-guided analyses that permit to restrict the investigation to one or more specific regions of interest (ROIs) of the brain. On the basis of the results obtained by Fias et al. (2007), we chose to focus our analysis on the voxel time series within bilateral hIPS and supplementary motor area (SMA) as regions of interest (see below). Third, the choice of classifier might be important and the use of both linear and nonlinear classifiers must be considered because linear ones can fail to produce satisfactory results, at least for some participants (O'Toole et al., 2007).

In this study we used support vector machines (SVM), by using linear and nonlinear kernels, as pattern recognition techniques for discriminating between the experimental conditions (i.e., number vs. letter comparison) from the fMRI data of Fias et al. (2007). The following sections describe extraction of the ROIs from the functional images, basic pre-processing, classifier training, analysis of classifier performance, and analysis of classification activation maps.

ROI selection

The functional images used for ROI extraction were those pre-processed by Fias et al. (2007) up to but excluding spatial smoothing. We considered three ROIs (see Fig. 1):

i) Functionally defined hIPS (ROI-1). We used local maxima of activations obtained by Fias et al. (2007) in the conjunction analysis of number comparison and letter comparison to define the centres of two spheres with radius $r = 8$ mm. The Talairach coordinates of the centres were [−39, −39, 36] and [45, −36, 48] for left and right hIPS, respectively. This yielded a set of 164 voxel time series of 660 volumes each. The selection of ROI-1 on the basis of a previous analysis of the same dataset raises the issue of non-independence (see Kriegeskorte et al., 2009, for a thorough discussion). In the present case, three factors moderate the (partial) non-independence. First, we did not select active voxels and we did not use any information at the level of individual participants (note that only the latter is relevant for multivariate classifiers). Second, we used spatially unsmoothed data, whereas Fias et al. employed a 6 mm (full-width at half-maximum) Gaussian kernel for smoothing. Third, the selected ROIs are very close to the coordinates of hIPS reported by Dehaene et al. (2003) in their meta-analysis of fMRI studies of numerical cognition. Nonetheless, to exclude any bias in the classifier results, we also considered an anatomically defined ROI, where we expected similar classification rates, and a functionally defined control region, where we expected chance performance.

ii) Anatomically defined IPS (ROI-2). The activations found by Fias et al. (2007) overlap with the location of the putative homolog of the anterior intraparietal area (Grefkes et al., 2002). Therefore, we defined this ROI according to the anatomical study of Choi et al. (2006) on the human IPS. We used two different subregions of the anterior IPS to create the anatomical ROI mask using SPM Anatomy toolbox (areas hIP1 and hIP2; http://www.fil.ion.ucl.ac.uk/spm/ext/#Anatomy). ROI extraction yielded a set of 327 voxel time series

iii) Supplementary motor area (ROI-3). This functionally defined ROI was used as a control region and it was selected according to the local maxima of activations obtained by Fias et al. (2007) in the conjunction analysis of number comparison and letter comparison. Two spheres with radius $r = 8$ mm and centres at [−6, 3, 53] and [12, 3, 45] were extracted for left and right SMA, respectively, yielding a set of 161 voxel time series. Since SMA

