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Title

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Journal

NeuroImage, 35(2)

ISSN

1053-8119

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Publication Date

2007-04-01

DOI

10.1016/j.neuroimage.2006.12.017

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Peer reviewed

Dissociated brain organization for single-digit addition and multiplication

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Received 3 September 2006; revised 4 December 2006; accepted 8 December 2006

Available online 23 December 2006

This study compared the patterns of brain activation elicited by single-digit addition and multiplication problems. 20 Chinese undergraduates were asked to verify whether arithmetic equations were true or false during functional magnetic resonance imaging. Results showed that both addition and multiplication were supported by a broad neural system that involved regions within SMA, precentral gyrus, intraparietal sulcus, occipital gyri, superior temporal gyrus, and middle frontal gyrus, as well as some subcortical structures. Nevertheless, addition problems elicited more activation in the intraparietal sulcus and middle occipital gyri at the right hemisphere, and superior occipital gyri at both hemispheres, whereas multiplication had more activation in precentral gyrus, supplementary motor areas, and posterior and anterior superior temporal gyrus at the left hemisphere. This pattern of dissociated activation supports our hypothesis that addition has greater reliance on visuospatial processing and multiplication on verbal processing.

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Keywords: Cognitive arithmetic; Addition; Multiplication; Arithmetic facts; Brain; fMRI

Introduction

Schoolchildren are taught to use two different types of strategies to learn arithmetic facts: procedural strategies and verbal memory strategy (e.g., Dehaene and Cohen, 1997; Roussel et al., 2002; Zhou and Dong, 2003). Procedural strategies, such as counting, transformation (e.g., $6+7=6+6+1$, $9+7=9+1+6$), and repeated addition ($3\times 4=3+3+3+3$), typically involve manipulation of visual Arabic digits. With the verbal memory strategy,

people repeatedly recite arithmetic facts so that the facts could be stored in memory as a type of modularized phonological associations between digit pairs and their answers. Schoolchildren are usually taught to use procedural strategies for simple addition and subtraction, but to use verbal memory strategy to memorize multiplication facts (e.g., Dehaene and Cohen, 1997; Roussel et al., 2002; Zhou and Dong, 2003). These differential strategies during the acquisition of arithmetic facts may play an important role in shaping their mental representations (e.g., Siegler and Shipley, 1995; Siegler and Shrager, 1984). It is possible that mental representations of addition and subtraction facts have greater reliance on the visuospatial memory than those of multiplication facts, whereas the latter had greater reliance on the verbal memory than the former (e.g., Zhou and Dong, 2003).

Some neuropsychological studies have shown such dissociation among simple arithmetic operations (e.g., Cohen et al., 2000; Dehaene and Cohen, 1997; Delazer and Benke, 1997; Lemer et al., 2003; Pesenti et al., 1994; van Harskamp et al., 2002, 2005). For example, injuries in the posterior part of the brain (e.g., intraparietal cortex) showed more damage to addition than to multiplication. In contrast, patients with lesions in the left perisylvian language region and those with low verbal fluency had more difficulty in single-digit multiplication than in addition and subtraction (e.g., Cohen et al., 2000; Dehaene and Cohen, 1997; Delazer and Benke, 1997; Lemer et al., 2003; Pesenti et al., 1994; van Harskamp et al., 2002, 2005). Recently, using the ERP technique, Zhou et al. (2006a) also showed neural dissociation among addition, subtraction, and multiplication. Compared with single-digit addition and subtraction, single-digit multiplication elicited a greater N300 at the left frontal electrodes peaking around 320 ms, and this implied a greater reliance on verbal processing (in the left frontal region) to retrieve simple multiplication facts than to perform addition and subtraction.

Compared to lesion and ERP studies, fMRI studies are better at localizing neural dissociation among simple arithmetic operations.

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Available online on ScienceDirect (www.sciencedirect.com).

So far, three neuroimaging studies have been conducted on simple arithmetic, but they yielded inconsistent results. One study (Lee, 2000) found that, compared to subtraction, multiplication elicited more activation in the left angular gyrus/supramarginal gyrus, right lingual gyrus, and right precentral gyrus, whereas subtraction had more activation in the bilateral intraparietal sulcus, inferior frontal gyrus, and posterior inferior temporal gyrus. In contrast, Kawashima et al. (2004) found that the right prefrontal and the left intraparietal cortex were activated more by multiplication than by addition and subtraction, but no regions of the brain were activated more by addition or subtraction than by multiplication. Finally, Chochon et al. (1999) used a variation of simple arithmetic problems in an fMRI study. They asked subjects to subtract a single-digit number presented on the screen from 11 for the subtraction task, and to multiply the target number by 3 for the multiplication task. Direct contrasts between multiplication and subtraction revealed that subtraction elicited more activation in several prefrontal areas and the right postcentral region than did multiplication, but multiplication did not show more activation in any areas.

