The Neural Origin of the Priming Distance Effect: Distance-Dependent Recovery of Parietal Activation Using Symbolic Magnitudes

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Abstract: Numerical magnitudes are known to be processed in areas around the intraparietal sulci of the brain. We used an fMRI-adaptation paradigm to investigate how they are actually coded at the neural level. In a number identification task, we manipulated the numerical distance between prime and target numbers (same, close, and far pairs) and their symbolic notation (Arabic and verbal numerals). We show that bilateral parietal activations present a distance-dependent recovery of activation positively correlated with the distance between primes and targets: the larger the prime-target distance, the higher the recovery of activation. Importantly, this effect is only present for trials where an Arabic numeral precedes a verbal numeral and not the reverse. Together, these findings reveal the neural origin of the behavioral priming distance effect and demonstrate that the relative importance of the semantic and nonsemantic pathways in a dual-route model of number processing is modulated by symbolic notation. *Hum Brain Mapp* 31:669–677, 2010. © 2009 Wiley-Liss, Inc.

Key words: event-related fMRI; adaptation; parietal cortex; intraparietal sulcus; number processing; priming distance effect

INTRODUCTION

Neuroimaging studies of number processing and calculation have shown that areas in and around the left and right Intraparietal sulcus (IPS) are activated whenever people

are engaged in numerical tasks. These tasks include comparing Arabic digits [Chochon et al., 1999; Fias et al., 2003; Pesenti et al., 2000; Pinel et al., 2001], producing or verifying the results of simple calculations [Pesenti et al., 2000; Simon et al., 2002; Zago et al., 2001], and identifying a predefined target in a continuous stream of numerals [Eger et al., 2003]. These IPS activations are observed with magnitudes presented as symbolic stimuli [i.e., as Arabic or verbal numerals; Eger et al., 2003], nonsymbolic discrete stimuli [such as dot patterns; Dormal and Pesenti, 2009; Piazza et al., 2004, 2007], or continuous stimuli [such as length of lines or amplitudes of angles; Dormal and Pesenti, 2009; Fias et al., 2003].

Recent behavioral and brain imaging studies have investigated how magnitudes are coded at the neural level. A good behavioral indicator of magnitude coding is the priming distance effect [Koechlin et al., 1999; Reynvoet et al., 2002], which refers to the observation that targets

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preceded by numerically close primes (e.g., “1” preceded by “2”) elicit faster responses than targets preceded by numerically far primes (e.g., “1” preceded by “4”). This effect was observed in comparison tasks [e.g., Koechlin et al., 1999], but also in tasks where processing magnitude information was less relevant, such as naming or parity judgment tasks [e.g., Reynvoet and Brysbaert, 1999]. It was observed for symbolic and nonsymbolic magnitudes [Koechlin et al., 1999], and appeared to be independent of notation changes between prime and target [Reynvoet et al., 2002], suggesting a notation-independent magnitude representation. This finding was implemented in a neural model assuming that each magnitude is represented by a node on a number line [Dehaene and Changeux, 1993; Verguts et al., 2005]. A magnitude (e.g., “1”) will not only activate its corresponding node but also the nodes of nearby magnitudes (e.g., “2”) with decreasing strength as a function of distance, leading to more similar coding schemes for numerically close magnitudes. This representational overlap will decrease response latencies to targets preceded by a numerically close number, hence the priming distance effect. This idea has received support from electrophysiological studies with primates, showing the existence of populations of number-sensitive neurons that were maximally active whenever a given numerosity was shown [Nieder and Miller, 2003, 2004]. Importantly, these neurons were also partially active when a nearby numerosity was presented, with decreased activation for larger distances.

Piazza et al. [2004] used an adaptation paradigm to investigate the coding schemes of nonsymbolic stimuli in humans. After passively viewing dot clusters with a fixed numerosity, participants were presented a dot cluster with a deviant numerosity. The presentation of this deviant numerosity led to a bilateral recovery of the BOLD signal in the IPS. Crucially, parametric analyses showed that the increase in activation was directly related to the numerical distance between the adapted and deviant dot clusters. Recently, this finding was replicated and extended to symbolic stimuli [Piazza et al., 2007]. In this study, participants were presented with nonsymbolic (i.e., dot clusters) or symbolic stimuli (i.e., Arabic numerals). After continuous presentation of highly similar magnitudes, distance-dependent recovery of the activation in the IPS and frontal regions was observed when a deviant magnitude was shown. Interestingly, this occurred irrespective of notation changes between the adapted and deviant magnitudes, supporting the idea of a notation-independent magnitude representation in the left and right IPS (for a recent review, see Cohen Kadosh and Walsh [in press]). These findings may reflect the mechanism behind the behavioral priming distance effect, but this should be tested further as previous adaptation studies used large magnitudes with long adaptation periods, whereas the priming distance effect is observed using small magnitudes and a single presentation of the prime number. Furthermore, Verguts et al. [2005] proposed that small and large sym-

bolic magnitudes are represented somewhat differently: due to their high frequency of use, small numbers have a sharper tuning curve and are thus more exactly represented. The magnitude representation of large numbers is believed to be fuzzier, likely due to the decreasing distance between their magnitude representations on the number line (i.e., compressed scaling) and/or wider tuning curves (i.e., increasing variability), both leading to a larger overlap of neighboring magnitude representations. Therefore, we believe this study to be a crucial extension of results previously reported by Piazza et al. [2004, 2007].