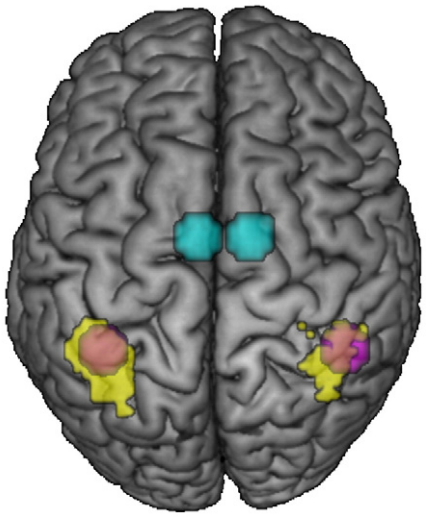

Fig. 1. Regions of interest (ROIs) used in the multivariate classifier analyses, transparently superimposed on top view of a standard template using MRICron software. ROI-1 (i.e., bilateral hIPS, in violet) and ROI-3 (i.e., bilateral SMA, in cyan) were spheres with 8 mm radius centered on the activation foci in Fias et al.'s (2007) conjunction analysis of number and letter comparison (Talairach coordinates: [−39, −39, 36] for left hIPS and [45, −36, 48] for right hIPS; [−6, 3, 53] for left SMA and [12, 3, 45] for right SMA). ROI-2 (in yellow) includes two subregions in the anterior part of IPS (Choi et al., 2006).

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is typically involved in response preparation, we did not expect it to reliably discriminate between number comparison and letter comparison tasks.

Basic pre-processing

After ROI extraction, the voxel time series were pre-processed through a series of commonly used steps: standardization, detrending and temporal filtering. In particular, each of the five runs was processed separately. The time series were first standardised to have zero mean and standard deviation one. Then, linear trends in each time series were removed. Finally, a temporal filter (moving average filter, window size of 5 volumes) was applied to remove the high frequency components in the signal. Moving average filters are normally used as low pass filters. The resulting time series were finally ready for the classification phase.

Classification phase

We performed two main analyses. The aim of the first one was to investigate the involvement of the hIPS regions in number and letter processing during the comparison tasks. We therefore trained both linear and nonlinear classifiers on the voxels within bilateral hIPS regions. In a second analysis we addressed the question of possible hemispheric asymmetries for number vs. letter comparison tasks. We therefore trained the SVM classifier to estimate the experimental conditions using only the voxel time series extracted from the left or the right hIPS.

When using linear SVM for classification, the critical parameter to tune is the regularization constant C that governs the error penalty term in the soft margin formulation of SVM by Vapnik (1999). Another crucial issue is the evaluation of the consistency of the generalization ability of the classifier, often measured through a cross-validation technique. In the nonlinear case, the only difference is that it is necessary to choose among different kernel functions (e.g., polynomial, radial basis function (RBF)) and their corresponding parameters (i.e., the polynomial degree or the width of the RBF).

We now describe the procedure we used for preparing data for training, for assessing the impact of different learning parameters on the generalization ability of the classifier, and for measuring the robustness of the results. All analyses were performed for each subject separately.

The fMRI dataset for the classification was created taking into account only the fMRI blocks referring to the two contrasted experimental conditions (i.e., number vs. letter comparison) and data were sampled in such a way to be considered independent for SVM training and testing. In particular, for each block, we discarded the first five volumes (relative to fixation, instructions and the first four trials) to capture a more stable fMRI signal and then created one sample averaging the remaining volume images (e.g., Pereira et al., 2009). Consequently, the target condition (i.e., number vs. letter comparison task) was coded in such a way as to have a vector $T_i \in \{+1, -1\}^N$, where i refers to the block and N is the number of blocks relative to both conditions in contrast (e.g., in this case $N=20$, one block per condition for each run), in which all the blocks corresponding to one target condition were labelled with $+1$, whereas all the other blocks with -1.

A cross-validation loop was used to find the classifier parameters yielding the best classification rate and to test generalization performance. We defined a grid of parameter combinations that included the value of the regularization constant C [range 1–10, with steps of 1] and the kernel function in the set [linear, polynomial, RBF]. The parameter of the nonlinear kernel functions (i.e., the polynomial degree and the RBF width) was fixed to 1. For each parameter combination, the SVM classifier was trained on the dataset using a modified version of leave-one-out cross-validation. At each step of the cross-validation loop, four samples were excluded from the training set. Two samples (one for each condition) served as validation set to optimize the learning parameters, whereas the other two (again, one per condition) were used to test generalization performance. Two classic performance indices were used as statistical measures of binary classification: accuracy and d′ sensitivity (both computed across the entire cross-validation loop). The best classifier was selected in terms of the maximum accuracy on the validation set. All results reported below refer to the generalization performance of the chosen classifier on the test set. We conducted a t-test on both generalization performance indices to obtain group statistics regarding the discriminability between number comparison and letter comparison.