The inconsistencies among the results of these three studies may be attributed to several factors. First, as mentioned above, there were variations in arithmetic problems used in different studies. Second, to avoid head movement, these three studies did not collect behavioral data while the subjects were being scanned. They were only asked to “think of” the answer, but not to report it orally. Therefore, subjects’ behavioral performance could not be recorded and evaluated, nor can it be assured that subjects were performing given tasks. Separate sessions of behavioral assessment revealed that arithmetic problems used in these studies had differential patterns of difficulties. In Chochon et al. (1999) study, subtraction was more difficult than multiplication, but in Kawashima et al. (2004) study, multiplication was more difficult than subtraction and addition. Lee (2000) did not provide any chronometric data. Therefore, difficulty levels of the arithmetic problems could also be a potential confounding factor in these studies.

The present study used the fMRI technique to test the dissociated processing hypothesis in simple arithmetic. We used an equation-verification paradigm with which subjects’ performance could be measured during scanning. This paradigm allowed us to collect chronometric data while avoiding potential artifacts from muscle movements in the face. In addition, based on previous studies (e.g., Zhou and Dong, 2003; Zhou et al., 2006a), we carefully matched the difficulty levels of addition and multiplication problems.

The following specific hypothesis was tested. Based on the research reviewed above, addition was expected to rely more on brain regions involved in visuospatial processing, whereas multiplication would rely on regions involved in verbal processing. Regions for visuospatial processing include intraparietal sulcus (e.g., inferior parietal lobule or superior parietal lobule) and occipital gyri (superior, middle or inferior gyrus) (e.g., Corbetta et al., 1998, 2000; Diwadkar et al., 2000; Jordan et al., 2002; LaBar et al., 1999; Linden et al., 2003; Nystrom et al., 2000; Podzebenko et al., 2002; Postle et al., 2004; Roland and Gulyas, 1995; Thomas et al., 1999; Vingerhoets et al., 2002; Zurowski et al., 2002). Brain regions for verbal processing include anterior and posterior superior temporal gyrus, motor areas, and complementary motor areas (e.g., Cowell et al., 2000; Hana-kawa et al., 2003; Hickok et al., 2000; Paus et al., 1996; Zhou et al., 2006a,b).

Methods

Participants

Twenty healthy right-handed university students (ten males and ten females) were recruited from Sichuan University, China. The average age of the subjects was 22.7 years, ranging from 18.3 to 29.8 years. They self-reported to have normal or corrected-to-normal eyesight. All were free from neurological and psychiatric disorders and had no brain abnormality on their T1-weighted high-resolution magnetic resonance images (MRI). They had not participated in any experiments similar to the present one (i.e., involving simple arithmetic tasks of addition, subtraction, and multiplication) during the past half a year. Informed written consent was obtained from each subject after procedures were fully explained. The experiment on these participants was approved by both the State Key Lab of Cognitive Neuroscience and Learning at Beijing Normal University and the Huaxi MR Research Center of Western China Hospital affiliated with Sichuan University.

Experimental design

We used a 2×2 within-subject design, with operation (one-digit addition vs. multiplication) and problem size (small vs. large) as independent variables.

Materials

Single-digit addition and multiplication problems were used in this study. Problems with 0 and 1 as an operand (e.g., $1+5$, $0+5$, 1×5 , 0×5) were not used because they are rule-based arithmetic facts (e.g., LeFevre and Liu, 1997). In addition, we did not include repeated-operand or “tie” problems (e.g., $3+3$ and 3×3) because they were found to have different operand encoding from the non-tie problems (e.g., Blankenberger, 2001; Gallistel and Gelman, 1992). The multiplication table used for Mainland Chinese typically includes only smaller-operand-first entries (e.g., $3 \times 7=21$, but not $7 \times 3=21$). Previous behavioral and neural studies have found the operand-order effect (e.g., LeFevre and Liu, 1997; Zhou and Dong, 2003; Zhou et al., in press). To solve the larger-operand-first problems (e.g., $7 \times 3=21$), subjects had to reorganize the problems as the smaller-operand-first problems (LeFevre and Liu, 1997). To eliminate a potential confounding effect from the order of operands during the retrieval of arithmetic facts, we only used the smaller-operand-first problems. Due to these constraints and the need to have a balanced set of problems across operations, there were only 28 problems we could use for each operation.

These addition and multiplication problems were further divided into “small” and “large” problems in order to examine and control for the confounding effect of task difficulty. Following Zhou and Dong’s (2003) study, “large” multiplication problems ($n=14$) included those with their product ranging from 28 to 72 and “small” multiplication problems ($n=14$) included those with products ranging from 6 to 24. Addition problems were grouped into 14 “small” (sums ranging from 5 to 11) and 14 “large” problems (sums ranging from 11 to 17) by using the same pairs of operands as in multiplication.

Because of the limited number of problems, to allow enough trials for the fMRI recording, we had to present each problem three times. Additionally, four problems (two small problems and two

large problems) were randomly selected from the whole set of problems for each operation and were turned into false equations by changing the answer. It should be pointed out that the false answers were not randomly generated. They had to meet the following requirements: (1) they came from the single-digit arithmetic table of the same operation type; (2) they were neighboring entries in the table (i.e., generated from equations with one of the operands plus or minus 1); and (3) they had to have the same number of digits (either one or two digits) as the true answer would have. The false answer would then be very similar to the true answer to avoid plausibility judgment during equation verification (e.g., Campbell and Tarling, 1996; Lemaire and Fayol, 1995). These false equations were also presented three times. There were 96 trials or problems for each type of operation.