fMRI-adaptation studies with a single presentation of the prime number and using small symbolic numerals have already been conducted [Cohen Kadosh et al., 2007; Naccache and Dehaene, 2001]. However, several issues remain unresolved in these studies. Firstly, although both studies are consistent with the idea of different neuronal sets coding for specific magnitudes, they are inconclusive as far as distance-dependent recovery of the fMR signal is concerned, because both studies were limited to conditions where primes and targets had either the same or a different magnitude. Such a design makes it impossible to dissociate adaptation effects, which exhibit a discrete, all-or-none function, from a continuous distance-dependent function as predicted by the neural model of small number representation developed by Verguts et al. [2005]. Secondly, contradictory results were found regarding the existence of a notation-independent magnitude representation in both hemispheres. When participants had to compare a target that was preceded by a prime, either in the same or in a different notation, decreased activation was found in the intraparietal sulci bilaterally, supporting the idea of a notation-independent magnitude representation in both hemispheres [Naccache and Dehaene, 2001]. However, these results were not replicated in a passive viewing task: when the same magnitude was presented twice in the same notation, a bilateral decrease in activation was found in the parietal regions, whereas recovery effects were limited to the left parietal cortex when prime and target were presented in different notations [Cohen Kadosh et al., 2007]. This led the authors to suggest that only the left parietal cortex contains a notation-independent magnitude representation.

To sum up, whether or not the adaptation to small numerical magnitudes in the IPS is an all-or-none or a progressive phenomenon, and whether or not it is affected by the symbolic notation is still unclear. Both these unresolved issues concerning adaptation effects motivated the present study. Participants were presented with two small consecutive numbers and had to indicate whether the target matched a predefined magnitude. Each pair consisted of two numbers referring to the same magnitude or two different magnitudes with the numerical distance between them being either small or large. Prime and target numbers were always in a different notation (i.e., an Arabic or verbal numeral) to exclude low-level

perceptual repetition effects. We hypothesized that the presentation of a different target number would lead to a recovery of parietal activation directly related to the numerical distance between primes and targets. More specifically, we expected a larger recovery of the parietal activation for trials where the distance between the prime and the target was large. In addition, we also wanted to compare the adaptation effects between the two types of trials (verbal numeral followed by an Arabic numeral or the other way around). Previous research has shown that there are notational differences between Arabic and verbal numerals in the way they are processed in a non-semantic task [e.g., Brysbaert, 2005]. Although both can be processed along semantic and nonsemantic pathways, it seems that Arabic numerals rely more on semantics than verbal numerals do. Since both notations might not activate the corresponding magnitude representation to the same extent, this difference between notations could affect adaptation effects.

METHODS

Participants

Thirteen healthy, male participants (age range: 19–30 years), recruited from an academic environment, took part in the study. All participants were right-handed, had no history of neurological or psychiatric disorders, had normal or corrected-to-normal vision, were native Dutch speaking, and were unaware of the purpose of the study. Written informed consent was obtained from all participants and they received payment for taking part in the study. The study was approved by the K.U. Leuven Medical Ethics Committee (ML3431).

Stimuli

The fixation stimulus was a cross (Arial font 18). The numbers [1, ÉÉN], [2, TWEE], [8, ACHT], and [9, NEGEN] were used as stimuli. They were presented as Arabic numerals (Arial font 18) or in Dutch as verbal numerals (Arial font 18, all capitals). In one trial, a prime and a target number were presented. If the prime was an Arabic numeral, the target was always a verbal numeral; conversely, if the prime was a verbal numeral, the target was always an Arabic numeral. All pairs of numbers were fully combined in both notations, resulting in 32 different trials involving one of the following conditions: (i) eight SAME pairs, where primes and targets had the same numerical value ("ONE"-"1," ..., "9"-"NINE"), (ii) eight CLOSE pairs, where the numerical distance between primes and targets was small (distance of 1; "ONE"-"2," ..., "8"-"NINE"), (iii) sixteen FAR pairs, where the numerical distance between primes and targets was large (distance of 6, 7, or 8; "ONE"-"8," ..., "2"-"NINE"). To equalize the number of trials in all

Figure 1.

Experimental design, example of a CLOSE trial. Prime and target numbers were presented for 600 ms each and were always a combination of an Arabic and verbal numeral to exclude any low-level perceptual repetition effect. The numerical distance between prime and target was systematically manipulated, resulting in three different conditions of interest: firstly, a condition where both quantities were identical (SAME), secondly, a condition where prime and target number were numerically close (CLOSE), and a final condition where the numerical distance between prime and target was larger (FAR).

conditions, the trials of the first two conditions were presented twice.

