



Common and segregated neural pathways for the processing of symbolic and nonsymbolic numerical magnitude: An fMRI study

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ABSTRACT

Numbers are everywhere in modern life. Looking out a window, one might see both symbolic numbers, like the numerals on a thermometer, and nonsymbolic quantities, such as the number of chickadees at a bird feeder. Although differences between symbolic and nonsymbolic numbers appear very salient, most research on numerical cognition has focused on similarities rather than differences between numerical stimulus formats. Thus, little is known about differences in the processing of symbolic and nonsymbolic numerical magnitudes. A recent computational model proposed that symbolic and nonsymbolic quantities undergo distinct encoding processes which then converge on a common neural representation of numerical magnitude (Verguts, T., Fias, W., 2004. Representation of number in animals and humans: a neural model. *J. Cogn. Neurosci.* 16 (9), 1493–1504.). Moreover, this model predicted that discrete brain regions underlie these encoding processes. Using functional magnetic resonance imaging, the present study tested the predictions of this model by examining the functional neuroanatomy of symbolic and nonsymbolic number processing. Nineteen adults compared the relative numerical magnitude of symbolic and nonsymbolic stimuli. An initial conjunction analysis revealed the right inferior parietal lobule to be significantly active in both symbolic and nonsymbolic numerical comparison. A contrast of the activation associated with symbolic and nonsymbolic stimuli revealed that both the left angular and superior temporal gyri were more activated for symbolic compared to nonsymbolic numerical magnitude judgments. The reverse comparison (nonsymbolic > symbolic) revealed several regions including the right posterior superior parietal lobe. These results reveal both format-general and format-specific processing of numerical stimuli in the brain. The potential roles of these regions in symbolic and nonsymbolic numerical processing are discussed.

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Introduction

Because a number is an abstract quality of a set, its meaning does not depend on the format in which that number is presented. In other words, whether one sees a numerical representation such as “6,” a verbal representation such as “six,” or a nonsymbolic representation such as six goldfinches in a bush, the “sixness” of the number is the same in all cases.

This abstract quality of numerical information has led to a substantial amount of research which has canvassed the brain in search of brain responses that reflect such an abstract representation of numerical magnitude. These empirical efforts have demonstrated that bilateral inferior parietal regions (most commonly the intraparietal sulcus (IPS)) respond to numerical magnitude across numerical stimulus formats. The IPS is modulated by numerical information when magnitudes are presented as numerals (Ansari et al., 2005; Chochon et al., 1999; Pesenti

et al., 2000), words (Dehaene et al., 1996; Pinel et al., 2001), or nonsymbolic arrays (Ansari and Dhital, 2006; Ansari et al., 2006; Piazza et al., 2004, 2007; Venkatraman et al., 2005). In addition, numerical information evokes IPS activation in both the visual and the auditory domains (Eger et al., 2003). It has, therefore, been contended that the IPS is a region of the brain that supports the representation of abstract numerical information (Dehaene et al., 2003). However, it should be noted that the idea of abstract numerical representation has been challenged by recent behavioral and neuroimaging research (Cohen Kadosh, 2008; Cohen Kadosh et al., 2007).

Irrespective of its validity, by focusing on the search for an abstract representation of numerical magnitude, the majority of existing research has deemphasized the importance of numerical stimulus format in the processing of numerical magnitude. Investigations into abstract brain representations are an exploration of commonalities in the neural structures underlying the processing of all numerical stimulus formats and, therefore, treat differences between these formats as a variable of no interest.

Behavioral studies have begun to reveal important variations in numerical processing that depend upon differences in numerical stimulus format. For example, a study performed by Campbell has

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shown that stimulus format differences are crucial in the domain of calculation (Campbell, 1994). Specifically, these authors compared simple addition and multiplication problems presented as either Hindu–Arabic numerals or number words. The error profiles of the two problem types differed depending upon the numerical stimulus format in which the problems were presented. Format differences have also been shown to be important even for low-level numerical processing such as numerical comparison. For example, a recent behavioral study showed that children with developmental dyscalculia performed at the same level as matched controls on relative magnitude judgments of nonsymbolic arrays, but performed much more poorly than their typically developing peers on judgments of Hindu–Arabic numerals (Rousselle and Noël, 2007). In addition, behavioral work by Holloway and Ansari demonstrated a similar effect in a sample of typically developing children (Holloway and Ansari, 2009). Specifically, these authors found that children's individual differences in the basic processing of symbolic, but not nonsymbolic numerical magnitudes are related to individual differences in mathematics achievement.

In addition to behavioral research pointing to important format-related differences in number processing, recent brain imaging research has found hemispheric differences in numerical representation that are dependent on stimulus format. In a recent study, Cohen Kadosh et al., compared the neural representation of numerical magnitude for Hindu–Arabic numerals and written number words using an fMRI adaptation design. In fMRI adaptation experiments, the neural response to stimulus repetition is measured, with the assumption that neural regions involved in the processing of a particular stimulus dimension will decrease in their activation as a function of stimulus repetition. In their fMRI adaptation study, Cohen Kadosh et al. found that while left IPS exhibited cross-format adaptation (decreased parietal response following repetition of number irrespective of the presentation format), the right IPS was only found to adapt its response to the repeated presentation of Arabic numerals, with no such pattern emerging for number words or cross-format pairs (Cohen Kadosh et al., 2007). These data suggested that the left IPS is related to format-independent numerical magnitude representation, while the right IPS shows some specificity for the representation of Hindu–Arabic numerals. In a related experiment also employing an fMRI adaptation design, Piazza et al. demonstrated that the representation of Arabic numerals in the left IPS is more finely tuned than the representation of nonsymbolic arrays in the left IPS (Piazza et al., 2007). These two sets of findings have led some to argue that the abstract representation of numerical magnitude in the left IPS could undergo important changes due to enculturation (Ansari, 2007) and moreover suggests that the IPS may contain both abstract and non-abstract representations of numerical quantity.

In a recent computational model Verguts and Fias have proposed a mechanism by which differences in the processing of symbolic (i.e. Hindu–Arabic numerals) and nonsymbolic representations (i.e. arrays of dots) of numerical magnitude develop (Verguts and Fias, 2004). Using nonsymbolic numerical input, these authors trained a neural network to represent discrete quantities. Their model included an “input field” in which the external representation of the number was presented, a “summation field” in which the external, nonsymbolic representation was summed and recoded so that it could be represented on a place-coded “number field”. To explain, the “summation field” represents the items in the set through an additive process called summation coding. In summation coding the size of the representation monotonically increases with the size of the quantity being represented. In contrast to the “summation field,” the “number field” corresponds to the internal representation of number and is defined by place coding. Place coding is a way of representing the total number of items in a set by representing that quantity with a specific “place” on a number line. Verguts and Fias showed that with repeated trials, a neural network with a pre-existing ability to sum the items of

a nonsymbolic array could learn how to internally represent nonsymbolic quantities using place coding.

Verguts and Fias then tested whether this model could be trained to learn symbolic representations of numerical magnitude, such as the Hindu–Arabic numerals. Specifically, the authors tested the hypothesis that symbolic numerical representations can be learned through a process of association with pre-existing nonsymbolic representations of numerical magnitude. Thus, they trained their model to associate symbolic numerals with the nonsymbolic representations that the model had learned previously. In each trial the presentation of symbolic inputs was paired with the presentation of nonsymbolic inputs. As a function of this training regime, the network eventually developed a so-called “symbolic field” which was used in place of the “summation field” to transform symbolic inputs into place-coded representations on the internal layer of the model. In other words, the network began representing a symbolic number by summing the associated nonsymbolic array, but as a function of training time, ceased using summation coding and began mapping symbolic inputs directly onto the internal place coding representation common to symbolic and nonsymbolic representations of numerical magnitude.

Based on the results, two testable predictions can be derived from this model. First, the model predicts that across different types of surface format, numerical information is internally represented in a common, place-coded representation. Second, the model suggests that, within the adult human brain, one should find that symbolic and nonsymbolic external representations of numerical information are processed with divergent encoding pathways.