In the case of linear SVM, analysis of the weight vector associated by the classifier to the training data can provide a map of the discriminating voxels (in nonlinear SVM, however, there is no direct way to characterise the most discriminating voxels). The discriminating maps were computed including those voxels that, during the cross-validation loop, had a positive weight value (number comparison) or a negative weight value (letter comparison) with a frequency greater than the mean frequency + 1 SD. We then averaged the selected voxel weights across the cross-validation runs. The discriminating maps were computed using the weight values of the selective voxels to index their relative contribution towards classification into a given condition (number vs. letter comparison).

Results

In this section we report the results obtained by training SVMs on the selected regions of interest. For each ROI, we illustrate these results in terms of classification performance on the test set.

ROI-1: Bilateral hIPS (Fias et al., 2007)

We trained SVMs on the voxel time series extracted from the bilateral hIPS for discriminating between letter comparison and number comparison tasks. The mean accuracy across all participants was 0.59 ± 0.03 (1 SE), which is significantly above the chance level of 0.5 ($t(16) = 3.13$, $p < 0.01$). Averaged across participants d′ sensitivity was 0.52 ± 0.18 (1 SE) which is significantly above the chance level of 0 ($t(16) = 2.87$, $p = 0.01$). For each participant, Table 1 reports the selected learning parameters (i.e., regularization constant C and kernel function) and the classifier performance expressed in terms of accuracy. The choice of the regularization constant C did not have a great impact on the final generalization performance. Indeed, for only 2 out of 17 participants the validation procedure selected $C = 2$. The selected kernel function was linear for eight of the participants. The RBF kernel was selected for six participants and the polynomial kernel for three participants. Fig. 2 shows the classification performance (d′) per participant.

To investigate possible hemispheric asymmetries in the discrimination between number and letter comparison tasks, we separately trained a set of SVM classifiers on the left and the right hIPS. The mean accuracy across all participants in left hIPS was 0.57 ± 0.02 (1 SE), which is significantly above the chance level of 0.5 ($t(16) = 2.86$, $p < 0.05$). Averaged across participants d′ sensitivity was 0.36 ± 0.13 (1 SE) which is significantly above the chance level of 0 ($t(16) = 2.7$, $p < 0.05$). For the right hIPS, mean accuracy across all participants was 0.58 ± 0.04 (1 SE), which is significantly above the chance level of 0.5 ($t(16) = 2.16$, $p < 0.05$). Averaged across participants, d′ sensitivity was 0.45 ± 0.22 (1 SE) which is marginally above the chance level of 0 ($t(16) = 2.04$, $p = 0.058$). Classifier performance was not statistically different for left vs. right hIPS (paired t-tests: $p > 0.7$ for both indices).

ROI-2: Bilateral anterior IPS (Choi et al., 2006)

We trained SVMs on the voxel time series extracted from the bilateral anterior IPS for discriminating between number and letter comparison tasks. The mean accuracy across all participants was 0.6 ± 0.04 (1 SE), which is significantly above the chance level of 0.5 (t

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Table 1
Accuracy and learning parameters selected for each participant in the SVM discrimination between letter and number comparison tasks in bilateral IPS (functional hIPS from Fias et al., 2007; anatomical IPS from Choi et al., 2006). Note: Rbf = radial basis function; Poly = polynomial.