Apparatus and imaging parameters

Functional MR investigation was carried out using a 3.0-T MR imaging system (EXCITE, General Electric, Milwaukee, USA) with an 8-channel phase array head coil. Subjects lay supine in the scanner with their heads immobilized. A single shot, T2*-weighted gradient-echo echo planar imaging (EPI) sequence was used for the fMRI scans, with slice thickness of 6 mm and no gap between slices, in-plane resolution of 3.75×3.75 mm, and TR/TE=3000 ms/30 ms. The field of view was 240×240 mm, and the acquisition matrix was 64×64 . Thirty contiguous axial slices parallel to AC–PC were acquired. One hundred and twenty three images were acquired with a total scan time of 548 s in a single run. Additionally, high-resolution T1-weighted anatomical images were acquired for each subject (three-dimensional, gradient-echo pulse sequence, TR/TE=25 ms/6 ms, FOV= 220×220 mm, 89–92 contiguous slices, matrix= 220×220 , and thickness=2 mm).

Scanning procedures

Fig. 1 shows the schematic representation of the experimental procedure for functional scanning. The functional scanning lasted 9 min and 8 s. The first 8 s was used to allow the machine's magnetization to stabilize. There were 18 blocks for the verification task, six blocks each for addition, multiplication, and fixation. Each block lasted for 30 s, with the first 2 s of each block used to orient participants about the upcoming task and the remaining 28 s for the experimental tasks. Previous research has shown strong evidence of interference among arithmetic operations when subjects had to switch among them (e.g., Campbell and Oliphant, 1992). To reduce such interference, different types of arithmetic problems were presented in separate blocks. The small and large problems were also presented in different blocks. The order for the two operations and the order for the large and small problems were counterbalanced across subjects.

Each block included 14 true arithmetic equations and 2 false ones. They were randomly presented within a block, with the constraint that consecutive problems did not have a common operand or the same solution. At the beginning of each block, the arithmetic operation to be performed was cued on the screen for 2 s with “Addition” for addition and “Multiplication” for multiplication. Then the problems were presented, each lasting 1 s. Subjects pressed a key to indicate whether the equations were true or false. Half of the subjects used their left index finger for true equations and their right index finger for false equations, and the other half responded in the opposite way. Subjects were encouraged to respond as quickly and accurately as possible. There was a blank of 750 ms between trials.

The arithmetic equations were projected onto the center of a translucent screen and viewed by the subjects through a mirror attached onto the head coil. The stimuli were presented in black against a light grey background, in the size of 48-dot matrix installed in the Window System 2000 (Chinese version). The numbers, the fixation symbol “*”, and the equal mark “=” were all bolded. For the problems with answers less than 10, a “#” sign in the same font type and size as the above was added to the most right side of arithmetic equation. Consequently, the addition and multiplication equations, regardless of problem size, had approximately matched visual field coverage. Before the formal test in the scanner, subjects were given 20 practice trials, randomly selected from the entire set of addition and multiplication problems (including both true and false equations).

Image processing and data analysis

Data analysis was performed using SPM2 for motion correction and statistical inference (Statistical Parametric Mapping, Wellcome Department of Cognitive Neurology, London, <http://www.fil.ion.ucl.ac.uk/spm/>). The functional data set acquired from the experiment consisted of 270 image volumes. The first four images were discarded to allow for the establishment of steady-state magnetization. Functional images were realigned to the first volume in the scanning session using affine transformations. A mean functional image volume was constructed for each participant from the realigned image volumes. This mean image volume was then used to determine parameters for spatial normalization. The normalization parameters were then applied to the corresponding functional image volumes for each participant. Spatial smoothing was performed on the normalized functional images using a Gaussian kernel 8-mm FWHM. Statistical analyses were conducted on the smoothed data using a delayed boxcar design with HRF. A high-pass filter (186 s) was applied in order to remove very low frequency effects and a low-pass filter (4 s) to remove the high-frequency noise. The global temporal trend was removed.

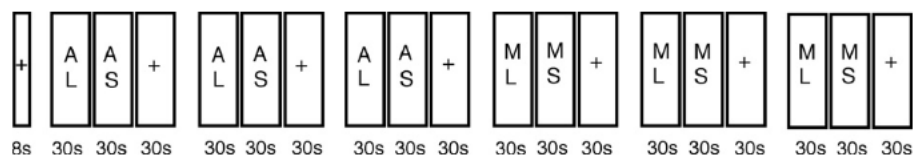


Fig. 1. Schematic representation for the procedure of fMRI acquisition. The order of two operations (addition and multiplication) and the order of two problem sizes (large and small) were counterbalanced across subjects. The 8 s at the beginning of the scanning session was used to stabilize MRI machine's magnetization. For each block, 2 s at the beginning was used to present the cue “Addition” or “Multiplication”, and the other 28 s to present problems. A: Addition; M: Multiplication; L: Large; S: Small.