In the present functional magnetic resonance imaging (fMRI) study, we tested these two predictions. To do so, we collected functional neuroimaging data while participants performed relative magnitude judgments on both symbolic (Hindu–Arabic numerals) and nonsymbolic (arrays of squares) stimuli. A numerical comparison task was chosen for this study as such tasks require participants to process the stimuli semantically, while also allowing for differences in stimulus format. Therefore, this task could be used to measure both semantic and stimulus format-related processing. To test the first prediction of the Verguts and Fias model, we investigated which brain areas were associated with the conjunction of symbolic and nonsymbolic numerical magnitude comparison. In this way, we were able to identify regions that showed common activation to both numerical stimulus formats. In accordance with the large corpus of research (for an overview see Dehaene et al., 2003) examining the neural correlates of numerical representation, we predicted that a conjunction of activation between symbolic and nonsymbolic numerical processing would be found in inferior parietal regions. Although our hypothesis is convergent with the findings reviewed by Dehaene et al., our analysis includes important differences from these previous studies.

To test the second prediction, we statistically contrasted the neural responses to symbolic and nonsymbolic numerical comparison. We expected to find differential regions involved in the processing of our two numerical stimulus formats. We hypothesized that regions of the superior parietal lobe would be particularly involved in nonsymbolic numerical processing, while regions in the left temporoparietal junction would be implicated in symbolic numerical processing. Because a similar analysis has not been previously reported in the literature, we based our hypothesis on ancillary sources of evidence. With respect to nonsymbolic comparison, recent work has shown that neurons found in the lateral intraparietal area (LIP) of macaque monkeys are involved in numerically summing an array of objects (Roitman et al., 2007). The existence of this type of summation coding in humans has been shown in a behavioral study (Roggemann et al., 2007). Importantly, a number of studies have suggested that the human homologue of the macaque LIP is found in the superior parietal lobe (Koyama et al., 2004; Sereno et al., 2001). Consistent with these data from non-human primates, Santens et al. (in press) have recently shown that the posterior parietal cortex exhibits a pattern of

increasing activation with increasing numerical size of nonsymbolic arrays. Based on these findings, it is reasonable to predict that nonsymbolic comparison will activate regions of the superior parietal cortex, potentially reflecting this region's involvement in the summation coding necessary for nonsymbolic number processing.

To formulate our anatomical hypotheses for symbolic comparison, we looked to neuroimaging studies of reading. Against the background of data showing that left temporoparietal regions are involved in integrating orthographic, phonological and lexical-semantic dimensions of words during reading (Booth et al., 2003; Price, 2000; Pugh et al., 2001a), we hypothesized that these regions may also play a role in symbolic number processing and, in particular, the association of numerical symbols with their quantitative referents.

Method

Participants

Nineteen (10 females) adults (*Mean age* = 23.5 years, *Range* = 18.4–28.25 years) participated in this study. All participants were healthy, right-handed, and had normal or corrected-to-normal vision. Participants were recruited from graduate and undergraduate faculties at Dartmouth College, Hanover, NH, USA. All participants gave informed consent in accordance with the Committee for the Protection of Human Subjects at Dartmouth College. All fMRI scans took place at the Dartmouth College Brain Imaging Center.

To ensure that the fMRI data were not confounded by motion artifacts, we applied stringent criteria for the inclusion of functional data based on participants' motion. Specifically, only functional runs whose overall motion was less than one voxel (3 mm) across the entire run were included in the analysis. In addition, only functional runs with less than 2 mm motion between sequential functional volumes were included in the analysis. Participants were required to have at least one run for each condition that met these motion parameters to be included in the analysis. Every run from each participant met these criteria and thus no runs were removed from the analysis.

Task design and stimuli

Stimuli

The stimuli for each of the four tasks described immediately below were created using Adobe PhotoShop software and presented using SuperLab software (Cedrus Corporation, San Pedro, CA). All stimuli were white presented on a black background measuring 600 × 800 pixels. Stimuli were presented equidistant from a fixation dot that appeared between individual trials. See Fig. 1 for an example of each stimuli type.

Symbolic task

In the symbolic task, Arabic numerals 1–9 were presented measuring 200 pixels in height. Participants were asked to choose which side of the screen contained the larger number. The stimuli pairs used were: 1–6, 1–7, 1–8, 2–3, 2–4, 2–7, 2–8, 2–9, 3–4, 3–5, 3–6, 3–9, 4–6, 4–7, 4–9, 5–2, 5–4, 5–8, 6–5, 7–1, 7–2, 7–4, 7–5, 7–6, 7–8, 8–1, 8–2, 8–3, 8–6, 9–2, 9–3, 9–6, and 9–7. The pairs 2–9, 8–1, and 8–3 were used twice resulting in a total of 36 stimulus pairs laterally counterbalanced across the three runs of the experiment for a total of 72 trials per condition. Blocks of trials consisted exclusively of either small numerical distances (1–3) or large numerical distances (5–7).

Nonsymbolic task

In the nonsymbolic comparison condition, the same stimuli were used as those reported in three recently published studies (Holloway and Ansari, 2009, *in press*; Price et al. 2007). Specifically, in this task, participants were asked to determine which of two arrays of white

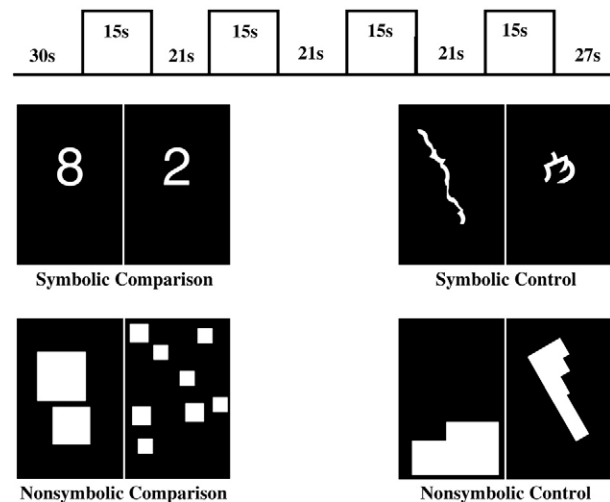


Fig. 1. Experimental timing information and examples of stimuli. During symbolic comparison, participants chose which of two Arabic numerals was numerically larger. During nonsymbolic comparison, participants chose which side of the screen contained more squares. The control tasks recombined the numerical comparison tasks into shapes and participants were asked to choose which of two shapes more closely resembled a diagonal line.

squares contained the larger numerosity. Each nonsymbolic trial matched the number-pair parameters of a corresponding symbolic trial, e.g. a symbolic number comparison of 3 vs. 7 would correspond to a nonsymbolic comparison of 3 squares vs. 7 squares. To control for the possible confound of continuous variables, the density, individual square size, and total area of each array was systematically varied across trials to ensure that numerosity could not be reliably predicted from variables continuous with it. Specifically, we first divided the 24 stimulus pairs into two groups of 12. In one of these groups, the larger numerosity had a larger overall area than the smaller numerosity. This pattern was reversed in the other group. Then, each group of 12 stimuli was further divided into two additional groups of 6 such that within each group of twelve, six of the stimuli with a greater overall area also had the greater density and six of the stimuli with a smaller overall area had the greater density. In addition to these controls, individual square size was also varied in each array. In this way, numerosity could not be reliably predicted from variables continuous with it.

Control tasks

The control tasks for both the symbolic and nonsymbolic comparison tasks involved judging which of two stimuli more closely resembled a diagonal line. In this way, the control task, like the experimental task, involved making a selection between the two sides of the display. For the symbolic control task, the stimuli were created by dividing the Arabic numerals into segments which were then rotated and reconnected in arbitrary shapes that either unambiguously approximated a diagonal line or did not (see Fig. 1 for an example of this). Our symbolic control stimuli were thus very similar to stimuli used by Göbel et al. (2004). Using a similar procedure, the nonsymbolic control task was created by combining the separate squares into either a shape that resembled a diagonal line or a shape that did not. The line-like stimuli were all constructed from the larger numerosity. In other words, when a participant was presented with a trial pairing 8 and 2 in the numerosity comparison tasks, a corresponding control task was created such that 8 was transformed into a line-like shape and 2 was transformed into a non-line-like shape. No visual information was added or subtracted from the stimuli. Thus the overall visual stimulation (the amount of white color in the display) in the control tasks is equivalent to the experimental tasks.