SVM classifier trained on bilateral hIPS regions						
Participant	Functional hIPS			Anatomical IPS		
	Accuracy	*C*	Kernel	Accuracy	*C*	Kernel
1	0.7	2	Rbf	0.7	1	Linear
2	0.5	1	Rbf	0.6	1	Linear
3	0.7	1	Poly	0.55	1	Poly
4	0.8	1	Linear	0.85	1	Linear
5	0.5	1	Linear	0.4	1	Rbf
6	0.65	1	Linear	0.55	1	Linear
7	0.4	1	Linear	0.25	1	Linear
8	0.55	1	Poly	0.55	1	Linear
9	0.45	1	Rbf	0.6	1	Linear
10	0.65	1	Linear	0.75	1	Poly
11	0.45	1	Rbf	0.5	1	Rbf
12	0.55	1	Linear	0.55	1	Poly
13	0.5	1	Linear	0.5	1	Linear
14	0.6	1	Rbf	0.6	1	Rbf
15	0.75	1	Poly	0.75	1	Linear
16	0.75	2	Linear	0.85	1	Linear
17	0.55	1	Rbf	0.65	1	Rbf

$(16) = 2.69$, $p < 0.05$). Averaged across participants d′ sensitivity was 0.53 ± 0.2 (1 SE) which is significantly above the chance level of 0 ($t(16) = 2.51$, $p < 0.05$). For each participant, Table 1 reports the selected learning parameters (i.e., regularization constant *C* and the kernel function) and the classifier performance expressed in terms of accuracy. The choice of the regularization constant *C* was not influential on the classifier performance (for all participants the selected value was $C = 1$, which is the default value). The RBF kernel was selected for four participants and the polynomial kernel for three participants. Fig. 2 shows the classification performance (d′) per participant.

Our findings on the anatomically defined ROI show that the results obtained on the functionally defined hIPS cannot be attributed to a bias due to (partial) non-independence in ROI selection (Kriegeskorte et al., 2009).

ROI-3: Bilateral SMA (Fias et al., 2007)

We trained SVMs on the voxel time series extracted from the bilateral SMA for discriminating between number and letter comparison tasks. The mean accuracy across all participants was 0.55 ± 0.009 (1 SE), and the mean d′ sensitivity was 0.27 ± 0.05 (1 SE). Both indices were not significantly different from chance level performance ($t(16) = 1.32$, $p > 0.2$ for accuracy and $t(16) = 1.28$, $p > 0.2$ for d′ sensitivity). The results obtained in this control ROI show that discrimination between number and letter comparison tasks is not possible in bilateral SMA, although these activation foci were obtained by Fias et al. (2007) in the same conjunction analysis that yielded bilateral hIPS activation.

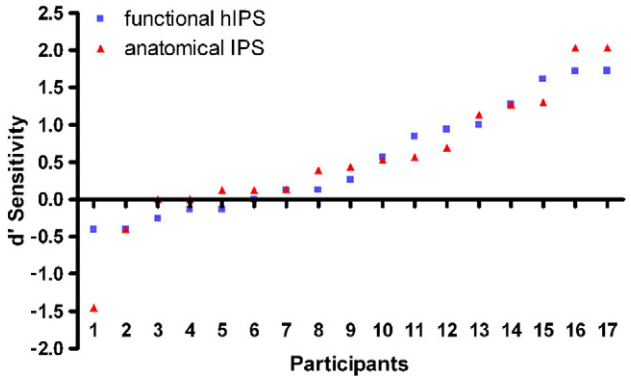

Fig. 2. SVM classification performance for each participant on functional (blue) and anatomical (red) hIPS. The classifier performance is expressed in terms of d′ sensitivity. Participants are sorted according to the d′ obtained for the discrimination between number and letter comparison tasks.

Discriminating maps

Fig. 3 shows the discriminating maps (i.e., number vs. letter comparison) obtained for the two participants (participants 4 and 16) for whom we obtained the best linear SVM classification accuracy on bilateral hIPS. Analyses of individual discriminating maps were not pursued because the classifier was nonlinear for more than half of the participants. Nonetheless, to investigate whether voxels discriminating between number and letter comparison can be consistently found across individual subjects, we trained a linear classifier on a new dataset that was the union of the individual datasets for all participants. Thus, the classifier was blind to individual differences because it had to discriminate the two conditions across examples that came from different participants. For each value of the *C* parameter (varying in the range [1–10]), the SVM classifier was trained on the dataset using a leave-one-subject-out cross-validation. At each step of the cross-validation loop, the data of two subjects were excluded from the training set (i.e., training was performed on the data from 15 subjects). The data of one subject held out from training served as validation set to optimize the *C* parameter, whereas the data of the other subject was used to test generalization performance. The generalization accuracy of the selected classifier (with $C = 5$) was 0.58, which is significantly above the chance level ($p < 0.001$, binomial test). This shows that the discrimination between number comparison and letter comparison is possible across a set of voxels that is shared across participants. The discriminating maps obtained from the classifier are shown in Fig. 4. The number of selected voxels was similar across hemispheres (left hIPS: 22 for numbers, 19 for letters; right hIPS: 18 for numbers, 26 for letters).