Design and Procedure

We used an fMRI-adaptation paradigm. In this paradigm, a given stimulus is repeatedly presented, which causes the BOLD signal to decrease due to a reduction of firing rates of a neuronal population [Grill-Spector and Malach, 2001]. Afterwards, a stimulus attribute is changed, which may lead to recovery of the BOLD signal, indicating that the adapted neuronal population contains neurons that are sensitive to the changed attribute. If the signal remains adapted, the neuronal population is invariant to this attribute.

All trials were presented to the participants in the following sequence (see Fig. 1). Each trial started with a fixation cross, presented centrally for 500 ms. The fixation cross was then replaced by the prime and target, which were consecutively presented centrally for 600 ms each, separated by a blank screen of 100 ms. When the target disappeared from the screen, a blank screen was presented for an additional 3,800 ms, resulting in an event length of 5,600 ms. Stimulus presentation was synchronized with the fMRI sequence at the beginning of each run. A jitter was induced, firstly by creating an event length (5,600 ms)

that was not a multiple of the TR (2,000 ms) and secondly by adding 32 null events, that is trials where nothing was presented on the screen for 5,600 ms, which equals the total length of an event. This resulted in a total number of 80 trials, each presented once in a run. The entire experiment contained four runs and lasted ~30 min. The order of the trials was counterbalanced for each run in such a way that each trial type followed every other trial type equally often. In addition, we also systematically rotated the positions of the trials across all runs, fully assuring that the average trial history preceding and following a given trial type was the same as for any other trial type.

Participants were asked to conduct a number identification task on the target number. They were instructed to focus on the fixation cross, followed by the prime and target, which were sequentially presented on the same location of the screen. They had to press a button as fast as possible with their left hand whenever the target matched a predefined number, which occurred in 25% of the trials. The predefined number was always one of the four numbers used in the experiment and was presented on the instruction screen as an Arabic and verbal numeral at the start of each run. A different number was used for each run, so that each number served as a response number once throughout the entire experiment. At the start of each run, the participants were informed on the number they had to respond to.

fMRI Data Acquisition and Processing

The fMRI images were acquired with a 3-T Intera MR scanner (Philips, Best, Netherlands), using an eight-element SENSE head coil (MRI Devices, Waukesha, WI). A functional time series consisted of whole-brain BOLD-weighted field-echo echo-planar images (FE-EPI) with TR/TE = 2,000/30 ms, in-plane resolution $2.75 \times 2.75 \text{ mm}^2$, acquisition matrix = 80×80 , SENSE reduction factor = 2, slice thickness = 3.75 mm, acquiring 36 horizontal slices covering the entire brain. At the end of each scanning session, a 3D high-resolution T1-weighted anatomical image (TR/TE = 9.68/4.6 ms, TI = 1,100 ms, field of view = 250 mm^2 , matrix = 256×256 , slice thickness = 1.2 mm, 182 slices, SENSE factor = 2) was acquired.

Data were processed and analyzed with SPM5 (<http://www.fil.ion.ucl.ac.uk/spm>) implemented in MATLAB (Mathworks, MA, USA). The first four images were discarded to allow for T1 equilibration. The remaining images were realigned to the first image and corrected for slice-timing. T1-weighted anatomical images were then coregistered to the first scan of the functional images. In a next step, the anatomical image was segmented and normalized to the standard template of the Montreal Neurological Institute by means of an affine fourth degree β -spline interpolation transformation and resampled to $2 \times 2 \times 2 \text{ mm}^3$ voxel size. The resulting spatial normalization file was subsequently used to normalize and rewrite the func-

tional images. Finally, functional images were spatially smoothed (FWHM 8 mm).

DATA ANALYSIS

Behavioral Data

Although the behavioral responses were registered online in the scanner, response times (RTs) were not recorded due to technical reasons. Participants were unaware of this technical problem. Therefore, they were asked to conduct the entire experiment once more in our laboratory after the scanning was completed. RTs from all response trials were analyzed in a repeated measures analysis of variance (ANOVA) with the distance between prime and target (3: same, close, and far) and trial type (2: Arabic-verbal and verbal-Arabic) as independent factors.

Imaging Data

In all analyses, only cerebral activations related to non-response trials were included. For each participant, condition-related changes in regional brain activity were estimated by a general linear model in which the responses evoked by each condition of interest were modeled by a standard canonical hemodynamic response function. The regions of interests were selected by conducting a whole-brain analysis comparing the activation during the presentation of number trials against all null events. This whole-brain group analysis was corrected for multiple comparisons at the cluster level ($P < 0.001$). To test our hypothesis, two analyses were conducted: one on the clusters resulting from the whole-brain analysis and the other on individually selected voxels. Firstly, the activation of the IPS clusters resulting from the whole-brain analysis was reduced for each condition (SAME, CLOSE, and FAR) with the average activation during null events. The results of these contrasts (betas), extracted using MarsBar [Brett et al., 2002], were then submitted to a linear contrast testing for a distance-dependent increase of activation using STATISTICA. As a control, the same analysis was performed for the activation of all significantly activated brain regions. Secondly, we focused on the areas around the IPS and investigated adaptation effects in these brain areas for each participant individually. This individual approach was motivated by a recent study showing that pooling activation across participants might reduce effects of interest and hence lead to smaller adaptation effects [Cohen Kadosh et al., 2007] and because previous research showed large anatomical interindividual variability along the IPS [Zilles et al., 2003]. In line with Piazza et al. [2007], a voxel-based analysis was conducted for each individual, by selecting the left and right parietal voxel that yielded the largest significant activation when conditions were compared against null events ($P < 0.05$, FEW-corrected) and that was closest to the left and right IPS regions