Task timing parameters

A total of 12 functional runs was collected for each participant, three runs for each of the four conditions (see Fig. 1). Each functional run contained blocks of only one type of comparison task. Functional runs began with 30 s of fixation followed by four 15-second blocks of trials made up of 6 trials each. Each trial was 2.5 s in length. The trials were further divided into 1200 ms of stimulus presentation followed by 1300 ms of fixation. Participants were instructed to choose which of the two sides of the screen corresponded to the correct answer. Subjects were asked to make the appropriate responses as quickly and accurately as possible by depressing the response button placed in their right hand if the correct answer was located on the right side of the screen and the response button placed in their left hand if the correct answer was located on the left side of the screen. The blocks of trials were separated by 21-second blocks of rest during which subjects were presented with a fixation dot and were not required to make any responses. After the final block of trials a block of rest was presented for 27 s before the run terminated. Thus, the total duration of each run was 3 min. Small and large distance blocks were alternated within a functional run.

Data acquisition

Functional and structural images were acquired in a 3T Phillips Intera Allegra whole-body MRI scanner (Phillips Medical Systems, The Netherlands) using an 8-Channel Phillips Sense head-coil. A gradient echo-planar imaging T2*-sequence sensitive to blood-oxygenation level-dependent (BOLD) contrast was used to acquire functional images. Functional images consisting of 30 non-contiguous slices were acquired in an interleaved order (4 mm thickness, 0.5 mm gap, 80 × 80 matrix, repetition time (TR): 3000 ms, echo time: 35 ms, flip angle: 90°, field of view 240 × 240 mm) covering the whole brain. For each functional run, 58 volumes were acquired. Each volume was collected using a standard Phillips MPRage 3-D sequence. Volumes consisted of 160 three-dimensional whole-brain high-resolution T1-weighted images collected in the sagittal plane and measuring 1 mm × 0.94 mm × 0.94 mm.

Data analysis

Both structural and functional images were analyzed using Brain Voyager QX 2.0.7 (Brain Innovation, Maastricht, Netherlands). The functional images were corrected for differences in slice time acquisition, head motion, and linear trends. In addition, functional images were spatially smoothed with a 6-mm full width at half maximum Gaussian smoothing kernel. Following initial automatic alignment, the alignment of functional images to the high-resolution T1 structural images was manually fine-tuned. The realigned functional data set was then transformed into Talairach space (Talairach and Tournoux, 1988).

A two-gamma hemodynamic response function was used to model the expected BOLD signal (Friston et al., 1998).

An initial whole-brain, random-effects conjunction analysis was conducted to reveal regions that responded to both numerical stimulus formats greater than their control conditions (symbolic – symbolic control and nonsymbolic – nonsymbolic control). That is, this conjunction revealed regions that were significantly more activated in the numerical than the control task for both types of stimulus format. Following the conjunction, we conducted a whole-brain random-effects analysis, which examined differences in BOLD response to the two numerical formats (i.e. symbolic and nonsymbolic). Before contrasting the two numerical formats with one another, we first subtracted out neural activation of the corresponding control tasks. Thus, this analysis revealed regions sensitive to differences in numerical stimulus format (symbolic – symbolic control) – (nonsymbolic – nonsymbolic control) after controlling for

response selection and aspects of visual processing common to numerical and control tasks.

The conjunction analysis and contrast of numerical stimulus format were initially calculated using an uncorrected statistical threshold of $p < 0.005$ and $p < 0.0001$, respectively. For the conjunction analysis, the lower statistical threshold was chosen since in a conjunction analysis two contrasts of interest must both significantly modulate the fMRI activation in a given region. For a conjunction analysis, the effective p -value is the square of the p -values for each component (In our case 0.005^2). Therefore, a more liberal threshold for such a conservative statistical procedure is justified. Both of the resulting statistical maps were subsequently corrected for multiple comparisons using cluster-size thresholding (Forman et al., 1995; Goebel et al., 2006). In this method, an initial voxel-level (uncorrected) threshold is set. Then, thresholded maps are submitted to a whole-slab correction criterion based on the estimate of the map's spatial smoothness and on an iterative procedure (Monte Carlo simulation) for estimating cluster-level false-positive rates. After 1000 iterations, the minimum cluster-size that yielded a cluster-level false-positive rate (α) of 0.05 (1%) was used to threshold the statistical maps. Put another way, this method calculates the size that a cluster would need to be (the cluster threshold) to survive a correction for multiple comparisons at a given statistical level. Only activations whose sizes meet or exceed the cluster threshold are allowed to remain in the statistical maps.

Region of interest (ROI) analyses were conducted for the sole purpose of extracting parameter estimates from regions showing significant whole-brain effects. For each ROI analysis described below, the region was first defined from areas that showed significant activations in the whole-brain analysis. In other words, our regions of interest were not defined *a priori*, but instead were defined by our actual data and intended simply as further explorations of the whole-brain effects. A general linear model (GLM) was performed across all of the voxels that comprised a given ROI, leading to an average activation of voxels within the region of interest for each condition and subject. The resulting parameter estimates (beta weights) are standardized scores (Z-scores). In each ROI analysis therefore, each subject has a beta weight from the GLM for each condition, which represents this average Z-scored magnitude of the activation for all voxels in a given ROI for each condition.

We performed two specific types of ROI analysis. For both the conjunction and the contrast of stimulus format, we extracted beta weights for the four experimental conditions (symbolic, symbolic control, nonsymbolic, and nonsymbolic control). This afforded further offline statistical analysis of the relative differences in BOLD response for each of these conditions in each region and allowed us to assess to what extent format differences are differences in activation or deactivation of brain regions.

The second ROI analysis examined the effect of numerical distance on the regions found in the conjunction analyses. We did not perform the analysis of distance on the regions elicited by differences in numerical stimulus format as numerical distance was not the primary focus of our stimulus-format analysis. We included the analysis of numerical distance to investigate whether regions elicited by the conjunction analysis were sensitive to the semantic dimension of numerical magnitude for both stimulus formats. The blocks of trials in the numerical comparison tasks were separated into small and large distances (see above), which allowed us to model the effect of symbolic and nonsymbolic numerical distance on the hemodynamic response. Accordingly, our second ROI extracted beta weights for the effect of symbolic and nonsymbolic numerical distance from the areas implicated in the conjunction analyses. Both the effects of symbolic and nonsymbolic distance were examined.

Finally, we performed a series of correlational analyses to rule out the possibility that the modulation of brain regions was due simply to differences in task difficulty between conditions. Specifically, we

examined whether the magnitude of differences in BOLD activity in regions showing differences between numerical notations correlated with differences in accuracy and response time between numerical notations. We reasoned that if the difference between the neural response to symbolic and nonsymbolic numerical processing in a given region was related to differences between reaction time and accuracy for symbolic and nonsymbolic numerical processing, then the neural activation could be related to a general feature of the tasks rather than to numerical processing per se. However, if no correlation exists between BOLD activity and task performance, then we can be reasonably more certain that our findings reflect numerical processing rather than general task performance.

Results

Behavioral results

Format differences in reaction time and accuracy of the numerical comparison tasks were analyzed in separate 2 (format: symbolic vs. nonsymbolic) by 2 (task: numerical vs. control) repeated measures analyses of variance. The effect of numerical distance on reaction time and accuracy was analyzed in a similar way using separate 2 (format: symbolic vs. nonsymbolic) by 2 (distance: small vs. large) repeated measures analyses of variance. For the distance effect analyses, the small distance level was created by averaging behavioral responses to distance 1–3 while the large distance level was formed by an average of behavioral responses to distance 5–7. For all analyses, significant interactions were further analyzed using Bonferroni-corrected *t*-tests. Because the accuracy data were skewed, we applied a logarithmic transformation to the data before submitting them to the analyses of variance and any follow-up *t*-tests.

Effect of format differences on reaction time

The analysis revealed a main effect of format in which the reaction times required for nonsymbolic comparison ($M = 548.1$, $SD = 128.8$) were found to be higher than those required for symbolic number comparison ($M = 493.1$, $SD = 109.5$), $F(1, 18) = 25.4$, $p < 0.001$, $\eta^2 = 0.59$. A main effect of task was also revealed by this analysis, such that the numerical comparison tasks ($M = 577.6$, $SD = 121$) required more time than the control tasks ($M = 463.6$, $SD = 121.2$), $F(1, 18) = 65.2$, $p < 0.001$, $\eta^2 = 0.78$. In addition, the effect of format

differed by task $F(1, 18) = 30.0$, $p < 0.001$, $\eta^2 = 0.62$. In the numerical task, reaction times during symbolic comparison ($M = 525.9$, $SD = 104.7$) were significantly shorter than reaction times during nonsymbolic comparison ($M = 629.4.1$, $SD = 146.6$), $t(18) = -5.7$, $p < 0.001$ corrected. In contrast, the reaction times of the control tasks did not differ by format $t(18) = -0.8$, *ns*.