Discussion

We demonstrated that hIPS activations for number comparison and letter comparison, which were found to be indistinguishable in conventional univariate analyses (Fias et al., 2007), can be reliably separated by multivariate classifiers. This clearly shows that the complete overlap between number and letter processing in hIPS was an artefact due to the limitations imposed by the conventional fMRI data analysis (i.e., spatial smoothing and univariate statistics).

From a theoretical perspective, our results rule out the hypothesis that IPS activation during number processing is associated with RT changes or with the comparison process per se (Cappelletti et al., 2010; Göbel et al., 2004), because number and letter comparison where indistinguishable in terms of RT and error rate (Fias et al., 2007). Moreover, classifiers trained on bilateral SMA did not reliably distinguish number comparison from letter comparison, even though this region was found to be jointly activated by the two tasks in the conjunction analysis performed by Fias et al. (2007).

In terms of the issue of possible hemispheric differences, the separate analyses performed on left and right hIPS ruled out any hemispheric asymmetry in terms of number vs. letter processing, which counters the claim that left parietal activation is not number selective (Cappelletti et al., 2010). As noted in the Introduction, number comparison and letter comparison produce very similar patterns of RTs, with the distance effect as main determinant of response latencies. This implies that the separability between number-selective and letter-selective neural patterns must be related to a more fundamental distinction between number comparison and letter comparison. Indeed, our results can be interpreted in terms of a dissociation between cardinal and ordinal

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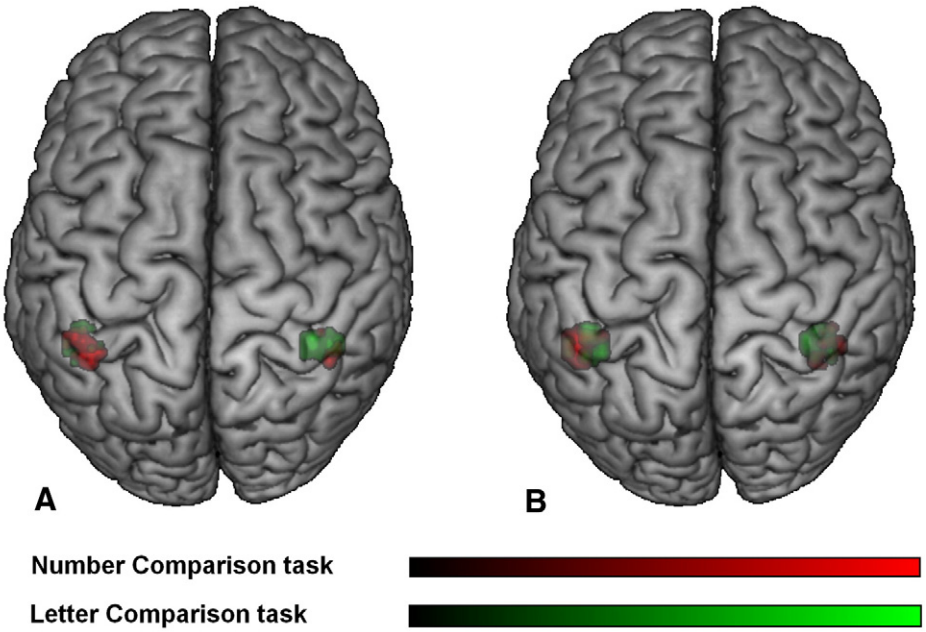