TABLE I. MNI coordinates of individual voxels in the left and right parietal regions, which were used as individual ROIs

Participant	Left parietal			Right parietal		
	<i>x</i>	<i>y</i>	<i>z</i>	<i>x</i>	<i>y</i>	<i>z</i>
1	-28	-58	56	34	-50	56
2	-32	-58	58	32	-54	54
3	-28	-62	54	30	-52	42
4	-38	-42	46	36	-52	42
5	-42	-40	40	32	-66	42
6	-28	-56	50	32	-62	40
7	-30	-52	52	28	-50	50
8	-56	-42	32	32	-40	40
9	-26	-52	38	34	-68	28
10	-52	-40	38	32	-50	48
11	-52	-40	30	52	-44	52
12	-54	-40	46	40	-46	46
13	-32	-60	54	34	-58	52
Mean	-38	-49	46	34	-53	45
SD	11.43	8.85	9.3	6	8.31	7.62

resulting from the whole-brain group analysis. For all participants, this resulted in a left and right parietal voxel, in which the adaptation effect was analyzed (see Table I for an overview of individual parietal voxels). For these voxels, the average activation in each condition was reduced with the average activation during null events. The results of these contrasts (betas) were submitted to a repeated measures ANOVA with trial type (2: verbal-Arabic vs. Arabic-verbal numerals), hemisphere (2: RH vs. LH), and numerical distance (3: same, close, vs. far) as the within-subject factors, followed by pairwise comparisons (using two-sample *t*-tests) using STATISTICA.

RESULTS

Behavioral Results

No errors were made. Mean RTs for SAME, CLOSE, and FAR trials were 434 ± 57 , 449 ± 51 , and 457 ± 79 ms, respectively. The main effect of distance was not significant [$F(1, 12) = 1.15$, $P = 0.33$], possibly due to the large variance caused by the small number of observations ($n = 16$) per condition for each participant. The type of trial had a significant main effect [$F(1, 12) = 10.34$, $P < 0.01$]: Arabic-verbal trials were responded to 33 ms slower than verbal-Arabic trials, indicating slower identification of verbal numeral targets. The interaction between distance and trial type was not significant ($F < 1$).

Imaging Results

The whole-brain group analysis, comparing the activation during number trials against all null events, resulted in a network including parietal, occipital, temporal, precentral, and cingulate areas (see Table II and Fig. 2). The

parietal regions were both located in the posterior part of the IPS, with the right region extending to the anterior part of the IPS (left: -28, -60, 46, right: 34, -50, 46). The occipital regions included the middle part of the left and right occipital gyri. A large cluster was found in the right temporal lobe, extending from the inferior and middle part of the temporal cortex to the fusiform gyrus. An additional activated cluster was found in the middle part of the right cingulate gyrus and in the right precentral cortex. Finally, significant activation was found in the left and right insula and also in the right premotor cortex. From all significantly activated areas, the parietal regions were the only regions where a distance-dependent increase of activation was observed [$F(1, 12) = 4.99$, $P < 0.05$].

As pooling activation across participants might have reduced effects of interests, a voxel-based analysis in and around the IPS was conducted at the individual level. This analysis revealed significantly more activation for Arabic-verbal numeral trials compared to verbal-Arabic numeral trials, leading to a significant effect of trial type [$F(1, 12) = 5.13$, $P < 0.05$]. A distance-dependent increase of activation was also found, resulting in a significant effect of distance [$F(2, 24) = 5.61$, $P < 0.05$]. A marginally significant effect of hemisphere was found [$F(1, 12) = 4.46$, $P = 0.057$], with more activation in the right hemisphere on average. The

TABLE II. MNI coordinates of regions showing activation during the number identification task (number trials–null events)

Cortical region	<i>x</i>	<i>y</i>	<i>z</i>	Cluster extent	Z score
R inf. parietal lobule	34	-50	46	338	5.51**
	28	-62	50		
L inf. parietal lobule	-28	-60	46	125	4.84*
	-32	-62	56		
R inf. temporal fusiform gyri	42	-58	-6	1,563	6.19**
	34	-92	-8		
L medial occipital fusiform gyri	36	-46	-18	521	544**
	-36	-58	-14		
Medical cingulate gyrus	-34	-74	-10	1,622	6.27**
	-36	-84	0		
R medial frontal gyrus	-2	10	46	191	6.09**
	6	14	46		
R precentral gyrus	2	20	34	114	5.44**
	32	40	20		
R thalamus	50	10	34	130	5.45**
	16	-22	12		
R insula	10	-12	14	215	5.06**
	36	26	0		
L insula	48	12	4	128	5.01**
	30	20	4		
	-30	26	4		
	-40	18	-8		

x, *y*, *z* = stereotaxic coordinates of peak-height voxels.