Effect of format differences on accuracy

Accuracy for all of the comparison tasks was all above 95%. Overall, more errors were made in the numerical tasks ($M = 0.97$, $SD = 0.02$) than the control tasks ($M = 0.99$, $SD = 0.01$), $F(1, 18) = 16.9$, $p < 0.01$, $\eta^2 = 0.48$. In addition, more errors were committed during the nonsymbolic condition ($M = 0.97$, $SD = 0.02$) than the symbolic condition ($M = 0.99$, $SD = 0.01$), $F(1, 18) = 19.9$, $p < 0.001$, $\eta^2 = 0.53$. Bonferroni-corrected post-hoc analyses of the significant interaction between task and format, $F(1, 18) = 13.4$, $p < 0.01$, $\eta^2 = 0.43$, suggested that the lower accuracy in the nonsymbolic ($M = 0.95$, $SD = 0.03$) compared with the symbolic condition ($M = 0.99$, $SD = 0.02$) was present in the numerical tasks, $t(18) = 4.7$, $p < 0.001$ corrected, but not the control tasks, $t(18) = 2.3$, *ns*.

Effect of distance on reaction time

Reaction time for performing symbolic comparison ($M = 525.9$, $SD = 104.7$) was lower than that required for nonsymbolic comparison ($M = 629.4.1$, $SD = 146.6$), $F(1, 18) = 32.1$, $p < 0.001$, $\eta^2 = 0.64$. In addition, numerical distance had a main effect on reaction time, $F(1, 18) = 117.6$, $p < 0.001$, $\eta^2 = 0.87$, with small distances ($M = 651.6$, $SD = 138.3$) requiring longer reaction times than large distances ($M = 503.6$, $SD = 109.1$). The effect of numerical distance on reaction time also depended upon the stimulus format, $F(1, 18) = 49.5$, $p < 0.001$, $\eta^2 = 0.73$. Specifically, reaction times to small distances were significantly longer in the nonsymbolic condition ($M = 743.9$, $SD = 183.3$) compared with the symbolic condition ($M = 559.3$, $SD = 109.4$), $t(18) = 6.7$, $p < 0.001$ corrected, whereas large distances did not differ between stimulus formats, $t(18) = 1.7$, *ns*.

Effect of distance on accuracy

The analysis of the accuracy data revealed results very similar to those of the reaction time data. A main effect of format was found, $F(1, 18) = 22.1$, $p < 0.001$, $\eta^2 = 0.55$. More errors were made in the nonsymbolic format ($M = 0.95$, $SD = 0.03$) than the symbolic format

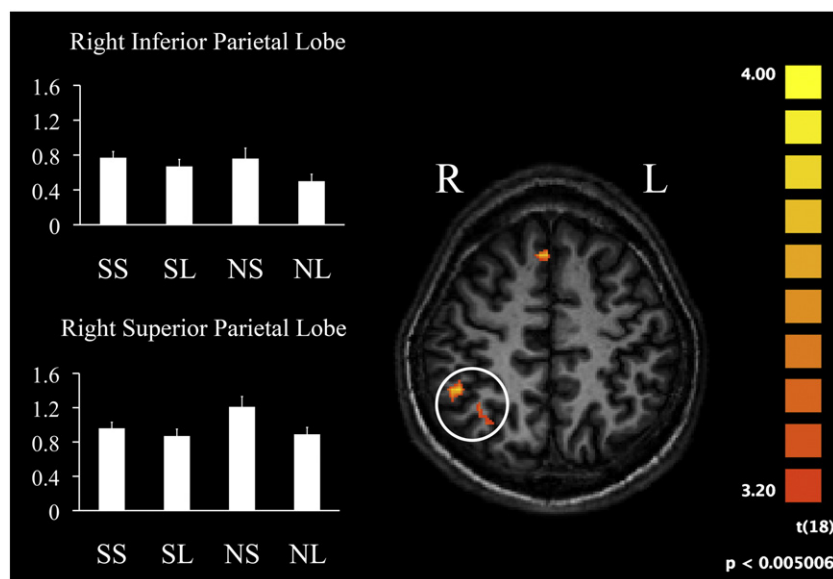


Fig. 2. Statistical map illustrating activation elicited by conjunction of symbolic and nonsymbolic comparison. Bar charts represent mean parameter estimates of activation across all participants in the inferior parietal lobe (above) and superior parietal lobe (below). Y-axis depicts BOLD signal represented in Z-scores. Error bars represent standard error of the mean.

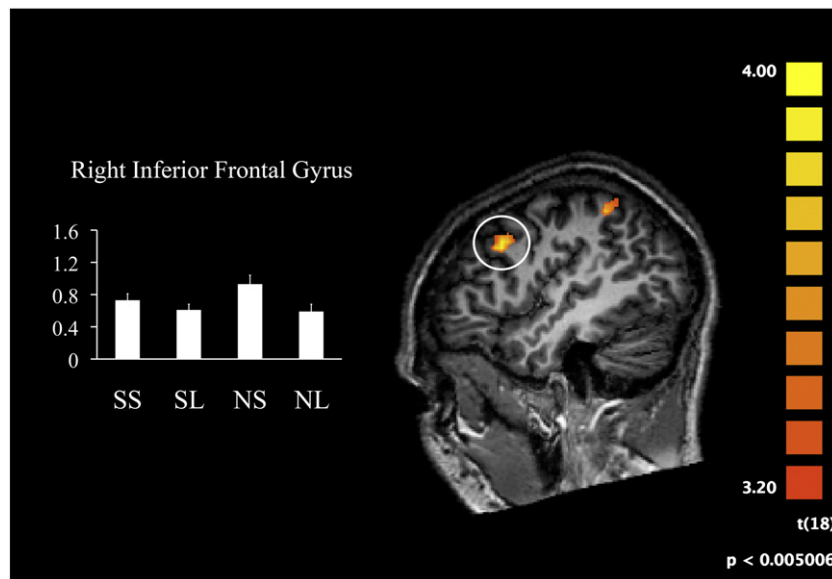


Fig. 3. Statistical map illustrating activation elicited by conjunction of symbolic and nonsymbolic comparison. Bar charts represent mean parameter estimates of activation across all participants in the right inferior frontal gyrus for symbolic small distance (SS), symbolic large distance (SL), nonsymbolic small distance (NS) and nonsymbolic large distance (NL). Y-axis depicts BOLD signal represented in Z-scores. Error bars represent standard error of the mean.

($M = 0.99$, $SD = 0.02$). A main effect of distance was found such that more errors were made for small numerical distances ($M = 0.95$, $SD = 0.03$) than for large distances ($M = 0.99$, $SD = 0.01$), $F(1, 18) = 30.3$, $p < 0.001$, $\eta^2 = 0.62$. In addition, an interaction was found between distance and format, $F(1, 18) = 20.6$, $p < 0.001$, $\eta^2 = 0.53$. For small distances, significantly more errors were made for the nonsymbolic stimuli ($M = 0.92$, $SD = 0.05$) than the symbolic stimuli ($M = 0.98$, $SD = 0.03$), $t(18) = 4.9$, $p < 0.001$. No difference between symbolic and nonsymbolic formats was found for the large distances, $t(18) = 0.1$, *ns*.

Imaging results

Conjunction analysis

In a first analysis, the conjunction of numerical stimulus format was analyzed by conducting a voxel-wise *t*-test to examine which areas were significantly modulated by both symbolic and nonsymbolic comparison relative to their control conditions (see Figs. 2 and 3 and Table 1). Results from the conjunction analysis revealed several distinct regions whose activity was significantly greater than their controls. Of particular note, two of the regions revealed by the conjunction analysis were the right inferior parietal lobule (IPL) and right superior parietal lobule (SPL). In addition, the conjunction analysis revealed several additional regions including the inferior frontal gyrus extending up into the middle frontal gyrus, a region of the right anterior insula, the anterior cingulate, and the right superior frontal gyrus extending ventro-laterally into the middle frontal gyrus.