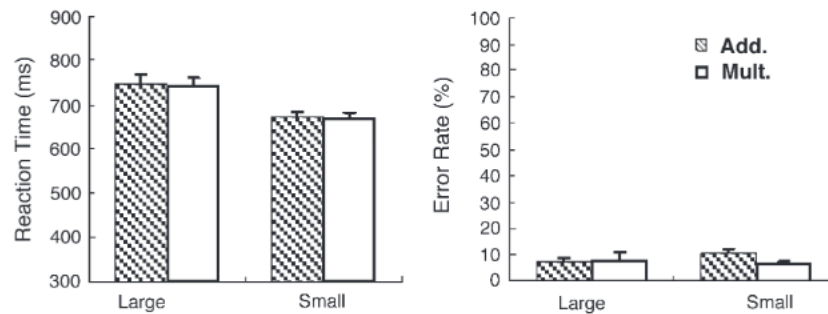


Fig. 2. Response times (ms) and error rates (%) for verifying single-digit addition and multiplication equations.

We first calculated parameter-estimated images for individual subjects across the entire brain. For each individual, we calculated contrasts (i.e., cognitive task minus fixation) to derive the activation maps for the four conditions (two operations by two problem sizes). Group effects were computed with a random-effect model. All reported areas of activation were significant above a threshold of $P < 0.001$ (uncorrected) when comparing experimental tasks to fixation or $P < 0.005$ (uncorrected) when comparing between tasks, with more than 15 voxels ($3 \times 3 \times 3$ mm).

In anatomical ROI (region of interest) analysis, the AAL template was used to define regions (Tzourio-Mazoyer et al., 2002). We selected specific brain regions in the frontal, parietal, occipital and temporal lobes believed to be responsible for visuospatial processing and language processing. The superior and inferior parietal lobules around intraparietal sulcus were selected

because previous studies have shown that these brain regions are involved in visual perception, visual mental imagery, visuospatial working memory, and spatial attention (e.g., Corbetta et al., 1998, 2000; Diwadkar et al., 2000; Jordan et al., 2002; LaBar et al., 1999; Linden et al., 2003; Nystrom et al., 2000; Podzebenko et al., 2002; Postle et al., 2004; Roland and Gulyas, 1995; Thomas et al., 1999; Vingerhoets et al., 2002; Zurowski et al., 2002). The occipital gyri (i.e., superior, middle, and inferior occipital gyri), as part of dorsal pathway for visuospatial processing, were also selected. Brain regions along the perisylvian language areas, including posterior superior temporal gyrus, supramarginal gyrus, angular gyrus, inferior frontal gyrus, and insula, were chosen to examine the involvement of verbal processing in the two types of arithmetic operations. Previous studies found that the posterior superior temporal gyrus could be activated during covert and overt speech

Table 1

Brain regions with significant activation relative to fixation: coordinates in Talairach space and T scores (x y z : T)

Regions	Addition		Multiplication	
	Large	Small	Large	Small
<i>Parietal</i>				
L. intraparietal s.	-27 -50 41: 12.79	-30 -47 41: 10.63	-27 -50 41: 10.34	-30 -59 47: 8.93
R. intraparietal s.	33 -59 50: 9.40	33 -59 50: 8.74	33 -59 50: 9.24	33 -59 50: 6.54
<i>Temporal</i>				
L. sup. temporal			-48 -40 24: 6.24	-48 -40 24: 6.09
L. sup. temporal (pole)			-48 3 -3: 5.25	-48 6 -3: 5.47
<i>Frontal</i>				
L. sup. motor area	-3 6 55: 16.76	-3 -6 55: 14.98	-3 3 58: 21.49	-3 3 58: 16.9
L. precentral g.	-45 5 33: 13.46	-42 5 33: 12.67	-45 4 30: 13.26	-42 4 27: 11.36
R. precentral g.	45 10 27: 9.44	48 8 36: 9.85	45 10 27: 8.28	50 8 36: 8.52
L. mid. frontal g.	-36 48 22: 6.08	-36 48 25: 6.18	-36 42 31: 7.69	-33 45 31: 7.36
R. mid. frontal g.	42 36 23: 7.58	36 39 23: 6.27	39 36 20: 5.96	39 42 20: 5.38
<i>Occipital</i>				
L. inf. occipital g.	-45 -69 -13: 10.53	-45 -69 -9: 12.64	-39 -70 -7: 10.58	-42 -70 -7: 9.29
R. inf. occipital g.	47 -63 -10: 5.93	42 -82 -6: 9.42	45 -62 -10: 6.23	45 -65 -9: 5.67
L. mid. occipital g.	-27 -72 31: 9.40	-27 -62 39: 7.20	-27 -72 26: 7.78	-27 -69 28: 7.24
R. mid. occipital g.	30 -67 33: 6.22	33 -59 39: 5.93		
<i>Subcortical</i>				
L. insula	-33 20 -1: 8.71	-33 20 -2: 7.60	-33 20 3: 9.41	-33 15 3: 7.79
R. insula	36 20 2: 8.58	33 20 2: 6.64	36 20 2: 11.19	36 18 0: 6.25
L. thalamus	-18 -11 17: 8.04	-15 -8 14: 7.18	-15 -8 14: 11.53	-15 -11 14: 6.89
R. thalamus	16 -11 17: 8.94	15 -11 14: 7.99	18 -8 14: 8.24	18 -8 14: 7.76

Note. Clusters that survived $p < 0.001$ (uncorrected) with spatial extent of $k > 15$ voxels were considered statistically significant. R, right hemisphere; L, left hemisphere; g, gyrus; inf, inferior; s, sulcus; sup, supplementary; temp, temporal.