Fig. 3. Discriminating maps (number comparison in red, letter comparison in green) for the two participants for whom linear SVM classification accuracy on bilateral hIPS was highest. The discriminating maps show voxels that are selective for number comparison (red) or letter comparison (green). The color scale indexes the relative contribution of each voxel towards classification into a given condition. The maps have been transparently superimposed on a standard template using MRICron software (http://www.cabiatl.com/mricro/mricron/index.html). A. Participant 4. B. Participant 16.

meanings. Such a dissociation has been reported in neuropsychological single case studies (Delazer and Butterworth, 1997; Turconi and Seron, 2002). Numbers and letters share the ordinal dimensions, but for numbers the cardinal dimension (i.e., numerical magnitude) is most prominent in a wide range of numerical tasks (and especially in number comparison). The results of our analyses show that distinct sets of voxels and/or distinct patterns of activity across voxels are involved in number and letter processing. The discriminating maps displayed in Figs. 3 and 4 indeed suggest that different voxels are involved. This would mean that ordinal judgments on non-numerical sequences and ordering numbers by magnitude are supported by different neuron populations within hIPS, as it is the case for discrete vs. continuous quantities (Tudusciuc and Nieder, 2007). One outstanding question is whether there is any systematicity in the topography of number and letter sequences in the IPS. Event-related designs would be better suited for this goal (see, e.g., Eger et al., 2009). A second question is whether processing of order information in hIPS is common to all non-numerical ordered sequences (e.g., letters vs. months), which would imply abstract coding of order irrespective of stimulus type. However, we predict that multivariate classifiers would separate ordered generation of months and numbers, which were found to elicit identical IPS activations using conventional analyses (Ischebeck et al., 2008).

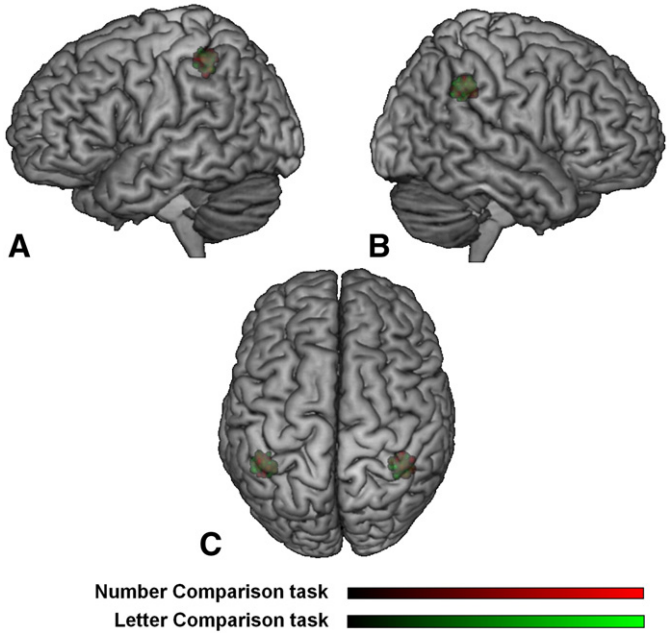

Fig. 4. Discriminating maps (number comparison in red, letter comparison in green) obtained by training a linear SVM classifier on bilateral hIPS data for all participants. The discriminating maps show voxels that are selective for number comparison (red) or letter comparison (green). The color scale indexes the relative contribution of each voxel towards classification into a given condition. The maps have been transparently superimposed on a standard template using MRICron software. A. Left view. B. Right view. C. Top view.

In conclusion, the present study illustrates the value of multivariate pattern recognition techniques for investigating fine-grained theoretical issues with fMRI. Moreover, our results show that multivariate analyses are mandatory to tackle subtle but important distinctions (for cognitive theory) such as cardinal vs. ordinal information or numerical vs. non-numerical ordered sequences.

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