* $P < 0.001$ corrected for multiple comparisons at cluster level;

** $P < 0.05$ FWE-corrected for multiple comparisons.

Figure 2.

Regions showing activation during the number identification task (number trials–null events). Statistical parametric maps are rendered on the SPM template (all $P < 0.001$, corrected for multiple comparisons at the cluster level). Only the parietal clusters showed a quantity-based adaptation recovery of activation.

interaction between hemisphere and distance, and the three-way interaction between trial type, hemisphere, and distance were nonsignificant (both $F < 1$). However, the interactions between trial type and hemisphere [$F(1, 12) = 2.12$, $P = 0.17$] and between trial type and distance [$F(2, 24) = 1.8$, $P = 0.19$] showed a trend toward significance. This possible difference across trial types was tentatively explored by repeating the first analysis for both trial types separately. The analysis for the Arabic-verbal numeral trials resulted in a significant effect of hemisphere [$F(1, 12) = 4.8$, $P = 0.05$], with more activation in the RH than in the LH on average. A distance-dependent increase of left and right parietal activations was observed, resulting in a significant effect of distance [$F(2, 24) = 8.12$, $P < 0.01$]. Pairwise comparisons revealed a significant difference between the SAME and CLOSE conditions [$t(12) = -3.13$;

$P < 0.005$], between the SAME and FAR conditions [$t(12) = -3.27$; $P < 0.005$], and a marginally significant difference between the CLOSE and FAR conditions [$t(12) = -1.7$; $P = 0.057$]. Finally, hemisphere and distance did not interact significantly ($F < 1$). The analysis for the verbal-Arabic numeral trials resulted in a marginally significant effect of hemisphere [$F(1, 12) = 3.79$, $P = 0.075$], with more activation in the RH than in the LH on average. The parietal activation did not increase with prime-target distance, resulting in a nonsignificant effect of distance ($F < 1$). Pairwise comparisons showed that none of the conditions differed significantly from each other [SAME vs. CLOSE, $t(12) = -1.2$, $P = 0.13$; SAME vs. FAR, $t < 1$; CLOSE vs. FAR, $t < 1$]. Finally, no significant interaction was found between hemisphere and distance ($F < 1$). The results are illustrated in Figure 3.

Figure 3.

Axial view of activation in the left and right IPS resulting from the whole-brain group analysis comparing activation for number trials relative to null events. The graphs show the activation levels for the SAME, CLOSE, and FAR conditions for both trial types separately in the left and right individual parietal voxels. Error bars represent one SEM.

DISCUSSION

This event-related fMRI study aimed at shedding light on the neural origin of the priming distance effect as observed in behavioral priming studies. More specifically, using small symbolic numbers, we tested whether numerically close numbers have more similar coding schemes compared to numerically far ones. Participants were shown a prime and a target number, while the numerical distance between them was manipulated. Conducting the number identification task resulted in an activated neural network including parietal, occipital, precentral, and cingulate regions. Bilateral activation in the intraparietal sulci as a consequence of number processing is in line with many other studies [e.g., Eger et al., 2003; Pesenti et al., 2000; Pinel et al., 2001]. The Euclidean distances between the present peaks and the left and right IPS clusters reported by Dehaene et al. [2003] in their meta-analysis of fMRI activations during various numerical tasks are 20 and 8 mm for the left and right IPS, respectively. Furthermore, the present foci largely overlap with the parietal clusters showing distance-dependent recovery reported by Piazza et al. [2007]. The activation in the occipital regions is probably due to the low-level processing of perceptual characteristics of the Arabic and verbal numerals. Arguing on the basis of previous research with numerical conflict tasks, the activation in the medial part of the cingulate gyrus, accompanied with precentral activation is likely to be caused by response demands or response conflict, independently of processing number semantics [e.g., Ansari et al., 2006a]. Response conflict was present in the task because for some trials, prime and target evoked different answers (response/no response). Since participants were asked to hold the response box in their left hand, this resulted in a significant cluster of activation in the right premotor cortex. Finally, the activation found in the left and right insula may be due to the vocalization of the stimuli. This region is known to be involved in phonological processing during reading [e.g., Fiez and Petersen, 1998].