Analysis of distance contrast in conjunction-defined regions

To examine the effect of numerical distance on these regions, we conducted a 2 (format: symbolic and nonsymbolic) by 2 (distance: small and large) repeated measures ANOVA on each of the six regions implicated in the conjunction analysis. After applying a Bonferroni correction to control for type I error inflation due to multiple comparisons, four of the six regions showed a significant main effect of numerical distance. These included both the inferior parietal lobe, $F(1, 18) = 10.0$, $p < 0.05$, $\eta^2 = 0.36$ and the superior parietal lobe, $F(1, 18) = 12.9$, $p < 0.05$, $\eta^2 = 0.42$ (see Table 1). In addition, the activation of the anterior insula, $F(1, 18) = 12.8$, $p < 0.05$, $\eta^2 = 0.42$ and the inferior frontal gyrus, $F(1, 18) = 14.1$, $p < 0.05$, $\eta^2 = 0.44$ also reflected significant modulation by numerical distance. Importantly, none of these regions showed a significant format \times distance interaction, which suggests that effect of numerical distance on the hemodynamic response was comparable in both symbolic and nonsymbolic comparison. The anterior cingulate, on the other hand, showed no main effect of distance, but a significant format \times distance interaction, $F(1, 18) = 9.5$, $p < 0.05$, $\eta^2 = 0.35$. Bonferroni-corrected *t*-tests indicated that this interaction is characterized by a significant effect of distance in the nonsymbolic condition, $t(18) = 3.2$, $p < 0.05$, but not the symbolic condition, $t(18) = 1.0$, *ns*. The superior frontal gyrus showed no significant effect of distance or a significant format \times distance interaction.

Contrast of stimulus format

To examine the effect of numerical stimulus format, we conducted a voxel-wise *t*-test to examine the brain for regions which showed

Table 1

List of the anatomical localization of the peak voxel for each activation, its coordinates, the number of voxels in each activated region, and the average *t*-statistic for each distinct activation elicited by the conjunction of stimulus format (symbolic – control) + (nonsymbolic – control).

Location	x	y	z	Voxels	t	S	SC	N	NC	SS	SL	NS	NL
R inferior frontal gyrus	48	13	31	1322	3.67	0.67	0.5	0.76	0.37	0.73	0.61	0.93	0.59
R inferior parietal lobe	45	−41	49	254	3.38	0.72	0.47	0.63	0.42	0.77	0.67	0.76	0.5
R anterior insula	32	20	4	1678	3.53	0.66	0.41	0.76	0.46	0.77	0.55	0.89	0.63
R superior parietal lobe	30	−51	44	333	3.38	0.91	0.79	1.05	0.75	0.96	0.87	1.21	0.89
R superior frontal gyrus	20	11	58	504	3.49	0.41	0.26	0.6	0.25	0.48	0.34	0.69	0.5
R anterior cingulate	5	23	38	1373	3.54	0.69	0.48	0.83	0.45	0.8	0.57	1.14	0.52

The right side of the table lists the average parameter estimate for the symbolic (S), symbolic control (SC), nonsymbolic (N), nonsymbolic control (NC), symbolic small distance (SS), symbolic large distance (SL), nonsymbolic small distance (NS), and nonsymbolic large distance (NL) conditions.

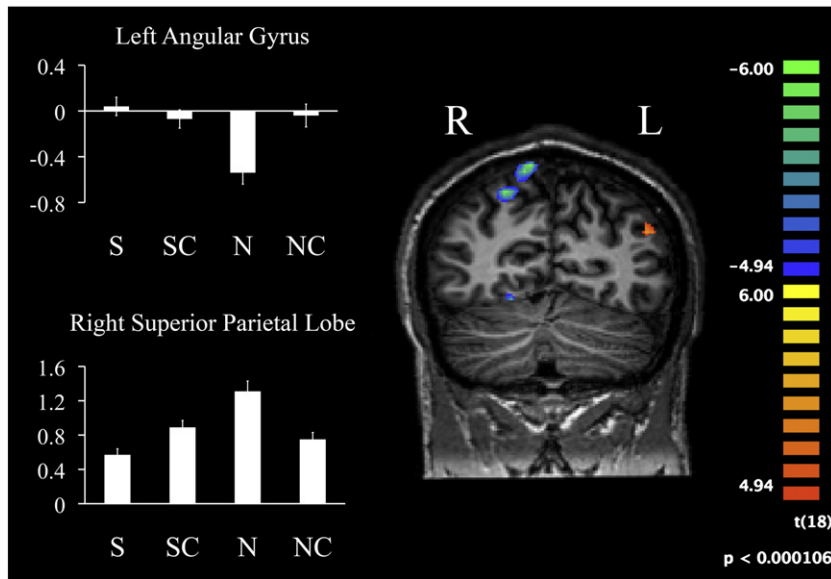


Fig. 4. Statistical map illustrating activations elicited by contrast of stimulus format. Activations in blue areas that were modulated more by the nonsymbolic compared with the symbolic tasks (after subtraction of the control tasks), while activations in orange represent regions showing greater activation for symbolic compared to nonsymbolic comparisons (after subtraction of the control tasks). Bar charts represent mean parameter estimates of activation across all participants in the left angular gyrus (above) and superior parietal lobe (below) for the symbolic condition (S), symbolic control condition (SC), nonsymbolic condition (N) and nonsymbolic control condition (NC). Y-axis depicts BOLD signal represented in Z-scores. Error bars represent standard error of the mean.

significant differences in activation between the symbolic and nonsymbolic stimulus formats after subtracting out activity associated with the control tasks (see Figs. 4 and 5 and Table 2). Nine regions were found. Seven of these areas showed greater activation in the nonsymbolic condition relative to the symbolic condition. These included the posterior portion of the right superior parietal lobe, the anterior portion of the right inferior occipital gyrus, the right cuneus, the posterior aspect of the left occipital gyrus extending ventrally into inferior occipital gyrus, the left superior occipital gyrus extending down into the middle occipital gyrus, and the left middle occipital gyrus extending ventrally into inferior occipital gyrus. In addition, one very large region was found centered on the right superior occipital gyrus, which extended into the middle occipital gyrus and, at its

extremes, to ventral aspects of the cuneus and very posterior aspects of the inferior parietal lobe. Note that the posterior right superior parietal lobe found in this contrast did not overlap with the more anterior portion of the superior parietal lobe elicited by the conjunction analysis (see Tables 1 and 2). Two regions showed greater modulation during the symbolic compared to the nonsymbolic comparison task. They include the left angular gyrus and the left superior and middle temporal gyrus near their border with the supramarginal gyrus.

Analysis of directionality of effects in contrast-defined regions

In previous studies, some of the activations found in temporoparietal regions such as the angular gyrus have been shown to be

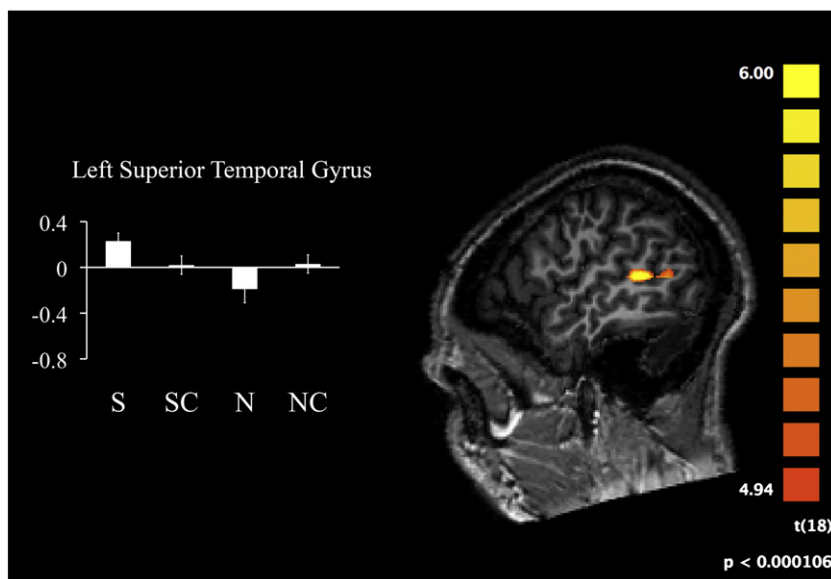


Fig. 5. Statistical map illustrating activations elicited by contrast of stimulus format. Orange represent regions showing greater activation for symbolic compared to nonsymbolic comparisons (after subtraction of the control tasks). Bar charts represent mean parameter estimates of activation across all participants in the left superior temporal gyrus for the symbolic condition (S), symbolic control condition (SC), nonsymbolic condition (N) and nonsymbolic control condition (NC). Y-axis depicts BOLD signal represented in Z-scores. Error bars represent standard error of the mean.