(e.g., Cowell et al., 2000; Hanakawa et al., 2003; Hickok et al., 2000; Paus et al., 1996). Meanwhile, the primary and supplementary motor areas were also considered due to their role in verbal production (e.g., Bohland and Guenther, 2006; Riecker et al., 2002; Wildgruber et al., 1996).

The dependent variables of this study were the intensity of activation (effect size). The intensity of activation in an anatomical region of interest was the average of effect sizes of all activated voxels (positive) for each condition, calculated based on the `con*.img` of SPM2. The tool we used was based on MarsBar (<http://www.marsbar.sourceforge.net/>) structural ROI analyses, but programmed in-house using Matlab 6.5 version (The MathWorks, Inc., MA, USA).

Results

One subject's behavioral data were lost due to a failure of the response box. The mean reaction time was calculated for the correct responses to all equations. Fig. 2 shows the mean reaction times and error rates. Two-factor repeated measures ANOVA with arithmetic operation and problem size as the within-subject factors showed a significant main effect of problem size, $F(1,18)=120.04$,

$MSe=857.66$, $P<0.001$. There was neither a significant main effect of operation nor a significant interaction between operation and problem size. The same ANOVA was conducted on error rates, and no significant effects were found.

The brain activation loci are shown in Table 1 by operation type and problem size. The supplementary motor area, intraparietal sulcus (including inferior and superior parietal lobules), precentral gyrus, middle frontal gyrus, and insula, and inferior occipital gyrus at the left and right hemispheres were activated by addition and multiplication, regardless of problem size. Multiplication, but not addition, significantly activated the posterior and anterior part of superior temporal gyrus. On the other hand, addition, but not multiplication, had significant activation in the right middle occipital gyrus.

Because the brain activation analyzed with direct contrasts among tasks was comparatively weak, the voxel-level P value was set to 0.005, uncorrected. Fig. 3 shows the results of direct activation contrasts: addition minus multiplication and multiplication minus addition, separately for the two problem sizes as well as combined across problem sizes. Addition had more activation in the posterior part of the brain, including bilateral superior occipital gyrus, right superior and inferior parietal lobules,