Contrary to previous studies using small symbolic magnitudes with only same and different pairs [Cohen Kadosh et al., 2007; Naccache and Dehaene, 2001], the present experiment manipulated the numerical distance between primes and targets, allowing us to investigate whether or not the recovery of parietal activation would exhibit a progressive distance-dependent rather than a discrete all-or-none function. We hypothesized that the recovery of parietal activation would be directly related to the numerical distance between primes and targets. The results support such a progressive distance-dependent recovery of bilateral parietal activation. We observed a significant increase with the least activation in the condition where primes and targets had the same magnitude and the highest activation when the numerical distance between primes and targets was the largest. This finding extends the adaptation effects already observed for larger nonsymbolic magnitudes (i.e., 16 and 32 adapted dots in Piazza et al. [2004]; 18 and 48 adapted dots or presented as Arabic numerals in Piazza et al. [2007]) to

small, symbolically presented magnitudes, in an fMRI study closely matched to behavioral priming experiments [Koechlin et al., 1999; Reynvoet et al., 2002]. This is a crucial extension because some authors [Verguts et al., 2005] have proposed that small symbolic numbers might be represented more precisely than larger symbolic numbers due to their high frequency of use.

Interestingly, the distance-dependent recovery of parietal activation was only observed for the Arabic-verbal numeral trials, whereas a similar effect was absent for the verbal-Arabic numeral trials. This difference suggests that Arabic and verbal primes did not access their magnitude representation to the same extent under the current conditions, leading to the absence of adaptation effects when a verbal numeral was shown first. In healthy individuals, there is a large body of evidence showing that Arabic numeral processing relies more on the semantic route than on the nonsemantic route [Brysbaert, 2005]. Several studies have revealed that Arabic numerals address their semantic representation very rapidly [e.g., Dehaene and Akhavein, 1995] even when their magnitude is completely irrelevant for the task at hand [Fias et al., 2001], whereas a few neuropsychological reports have provided some support for a nonsemantic processing of Arabic numerals [e.g., Dehaene and Cohen, 1997]. Moreover, findings including verbal numerals are consistent with the view that nonsemantic processing routes are dominant when magnitude information is irrelevant for the task at hand [e.g., Fias et al., 2001; Ito and Hatta, 2003]. This nicely fits with the proposal of a dual-route architecture containing semantic and nonsemantic number processing routes along which both Arabic and verbal numerals can be processed depending on their notation and task context [Brysbaert, 2005]. Such a dual-route model is in line with neuropsychological data [Cappelletti et al., 2001; Cohen et al., 1994] and with current models of written word naming that all consist of multiple routes from alphabetic input to spoken output [e.g., Coltheart et al., 2001].

Importantly, one might argue that the absence of any difference between the same, close, and far pairs in the verbal-Arabic trials in combination with a lower activation level for these trials reflects the presence of an equally large adaptation effect in all three conditions rather than the absence of adaptation. Theoretically, it is more likely to assume the absence of a priming effect in all three conditions in the case of verbal-Arabic stimuli, rather than to assume the presence of an equally large priming effect. According to the model of Verguts et al. [2005], the overlap of magnitude representations leads to a strong activation of neighboring magnitudes and less activation of magnitudes numerically further away, resulting in the typical priming distance effect as observed in many previous behavioral studies [e.g., Koechlin et al., 1999; Reynvoet et al., 2002]. In addition, previous behavioral studies showed that when the numerical distance between primes and targets became larger than 3 or 4, there was hardly any effect of the prime on the target [e.g., Roggeman et al., 2007]. In our study, the numerical distance between primes and targets in the far condition varied between 6

and 9 leading to little or no priming. Therefore, this condition can serve as a baseline to examine adaptation effects in the other conditions. Under this assumption, the observed lower activation level in the verbal-Arabic condition can be explained as follows. The target number (either an Arabic numeral or a verbal numeral) was always processed up to the semantic level since participants were asked to conduct the task on the target number. However, using a nonsemantic task led to an asymmetry in the automatic activation of the semantics of the Arabic and verbal primes. According to the dual route model, in this situation, only Arabic primes were processed semantically, whereas verbal primes were processed along a nonsemantic route. Indeed, verbal numerals are less tightly linked to their semantics compared to Arabic numerals: more pronounced bilateral IPS activation was found for Arabic digits relative to verbal numerals, suggesting greater semantic involvement when processing Arabic numerals [Pinel et al., 2001]. As a result, both the prime and the target of the Arabic-verbal trials activated their semantics leading to more activation in the IPS compared to verbal-Arabic trials in which only the target number activated its semantics.

Brysbaert's [2005] proposal that semantic processing of a numeral is dependent on an interaction between task demands and notation can also explain the differences between the present study and the study of Naccache and Dehaene [2001]. Adaptation effects require semantic processing of the prime and, as noted above, this semantic access may be dependent on the cognitive demand of the task. The cognitive demand was higher in the study of Naccache and Dehaene (i.e., comparison) than in the present study (i.e., identification), which explains the semantic processing of all verbal numerals, both as prime and target, in the former study. As mentioned previously, the verbal numerals in our study were only processed semantically when they served as targets on which the task had to be conducted. With verbal primes, the task appeared insufficiently semantic to activate the semantics of the prime. Further research directly comparing task demands is required to test this to a further extent.