Table 2

List of the anatomical localization of the peak voxel for each activation, its coordinates, the number of voxels in the activation, and the average *t*-statistic for each distinct activation elicited by the contrast of stimulus format (symbolic – control) – (nonsymbolic – control).

Location	<i>x</i>	<i>y</i>	<i>z</i>	Voxels	<i>t</i>	S	SC	N	NC
R inferior occipital gyrus	49	–54	–2	122	–5.35	0.49	0.72	0.83	0.67
R superior occipital gyrus	29	–79	19	5183	–5.72	0.80	1.21	1.72	1.18
R superior parietal lobe	18	–64	53	2527	–5.51	0.57	0.89	1.31	0.75
R cuneus	9	–89	20	1294	–5.82	0.41	0.72	1.61	1.07
L superior occipital gyrus	–27	–77	23	1651	–5.47	0.76	1.17	1.60	1.12
L posterior superior occipital gyrus	–23	–91	18	161	–5.28	0.64	1.01	1.44	0.91
L middle occipital gyrus	–32	–84	6	252	–5.33	0.80	1.16	1.28	0.97
L angular gyrus	–43	–67	30	85	5.12	0.04	–0.07	–0.54	–0.04
L superior temporal gyrus	–52	–44	11	496	5.48	0.23	0.02	–0.19	0.03

Right side of the table lists the average parameter estimate for the symbolic (S), symbolic control (SC), nonsymbolic (N), and nonsymbolic control (NC) conditions.

reflective of relative deactivation in this region (Ischebeck et al., 2006; Shulman et al., 2007). We, therefore, examined the beta weights from each of the regions elicited by our contrast of stimulus format to determine the directionality of the effects. Of the nine regions found, only two of these involved relative deactivations. We examined the effects of task and format more closely in these two regions using separate 2 (format: symbolic vs. nonsymbolic) by 2 (task: numerical vs. control) repeated measures analyses of variance, corrected for multiple comparisons using the Bonferroni method. In the angular gyrus, our analysis revealed both a significant main effect of format, $F(1, 18) = 16.0, p < 0.01, \eta^2 = 0.47$, and a significant main effect of task, $F(1, 18) = 10.3, p < 0.01, \eta^2 = 0.36$. These effects were not interpreted in light of the significant interaction between task and format $F(1, 18) = 36.2, p < 0.01, \eta^2 = 0.69$. Bonferroni correct *t*-tests indicated that the interaction was characterized by a significant difference between symbolic and nonsymbolic numerical comparison, $t(18) = -7.1, p < 0.01$, but no difference between the control conditions, $t(18) = -0.307, ns$. In addition, a one-sample *t*-tests revealed that the difference between the symbolic and nonsymbolic numerical tasks was characterized by a significant deactivation of the angular gyrus during the nonsymbolic condition, $t(18) = -5.1, p < 0.001$ and no significant modulation in the symbolic condition, $t(18) = 0.52, ns$ (for a visual representation of this see Fig. 4). Thus, the interaction was characterized by a significant difference in numerical conditions (i.e. deactivation during nonsymbolic and no significant modulation during symbolic) and no difference in modulation of the angular gyrus during the control conditions.

An identical analysis was conducted on the parameter estimates from the superior temporal gyrus. Neural activity in this region was characterized by a significant effect of format $F(1, 18) = 21.9, p < 0.001, \eta^2 = 0.55$ and a significant interaction between format and task, $F(1, 18) = 64.9, p < 0.01, \eta^2 = 0.78$. Bonferroni-corrected *t*-tests indicated that the interaction was defined by a significant difference between the numerical comparison conditions, $t(18) = -7.0, p < 0.01$, but no difference between the control conditions, $t(18) = -0.079, ns$. One-sample *t*-tests revealed that the difference in activation between the symbolic and nonsymbolic numerical tasks was due to a significant deactivation during the nonsymbolic numerical comparison, $t(18) = -2.8, p < 0.05$ and a significant activation in the symbolic condition, $t(18) = 3.5, p < 0.01$ (for a visual representation of this see Fig. 5). In the superior temporal gyrus, the interaction was defined by a significant difference in numerical conditions (i.e. deactivation during nonsymbolic and significant activation during symbolic) and no significant modulation of this region during the control conditions.

Test of correlation between parameter estimates and behavioral measures

The behavioral data above revealed a difference in reaction time and accuracy between the symbolic and nonsymbolic numerical tasks.

To rule out the possibility that format-related differences in brain activation were solely related to differences in general task performance, we performed a series of correlational analyses. Thus, for each subject we calculated two performance scores that reflected the difference in reaction time and accuracy between the symbolic and nonsymbolic numerical conditions. We also calculated scores reflecting the difference in BOLD activity between the symbolic and nonsymbolic numerical conditions for each region that showed a significant effect of stimulus format. No significant correlations were found between BOLD activity and performance, which suggests that the brain activation differences cannot be entirely explained by differences in task performance.

Discussion

In this study, we investigated the neural correlates of symbolic and nonsymbolic numerical processing to elucidate commonalities and differences between the processing of numerical stimulus formats in the adult human brain. To examine which brain regions responded to both symbolic and nonsymbolic formats of stimulus presentation, we investigated the conjunction of neural response to symbolic and nonsymbolic comparison. This was followed by a contrast of numerical stimulus format to identify regions that responded differentially to symbolic and nonsymbolic numerical processing. Below we discuss the results from these analyses in turn.

Conjunction of stimulus format

The conjunction of symbolic and nonsymbolic stimulus formats revealed several areas previously shown to be engaged by numerical comparison including the right superior parietal lobe (Chochon et al., 1999; Eger et al., 2003; Pesenti et al., 2000), the right superior frontal gyrus (Chochon et al., 1999; Pinel et al., 1999), the inferior frontal gyrus (Pinel et al., 1999), and the right anterior cingulate (Chochon et al., 1999; Pinel et al., 1999). Most notably, this analysis supported our prediction that inferior parietal regions would be activated by the conjunction of symbolic and nonsymbolic numerical comparison. This result is commensurate with a growing body of neuroimaging studies showing that this region is engaged by numerical processing tasks in symbolic formats (Ansari et al., 2005; Chochon et al., 1999; Eger et al., 2003; Pesenti et al., 2000; Pinel et al., 2001, 1999), nonsymbolic formats (Ansari and Dhital, 2006; Ansari et al., 2006; Piazza et al., 2004, 2007), and both (Venkatraman et al., 2005). Our findings also converge with previous research by Fias et al. who demonstrated the IPL to be involved in the processing of both numerical (Hindu–Arabic numerals) and non-numerical (line length and angle size) magnitudes (Fias et al., 2003).

However, the notion that parietal responses during number comparison are specifically related to the processing of numerical magnitude has not been uncontroversial. In particular, Göbel et al. have challenged the findings of previous numerical comparison

studies implicating the parietal cortex in the processing and representation of numerical magnitude by demonstrating that inferior parietal regions (in particular the intraparietal sulcus) are engaged to an equal extent when participants are required to select one of two non-numerical stimuli (Göbel et al., 2004). Since all numerical comparison tasks contain a response selection component, it is difficult to determine whether the activation in response to numerical comparison is reflective of numerical processing or response selection. However, by using control stimuli very similar to the stimuli used by Göbel et al., we were able to avoid this confound. The activations shown in the present study were present even after controlling for response selection components of the tasks (selecting one of two sides of the display by means of a button press).

The results of the conjunction analysis revealed inferior parietal activation that was found to be right lateralized. Similar lateralization has been demonstrated in other neuroimaging research of numerical processing. In particular, Chochon et al. compared numerical comparison to arithmetic tasks. They showed that the right, but not left, parietal cortex is modulated by nonverbal numerical processing and thus concluded that the right parietal lobe houses an analog representation of numerical magnitude (Chochon et al., 1999). This conclusion was later supported by Piazza et al. who demonstrated format-general representation of numerical magnitude only in the right parietal lobe (Piazza et al., 2007). The present data converge with these previous data and implicate the right parietal lobe in format-general numerical representation.

Recently, Cantlon et al. (in press) reported left parietal regions are involved in the ontogenetic development of a format-independent representation of numerical magnitude. In this study, the authors used comparison tasks that were highly similar to the ones used in this study. Using a conjunction analysis between symbolic and nonsymbolic numerical comparison, the authors showed that adults show stronger activation relative to children in the left superior parietal cortex. While our data are broadly commensurate with those reported by Cantlon and colleagues in that both studies implicate parietal regions in the format-independent processing of numerical magnitude, the specific regions revealed in these studies (right inferior parietal lobe in our study and left superior parietal lobe in Cantlon et al.'s study) are quite distinct. The differences in the parietal activation between the two studies are likely due to our use of a control task in addition to the numerical comparison tasks. It will be important for future studies of the development of numerical representation to include appropriate control tasks to distinguish developmental differences in number-related activation from developmental differences in task- and domain-general response selection mechanisms.