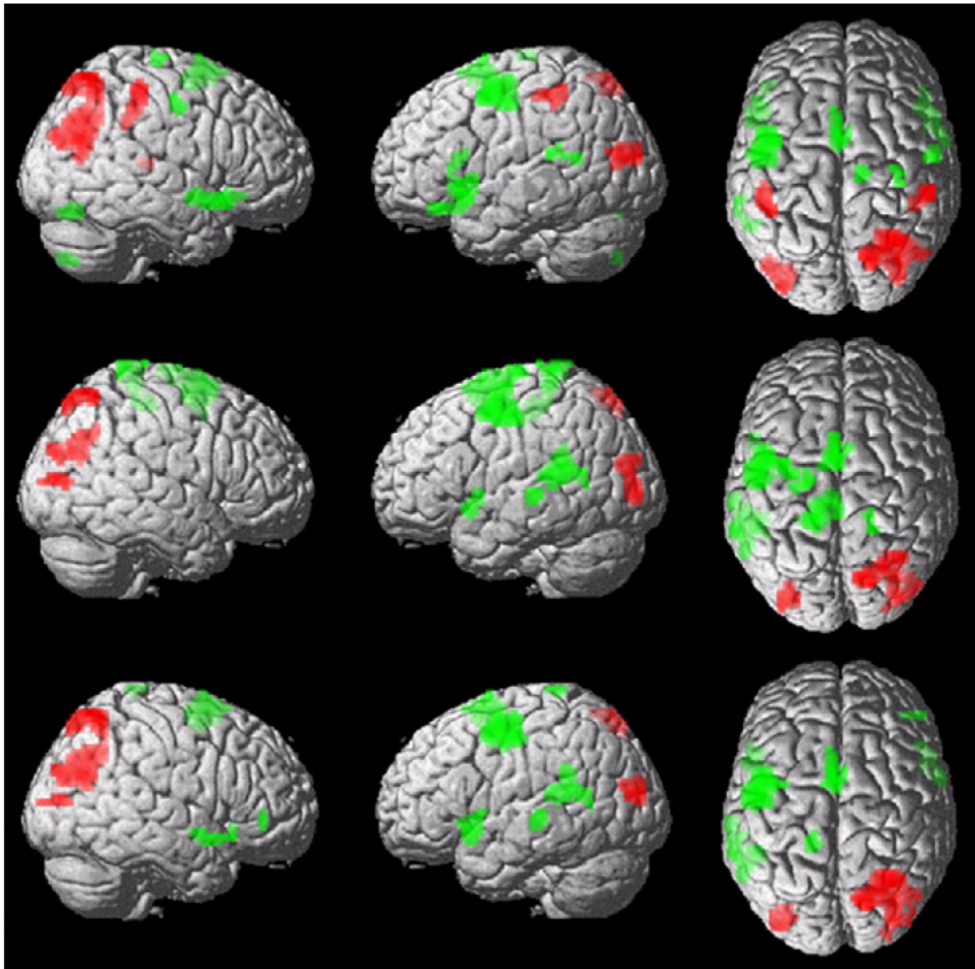


Fig. 3. The contrasts of brain activations between addition and multiplication. Top panel is for large problems; the middle for small problems, and the bottom for the combination of the two types of problems. Red marks more activation for addition, and green for multiplication. Statistical parameters: $P<0.005$ uncorrected, with spatial extent $k>15$ voxels.

and superior and middle occipital gyrus. In contrast, multiplication had more activation than addition in the left supplementary motor area, left precentral gyrus, and left posterior and anterior superior temporal gyrus.

Fig. 4 shows direct activation contrasts between large and small problems. Large problems, regardless of addition and multiplication, had more activation in supplementary motor area, bilateral precentral gyrus, insula, and left intraparietal sulcus. Small problems had more activation at the left angular gyrus, left superior frontal gyrus and left superior medial frontal gyrus. The brain patterns for the problem-size effect were obviously different from those for the operation effect.

Anatomical ROI analysis was conducted to further validate the operation and problem-size effects. As mentioned in the Introduction, the anatomical regions responsible for visuospatial processing and language processing were selected (see Fig. 5). The activation intensity was entered into two-factor repeated measures ANOVA with operation (addition vs. multiplication) and problem size (small vs. large size) as within-subject factors. Compared to multiplication, addition had more activation in left superior occipital lobule, $F(1,19)=4.74$, $MSe=0.017$, $P<0.05$; right superior and middle occipital gyrus, $F(1,19)=11.28$, $MSe=0.036$, $P<0.005$; $F(1,19)=$

8.65, $MSe=0.022$, $P<0.01$; and (marginally) right superior and inferior parietal lobules, $F(1,19)=3.70$, $MSe=0.045$, $0.05<P<0.10$; $F(1,19)=3.23$, $MSe=0.024$, $0.05<P<0.10$. On the other hand, multiplication had more activation in the left precentral gyrus, $F(1,19)=8.09$, $MSe=0.017$, $P<0.01$; supplementary motor area, $F(1,19)=8.54$, $MSe=0.019$, $P<0.01$; superior temporal gyrus, $F(1,19)=16.50$, $MSe=0.007$, $P<0.001$; and in superior temporal gyrus (pole), $F(1,19)=11.28$, $MSe=0.036$, $P<0.005$.

Large problems, regardless of operation type, had more activation at the left precentral gyrus, $F(1,19)=25.65$, $MSe=0.009$, $P<0.001$, but not at the right precentral gyrus. The problem-size effect was also found at bilateral insula, $F(1,19)=14.50$, $MSe=0.004$, $P<0.001$, for the left insula, and $F(1,19)=27.71$, $MSe=0.007$, $P<0.001$, for the right insula; bilateral inferior frontal gyrus, $F(1,19)=21.89$, $MSe=0.007$, $P<0.001$; $F(1,19)=9.83$, $MSe=0.018$, $P<0.01$; bilateral supplementary motor area, $F(1,19)=12.26$, $MSe=0.014$, $P<0.05$; $F(1,19)=7.44$, $MSe=0.012$, $P<0.05$; and bilateral inferior frontal gyrus, $F(1,19)=22.01$, $MSe=0.009$, $P<0.001$; $F(1,19)=10.84$, $MSe=0.017$, $P<0.005$. The left inferior occipital gyrus was activated more by large problems than by small problems, $F(1,19)=5.30$, $MSe=0.035$, $P<0.05$. The problem-size effect was