Although the dual-route model provides an explanation for the differences found between the present study and the study of Naccache and Dehaene [2001], it is inconsistent with the results of the study of Cohen Kadosh et al. [2007]. According to this model, verbal numerals should be dominantly processed through a nonsemantic route in case of a nonsemantic task. Although a nonsemantic task (i.e., passive viewing) was used by Cohen Kadosh et al. [2007], a significant repetition priming effect was observed in the left hemisphere in the verbal-verbal condition. However, this result must be interpreted with care for the following reasons. Given that the entire parietal cortex was predefined as a region of interest and given the presence of a large variability between the anatomical locations of the individual parietal regions, it is possible that the repetition suppression effect in the left parietal cortex for the verbal condition was due to the involvement of processes other than magnitude processing. For instance, a

study of Dehaene et al. [2004; Experiment 1] investigated cross-case repetition priming (i.e., prime in upper case and target in lower case, or the other way around). Such a condition is very similar to the verbal-verbal condition of Cohen Kadosh et al. [2007] who also examined repetition priming with primes and targets presented in different fonts. Cross-case repetition suppression effects also occurred in the left parietal cortex, suggesting that the priming effect observed in the verbal-verbal condition in the left hemisphere was a verbal priming effect, rather than a magnitude-related priming effect. Although the presence of a cross-notation adaptation effect would argue against this reasoning, a closer look at the data reveals no significant effect of quantity adaptation on the mixed notation condition, but only a main effect of quantity adaptation over all conditions. Additional evidence comes from a study by Simon et al. [2002] showing that phonological processes activate the horizontal part of the left IPS, which overlaps with activations related to mental arithmetic.

It has been found that number processing and response selection or even response planning may lead to common activations in the parietal cortex [Göbel et al., 2004]. It is worth noting that cross-notation adaptation and recovery of parietal activation in the present study cannot be attributed to response selection nor to response planning, since all trials requiring a response were excluded from the analyses. Furthermore, since all numbers were equally divided over all conditions, leading to an equal distribution of response and no-response trials, response planning was present to the same extent in all three conditions. Therefore, the observed IPS activation and the differences across conditions cannot be explained by response planning, but most likely only stems from differences in the numerical distance between prime and target. Additional evidence against the response planning account comes from a study of Ansari et al. [2006b] showing distance effects in the IPS with a task that did not involve any response selection.

To conclude, the present study has shown for the first time that bilateral parietal activation recovered in a progressive way as a function of the numerical distance between a prime and a target number, both presented as small symbolic numbers. Therefore, the results reveal the neural origin of the frequently reported behavioral distance-dependent priming distance effect. Importantly, this effect was only present for trials where a verbal numeral was preceded by an Arabic numeral and absent on trials where an Arabic numeral was preceded by a verbal numeral, which is in line with an asymmetric access to semantics for both notations. The observed cross-notation adaptation and recovery of bilateral parietal activation support the idea of a notation-independent representation of magnitudes in both parietal cortices.