Contrast of stimulus format

Regions responding to nonsymbolic numerical processing

The contrast of numerical stimulus format revealed regions that were differentially activated by the surface format in which quantities were represented. It should be noted that these format-related differences emerged after subtracting away the variance related to the control tasks. These control tasks included a response selection component (depressing a button underneath the side of the display that most closely resembled a line) and were equated with the experimental tasks in terms of the number of white pixels that were visually presented.

The contrast of nonsymbolic vs. symbolic number comparison revealed a large area of the visual cortex, which reflects the greater visual demands of the nonsymbolic condition. This activation could reflect aspects of visual processing that were not accounted for by the control task such as processing the density of an array. However, it is also possible that some of the activation in

the visual cortex reflects visual processing necessary for nonsymbolic numerical processes such as the individuation and summation of the white squares. Future studies specifically targeting the role of visual aspects in nonsymbolic numerical processing are needed to clarify this issue further. In addition to these visual regions, the nonsymbolic condition also activated a region of the right posterior superior parietal lobe—an area that has previously been implicated in nonsymbolic number processing by several other studies (Ansari et al., 2006; Cantlon et al., 2006; Piazza et al., 2004, 2007).

The involvement of the posterior superior parietal lobe in nonsymbolic numerical processing confirms our prediction put forward in the introduction. Specifically, at the outset of this paper we proposed that this region would be involved in nonsymbolic numerical processing due to its role in the summation coding necessary for processing nonsymbolic quantities. Indirect support for the role of the posterior superior parietal lobe in summation coding can be found in recent research in monkeys and humans. Roitman et al. recently demonstrated that the LIP of macaque monkeys contains neurons whose firing rate increases monotonically with the number of nonsymbolic items presented (Roitman et al., 2007). Thus, the behavior of these neurons reflects a summing of the objects (summation coding) in a visually presented nonsymbolic array. Behavioral research has demonstrated the existence of summation coding in humans (Roggeman et al., 2007). Furthermore, recent neuroimaging work has demonstrated that the superior parietal lobe (Talairach coordinates: 21, −67, 57) is involved in nonsymbolic, but not symbolic, numerical processing and, consistent with the summation coding, is modulated by the set size of nonsymbolic numerical magnitudes (Santens et al., in press). Other neuroimaging work has provided evidence that the superior parietal lobe in humans is the homologue to the LIP of macaque monkeys (Koyama et al., 2004; Sereno et al., 2001). More specifically, Koyama and colleagues elicited LIP activation in macaque monkeys and SPL activity in humans using identical visually-guided saccade tasks. The authors reported bilateral activity in the human SPL that was homologous to the LIP activation in macaques. The Talairach coordinates of the peak voxel for the right SPL in that study was reported as 19, −63, 49. To quantify the proximity of that activation with the SPL activation elicited by our contrast of stimulus format, we calculated the Euclidean distance between them: $d = \sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2}$. The activations reported by Santens et al. and Koyama and colleagues are quite close ($d = 4.69$ and 4.24 , respectively) to the peak voxel of our SPL: 18, −64, 53. Taken together, these data support our claim that the activity of the superior parietal lobe in nonsymbolic comparison may reflect this region's role in summation coding.

This explanation is also consistent with the predictions put forward in the Verguts and Fias (2004) model. This model predicts that nonsymbolic quantities initially undergo a format-specific summation process and are subsequently represented in a format-general, place-coded manner. Against the background of this model, our data suggest that the posterior superior parietal lobe is involved in the summation coding necessary for enumerating a nonsymbolic array.

Importantly, the right superior parietal activation elicited by the contrast of stimulus format did not overlap with the right superior parietal activation elicited by the conjunction analysis, $d = 19.8$. Specifically, the region from the conjunction analysis (peaking at 30, −51, 44) was more ventral, lateral and anterior relative to the region from the contrast of stimulus format peaking at (18, −64, 53). In addition, this region from the conjunction analysis, was much further removed, relative to the superior parietal lobe elicited by the contrast of stimulus format, from the purported homologue of the LIP reported by Koyama and colleagues, $d = 17.0$.

Further research should clarify how the involvement of the posterior superior parietal lobe in nonsymbolic processing is related to other processes associated with this region such as saccadic eye movements (Koyama et al., 2004) or visual attention (Corbetta and Shulman, 2002; Simon et al., 2002). Indeed, because our study did not control for participants' eye movements, it is impossible to completely disambiguate eye movements from summation coding in the superior parietal lobe using the current data. It is therefore possible that the activation we show in the superior parietal lobe is related to saccadic eye movements. However, it should be kept in mind that eye movements are an integral part of the process underlying the enumeration of arrays of items. One possibility is that over the course of evolution, domain-general competencies such as visual attention and saccades served as a foundation upon which a summation system was built.

Regions involved in symbolic number processing

The contrast of stimulus format revealed two regions in the left hemisphere which showed statistically greater modulation in response to symbolic relative to nonsymbolic comparison: the left angular and the left superior temporal gyri. The left angular gyrus has long been associated with numerical processing. For example, damage to this region is associated with a variety of symptoms including impairments in calculation (Gerstmann, 1940). Several neuroimaging studies have demonstrated empirically that the left angular gyrus is important for calculation (Burbaud et al., 1995; Roland and Friberg, 1985; Rueckert et al., 1996), may be more involved in exact than approximate calculation (Dehaene et al., 1999; Venkatraman et al., 2006), and is likely involved in arithmetic fact retrieval (Delazer et al., 2003; Delazer et al., 2005; Grabner et al., 2009). The present study is the first to demonstrate the role of the left angular gyrus in basic numerical processing in the absence of calculation. Our data suggests that this region is not restricted to the retrieval of arithmetic facts, but instead, with the superior temporal gyrus, may play a more general role in symbolic numerical processing.

Convergent evidence for the left angular gyrus' specific involvement in basic symbolic numerical processing can be found in a recent study examining the neural correlates of calculation in adults (Grabner et al., 2007). Specifically, this study compared the effect of individual differences in mathematical competence on brain activation patterns during single and multi-digit multiplication as well as a control task where participants judged whether three Hindu–Arabic numerals were identical or not. Interestingly, the authors showed that even in the control task, which involved absolutely no calculation, but merely asemantic processing of Arabic numerals, mathematical competence modulated activation of the left angular gyrus in a similar way as for calculation. Against the background of these results, the authors argued that the differences in angular gyrus activation could reflect group differences in the amount of stimulus-driven access to the semantic information represented by the symbolic numerals.

Another region directly adjacent to both of the neural loci found in our study, the left supramarginal gyrus, has also been implicated in symbolic numerical processing. Roux et al. showed that direct electrostimulation of the cortex disrupted reading of numerical symbols in the supramarginal gyrus of the dominant hemisphere (Roux et al., 2008). Further evidence to implicate the left temporoparietal cortex in the processing of numerical symbols comes from a neuropsychological study. In their study of a patient with a focal lesion of white matter directly beneath the left anterior supramarginal gyrus, Polk et al. presented evidence for a specific role of the supramarginal gyrus in symbolic but not nonsymbolic number processing (Polk et al., 2001). As a result of the lesion, the patient presented with a severe deficit in the processing of numerical symbols, while retaining intact nonsymbolic numerical processing.

Together with these findings, our study could suggest a broader role of the left temporoparietal junction (composed of the angular, supramarginal gyri and the posterior aspect of the superior temporal gyrus) in symbolic number processing. While the exact role of the left angular and superior temporal gyri in symbolic number processing cannot be directly addressed by our data, a review of neuroimaging studies of reading yields an interesting possibility for how they may be involved in processing numerical symbols. Neuroimaging research has found the left angular gyrus (Booth et al., 2003; Joseph et al., 2006; McDermott et al., 2003; Pugh et al., 2001a,b) and left superior temporal regions (Raij et al., 2000; van Atteveldt et al., 2004) to be involved in the integration of letters (graphemes) with speech sounds (phonemes). We propose that our results may reflect similar roles for these regions in the numerical domain. The greater involvement of the left angular and superior temporal gyri in symbolic relative to nonsymbolic processing could reflect this region's role in processing the connection between numerical symbols and their quantitative referents. In the case of the left angular gyrus, the symbol-to-referent mapping hypothesis can explain both our findings and previous work implicating this site in calculation. The association between an arithmetic equation and its result, on the one hand, and the mapping between a numerical symbols and its numerical magnitude, on the other hand, could both involve the angular gyrus. Here the common denominator is the role it may play in mapping between a visual form and its semantic referent. This hypothesis is directly in line with the one put forth by Grabner and colleagues, suggesting that “in addition to being involved in the automatic retrieval of arithmetic facts, the angular gyrus also mediates the mapping between symbols and numerical magnitudes” (p. 354).