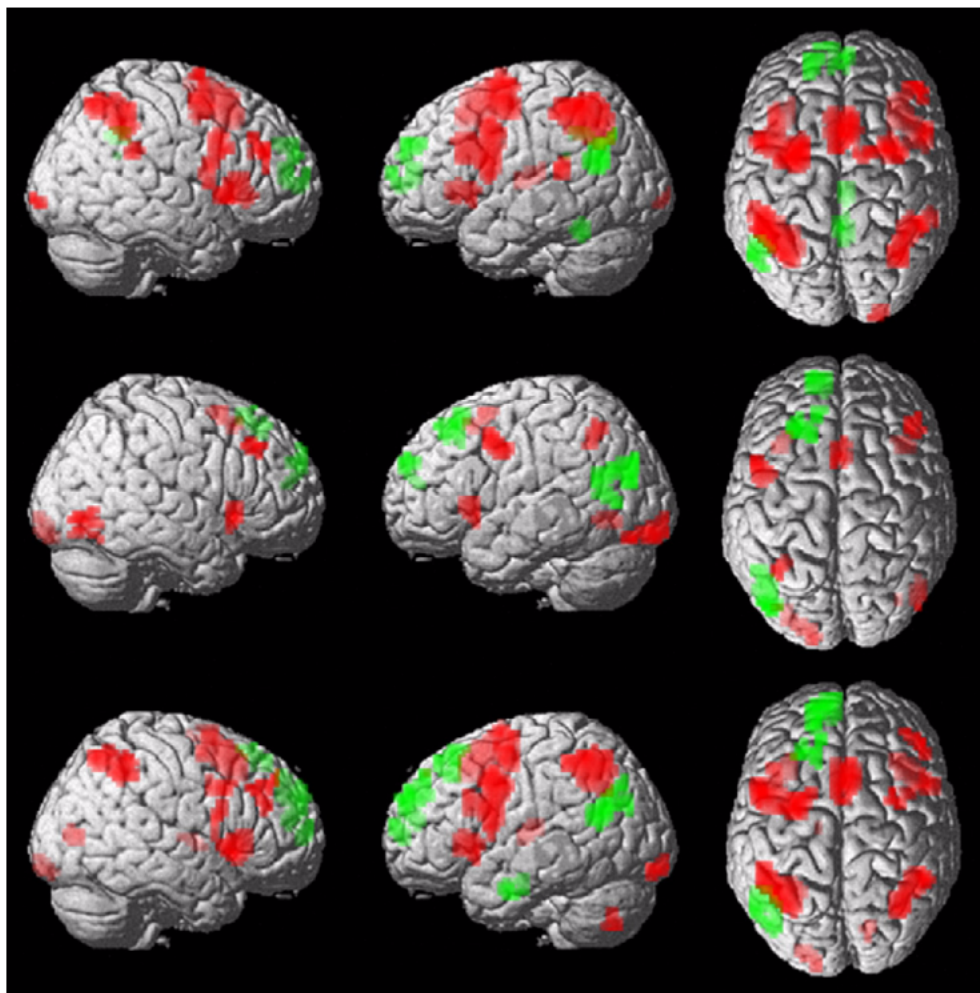


Fig. 4. The contrasts of brain activations between small and large problems. Top panel is for addition problems; the middle for multiplication problems, and the bottom for the combination of the two types of problems (regardless of operation). Red marks more activation for large problems, and green for small problems. Statistical parameters: $P<0.005$ uncorrected, with spatial extent $k>15$ voxels.

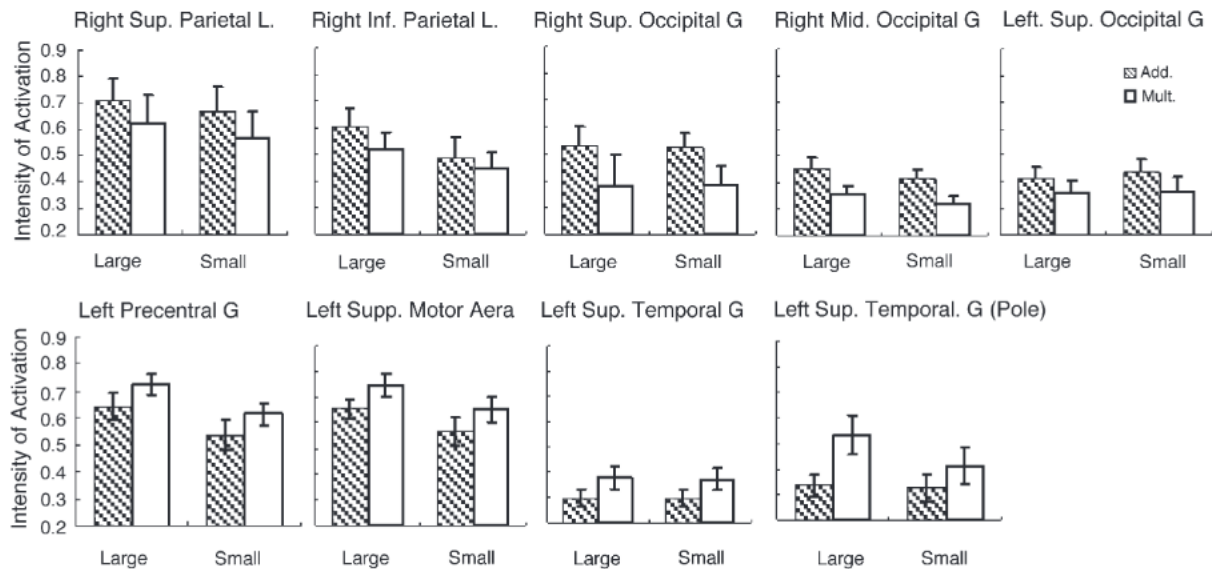


Fig. 5. The anatomical ROI analysis on intensity (effect size) of activation in parietal, occipital, motor and temporal regions.

found in the temporal lobe. As shown in Fig. 4, small problems had more activation at the left parietal–temporal–occipital association areas (including angular gyrus), superior frontal gyrus, and superior medial frontal gyrus. Actually, there was deactivation in these brain regions. Thus, the anatomical ROI analysis based on positive intensity values could not find any significant differences.