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REFERENCES

- Ansari D, Fugelsang J, Dhital B, Venkatraman V (2006a): Dissociating response-conflict from numerical magnitude processing in the brain: An event-related fMRI study, *Neuroimage* 32:799–805.
- Ansari D, Dhital B, Soon CS (2006b): Parametric effects of numerical distance on the intraparietal sulcus during passive viewing of rapid numerosity changes. *Brain res* 1067:181–188.
- Brett M, Anton J-L, Valabregue R, Poline J-B (2002): Region of interest analysis using an SPM toolbox. Presented at the 8th International Conference on Functional Mapping of the Human Brain, June 2–6, 2002, Sendai, Japan. Available on CD-ROM in *Neuroimage* 16(2) (abstract).
- Brysbaert M (2005): Number recognition in different formats. In: Campbell JID, editor. *Handbook of Mathematical Cognition*. Hove: Psychology Press.
- Cappelletti M, Butterworth B, Kopelman M (2001): Spared numerical abilities in a case of semantic dementia. *Neuropsychologia* 39:1224–1239.
- Chochon F, Cohen L, Van de Moortele PF, Dehaene S (1999): Differential contributions of the left and right inferior parietal lobules to number processing. *J Cogn Neurosci* 11:617–630.
- Cohen L, Dehaene S, Verstichel P (1994): Number words and number non-words—A case of deep dyslexia extending to Arabic numerals. *Brain* 117:267–279.
- Cohen Kadosh R, Cohen Kadosh K, Kaas A, Avishai H, Goebel R (2007): Notation-dependent and -independent representations of numbers in the parietal lobes. *Neuron* 53:307–314.
- Cohen Kadosh R, Walsh V (2009): Numerical representation in the parietal lobes: Abstract or not abstract? *Behav Brain Sci* 32:313–328.
- Coltheart M, Rastle K, Perry C, Langdon R, Ziegler JC (2001): DRC: A dual route cascaded model of visual word recognition and reading aloud. *Psychol Rev* 108:204–256.
- Dehaene S, Akhavein R (1995): Attention, automaticity and levels of representation in number processing. *J Exp Psychol Learn Mem Cogn* 21:314–326.
- Dehaene S, Changeux J-P (1993): Development of elementary numerical abilities: A neuronal model. *J Cogn Neurosci* 5:390–407.
- Dehaene S, Cohen L (1997): Cerebral pathways for calculation: Double dissociation between rote verbal and quantitative knowledge of arithmetic. *Cortex* 33:219–250.
- Dehaene S, Jobert A, Naccache L, Ciuciu P, Poline JB, Le Bihan D, Cohen L (2004): Letter binding and invariant recognition of masked words: Behavioral and neuroimaging evidence. *Psychol Sci* 15:307–313.
- Dehaene S, Piazza M, Pinel P, Cohen L (2003): Three parietal circuits for number processing. *Cogn Neuropsychol* 20:487–506.
- Dormal V, Pesenti M (2009): Common and specific contributions of the intraparietal sulci to numerosity and length processing. *Hum Brain Mapp* 30:2466–2476.
- Eger E, Sterzer P, Russ MO, Giraud A-L, Kleinschmidt A (2003): A supramodal number representation in human intraparietal cortex. *Neuron* 37:719–725.
- Fias W, Lammertyn J, Reynvoet B, Dupont P, Orban GA (2003): Parietal representation of symbolic and nonsymbolic magnitude. *J Cogn Neurosci* 15:47–56.
- Fias W, Reynvoet B, Brysbaert M (2001): Are Arabic numerals processed as pictures in a Stroop interference task? *Psychol Res* 65:242–249.
- Fiez JA, Petersen SE (1998): Neuroimaging studies of word reading. *Proc Natl Acad Sci USA* 95:119–122.
- Göbel SM, Johansen-Berg H, Behrens T, Rushworth MFS (2004): Response-selection-related parietal activation during number comparison. *J Cogn Neurosci* 16:1536–1551.
- Grill-Spector K, Malach R (2001): fMR-adaptation: A tool for studying the functional properties of human cortical neurons. *Acta Psychol* 107:293–321.
- Ito Y, Hatta T (2003): Semantic processing of Arabic, Kanji, and Kana numbers: Evidence from interference in physical and numerical size judgments. *Mem Cognit* 31:360–368.
- Koechlin E, Naccache L, Block E, Dehaene S (1999): Primed numbers: Exploring the modularity of numerical representations with masked and unmasked semantic priming. *J Exp Psychol Hum Percept Perform* 25:1882–1905.
- Naccache L, Dehaene S (2001): The priming method: Imaging unconscious repetition priming reveals an abstract representation of number in the parietal lobes. *Cereb Cortex* 11:966–974.
- Nieder A, Miller EK (2003): Coding of cognitive magnitude: Compressed scaling of numerical information in the primate prefrontal cortex. *Neuron* 37:149–157.
- Nieder A, Miller EK (2004): A parieto-frontal network for visual numerical information in the monkey. *Proc Nat Acad Sci USA* 101:7457–7462.
- Pesenti M, Thioux M, Seron X, De Volder A (2000): Neuroanatomical substrates of the Arabic number processing, numerical comparison and simple addition: A PET-study. *J Cogn Neurosci* 12:461–479.
- Piazza M, Izard V, Pinel P, Le Bihan D, Dehaene S (2004): Tuning curves for approximate numerosity in the human intraparietal sulcus. *Neuron* 44:547–555.
- Piazza M, Pinel P, Le Bihan D, Dehaene S (2007): A magnitude code common to numerosities and number symbols in human intraparietal cortex. *Neuron* 53:293–305.
- Pinel P, Dehaene S, Rivière D, Le Bihan D (2001): Modulation of parietal activation by semantic distance in a number comparison task. *Neuroimage* 14:1013–1026.
- Reynvoet B, Brysbaert M (1999): Single-digit and two-digit Arabic numerals address the same semantic number line. *Cognition* 72:191–201.
- Reynvoet B, Brysbaert M, Fias W (2002): Semantic priming in number naming. *Q J Exp Psychol A* 55:1127–1139.
- Roggeman C, Verguts T, Fias W (2007): Priming reveals differential coding of symbolic and non-symbolic quantities. *Cognition* 105:380–394.
- Simon O, Mangin J-F, Cohen L, Le Bihan DL, Dehaene S (2002): Topographical layout of hand, eye, calculation, and language-related areas in the human parietal lobe. *Neuron* 33:475–487.
- Verguts T, Fias W, Stevens M (2005): A model of exact small-number representation. *Psychon Bull Rev* 12:66–80.
- Zago L, Pesenti M, Mellet E, Crivello F, Mazoyer B, Tzourio-Mazoyer N (2001): Neural correlates of simple and complex mental calculation. *Neuroimage* 13:314–327.
- Zilles K, Eickhoff S, Palmero-Gallagher N (2003): The human parietal cortex: A novel approach to its architectonic mapping. In: Siegel AM, Andersen RA, Freund H-J, Spencer DD, editors. *The Parietal Lobes*. New York: Lippincott Williams & Wilkins. pp 1–22.