Compared to the nonsymbolic condition, the degree to which our symbolic findings converge with the model put forth by Verguts and Fias is less straightforward. While these authors predicted that nonsymbolic processing would require summation coding, the nature of the “symbolic field” in their model was described in much less detail. However, one feature must be present in order for this input field to be truly symbolic. A symbolic relationship requires there to be an integration of at least two distinct types of representation. For example, the symbolic relationship imbedded in a written word requires the reader to integrate a visual representation with an auditory representation which is itself symbolically related to a semantic representation. Thus, a given symbolic relationship involves distinct representations and the connection between them. Therefore, although not explicitly stated by Verguts and Fias, the processing underlying the “symbolic (number) field” should be characterized by similar properties. Put most simply, such symbolic processing would involve a visual external representation of the numeral, a semantic internal representation of numerical magnitude (shown in this study to be housed in the right parietal lobe) and a connection between these. As these brain regions have not been associated with basic visual processing, we contend that the angular and superior temporal gyri are not involved in the processing of the visual features of the symbolic (Hindu–Arabic) numerals. Instead, and especially given their involvement in cross-modal integration in reading, we suggest that these regions process the symbolic relationship between the visual and numerical representations of symbolic numerals.

An alternate explanation of the activity of the temporoparietal junction in our study is that it reflects the processing of verbal number words associated with numerical symbols rather than a connection between symbols and their semantic referents. In his influential “Triple Code Model,” Dehaene suggests that one aspect of numerical information is verbal in nature (Dehaene, 1992) and that this verbal code is localized in the left angular gyrus (Dehaene et al., 2003). It is possible that the participants in our study were covertly saying the names of the Arabic numerals during symbolic numerical comparison. Thus, our data are commensurate either with the verbal hypothesis of Dehaene or with the symbol-to-referent mapping

hypothesis put forth by Grabner and colleagues. To distinguish between these hypotheses, future studies must be designed that decompose symbolic number processing into its verbal and non-verbal components.

It should be mentioned that other recent data suggest that the prefrontal cortex is important for the creation of neural associations between numerical symbols and parietally mediated numerical representations in monkeys (Diester and Nieder, 2007). In a training study, these authors trained monkeys to associate symbolic numerals with nonsymbolic numerical arrays. The authors found neurons in the prefrontal cortex that respond preferentially to symbolic and nonsymbolic numbers as well as neurons that respond to both stimulus formats and suggested that this region is involved in forming the connection between a numerical symbol and numerical representations. These data do not necessarily conflict with ours. Indeed, our conjunction analysis revealed right inferior frontal gyrus activation during the processing of both symbolically and nonsymbolically presented numerical information. Unlike Diester and Nieder, however, we found no evidence of prefrontal activation that reflects preferential processing of symbolic or nonsymbolic numerical processing alone. Taken together with the results presented by Diester and Nieder, our findings could suggest that while prefrontal areas are involved in the initial establishment of associations between numerical symbols and quantitative referents, the temporoparietal region revealed in our data reflects development of efficient activation and retrieval of those associations. However, this explanation does not completely account for why the prefrontal cortex is activated by both symbolic and nonsymbolic numerical information. Future research must clarify the role of the prefrontal cortex in the numerical processing of both children and adults.

It is important to note that the activity in the angular gyrus is defined by deactivations relative to baseline. Although relatively common (Dehaene et al., 1996; Grabner et al., 2007; Ischebeck et al., 2006; Rickard et al., 2000; Shulman et al., 2007; Venkatraman et al., 2006; Zago et al., 2001), the nature of such deactivations is currently unresolved in the literature. One possibility is that the deactivations in the angular gyrus relate to task difficulty. Two of the above studies observed that greater deactivation was found in response to increased difficulty of the tasks being performed (Ischebeck et al., 2006; Zago et al., 2001). However, the deactivation in our study cannot be explained through a similar appeal to task difficulty. Our pattern of reaction times showed that the nonsymbolic comparison was more difficult than symbolic comparison, which in turn, was more difficult than either control task. If activity in this region were defined solely by task difficulty, one would expect to see greater deactivation in the more demanding symbolic condition than the control tasks. However, inspection of the beta weights suggest that the activity in response to the symbolic condition in the left angular gyrus was actually slightly, non-significantly higher than the activation related to the control tasks. Thus a pure task difficulty explanation cannot hold, as it should generalize to differences between the symbolic and control tasks, where a reaction time difference was also found.

A different explanation for neural deactivation has been put forth by Shulman et al. in a study of visual attention (Shulman et al., 2007). These authors showed that when participants searched presentations of distracter objects for a visual target, the right supramarginal gyrus (a region adjacent to the angular and superior temporal gyri) was significantly deactivated until the target was detected. Shulman et al. suggested that deactivation of this region inhibits stimulus-driven reorientation of attention to inappropriate stimuli and, in this way, acts as a neural stimulus filter. In this view, deactivation can serve a functional role in the performance of cognitive tasks.

We have proposed that the left temporoparietal areas found in our study are a network of brain regions that serve to process the connection between numerical symbols and their quantitative referents. Against the background of the Shulman et al. findings, we

tentatively hypothesize that deactivation of the left TPJ may serve a key function in the symbol-to-referent mapping attributed to this region. Specifically, the deactivation of the TPJ in response to nonsymbolic stimuli, in concert with its activation in response to symbolic stimuli (in the superior temporal gyrus), could reflect these regions' joint role as a stimulus filter or gateway that allows differential access to numerical representations dependent upon the stimulus format of the number being presented. When individuals are presented with a nonsymbolic numerical array, access to the quantity represented by the array may be indirect and mediated through the summation coding of the right superior parietal lobe. In contrast, presentation of an Arabic numeral could trigger a more direct access to the numerical representation with which it is associated and, hence, an absence of suppression (relative to baseline). Thus, the filter would not be engaged when representations can be mapped onto their semantic referents without further processing. This hypothesis should be explored using functional connectivity analysis in the context of an event-related fMRI study. It should be acknowledged that in the presence of significant deactivation in the left AG during nonsymbolic comparison and no significant activation during symbolic comparison, it is difficult to ascertain, from the present findings, whether the pattern of relative deactivation of the left AG in the present study indicates anything about the processing of the symbolic stimuli or whether it merely reflects a function relevant to the processing of the nonsymbolic stimuli. Thus the present hypothesis of a filtering mechanism is speculative and requires follow-up research. In contrast the pattern of activation from the left STG is much clearer, where significant activation during symbolic but neither nonsymbolic nor control conditions is observed. Thus, our data provide clearer support for the involvement of the left STG in symbolic number processing than they do for the left AG.

In sum, the present study revealed brain regions involved in processing different numerical stimulus formats. We have shown a pattern of results that fits into the model of stimulus format processing put forth by Verguts and Fias (2004). These authors predicted that differential pathways are responsible for encoding a quantity from either symbolically or nonsymbolically represented numbers. These differential pathways were then predicted to converge on a format-general representation of numerical magnitude. Our data provide support for these predictions and identify key regions that might mediate different functions predicted by the Verguts and Fias model. In particular, a comparison of symbolic and nonsymbolic numerical processing reveals different regions involved in these numerical stimulus formats in the left temporoparietal regions and the right posterior superior parietal lobe, respectively. In addition, we demonstrated that a conjunction between symbolic and nonsymbolic numerical processing reveals regions in the right inferior parietal lobe and anterior superior parietal lobe, regions long associated with numerical representation. Thus, this study starts to map out the pathways that mediate numerical stimulus format processing in the human brain. We have demonstrated that while there is evidence for a common abstract representation of numerical magnitude, there are also important differences in the pathways mediating the mapping from external representations to internal ones. These mappings should be investigated developmentally to clarify more precisely how this mapping emerges through interplay of education and brain maturation.

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