Anatomical ROI analysis was also conducted to test the laterality effect in the brain regions. Activation intensity was entered into two-factor repeated measures ANOVA with laterality (left vs. right) and operation (addition vs. multiplication) as within-subject factors. At the inferior and middle occipital gyri, left hemisphere had more activation than right hemisphere, $F(1,19)=7.24$, $MSe=0.12$, $P<0.05$, and $F(1,19)=9.21$, $MSe=0.05$, $P<0.01$. The main laterality effect was evident at the precentral gyri and supplementary motor area, $F(1,19)=15.25$, $MSe=0.12$, $P<0.005$, and $F(1,19)=15.05$, $MSe=0.06$, $P<0.001$. No laterality effect was found for other brain regions.

Discussion

The present study explored the brain organization for single-digit addition and multiplication. Addition and multiplication activated similar brain regions, including the supplementary motor area, intraparietal sulcus (inferior and superior parietal lobules), precentral gyrus, middle frontal gyrus, insula, and inferior occipital gyrus at the left and right hemispheres. We also found neural dissociation between addition and multiplication. Addition problems elicited more activation in the intraparietal sulcus (superior and inferior parietal lobules) and middle occipital gyri at the right hemisphere, and superior occipital gyrus at both hemispheres, whereas multiplication had more activation in precentral gyrus, supplementary motor areas, and posterior and anterior superior temporal gyrus at the left hemisphere. In terms of the problem-size effect, we found that large problems had more activation in the supplementary motor area, precentral gyrus, and insula at both hemispheres, and intraparietal sulcus at the left hemisphere. Small problems had

more activation in the left parietal–temporal–occipital association area (including angular gyrus), superior frontal gyrus and medial superior frontal gyrus at the left hemisphere. These findings support our hypothesis that the retrieval of addition facts has a greater reliance on visuospatial processing, and the retrieval of multiplication facts has a greater reliance on verbal processing.

Mental processes in arithmetic equation verification

Based on the behavioral data, our subjects (Chinese college students) typically solved addition and multiplication within about 700 ms after the presentation of stimuli. Within that period for the verification of an arithmetic equation, subjects had to go through the following processes: encoding two visually presented digits, retrieving or calculating the answer, matching the answer with the proposed solution, and finally pressing the left or the right key to make a behavioral judgment. Chinese adults have been reported to use mainly the direct retrieval strategy for multiplication facts (e.g., Geary, 1996), and only occasionally to use non-retrieval procedures (e.g., repeated addition, $2 \times 4 = 4 + 4$; number series, $3 \times 5 = 5, 10, 15$; derived facts, $6 \times 7 = [6 \times 6] + 6$). It should be noted, however, in the arithmetic equation verification, subjects could sometimes use another strategy—plausibility judgment (e.g., Campbell and Tarling, 1996; Lemaire and Fayol, 1995). That is, instead of retrieving the answers to the arithmetic problems, subjects could assess whether an equation was implausible (e.g., implausible equations include those with answers smaller than the operands in addition and multiplication, those with answers that are not in the table of number facts). To minimize this potential problem, we chose false answers for the arithmetic equations that were very close to the true answers (see Methods section). We also used more true equations than false equations to further reduce plausibility judgment. In sum, by refining the design of arithmetic problems, we were able to minimize the effects of some known confounding factors (i.e., differing difficulty levels of problems for different operations, a lack of on-line behavioral data, and plausibility judgment for the verification paradigm). Therefore, our imaging results should

reflect true differences in the retrieval of arithmetic facts between addition and multiplication.

Visuospatial processing

Compared to multiplication, addition had more activation at the posterior regions of the brain. These brain regions included bilateral superior occipital gyrus, right superior and inferior parietal lobules, and right middle occipital gyrus. These brain regions in the parietal lobe (e.g., superior and inferior parietal lobules) and occipital lobe (e.g., superior and middle gyri) are known to be involved in visual perception, visual mental imagery, visuospatial working memory, and spatial attention (e.g. Corbetta et al., 1998, 2000; Diwadkar et al., 2000; Jordan et al., 2002; LaBar et al., 1999; Linden et al., 2003; Nystrom et al., 2000; Podzbenko et al., 2002; Postle et al., 2004; Roland and Gulyas, 1995; Thomas et al., 1999; Vingerhoets et al., 2002; Zurowski et al., 2002). Thus, the greater activation for addition than for multiplication in these regions could be reasonably interpreted as a result of a greater reliance on visuospatial processing during the retrieval of addition facts. As mentioned in the Introduction, addition facts tended to be represented in the visual Arabic format due to early acquisition experiences. The mental imagery of number sequences involved in addition is believed to activate the visuospatial processing.

We should note that the posterior part of the brain (e.g., IPS) is also sensitive to working memory load. For example, previous research has shown that IPS is typically activated when there are increased demands on working memory (Jonides et al., 1997, 1998; Klingberg et al., 1997; Kong et al., 2005). The problem-size effect in IPS in the present study was likely due to the differences in problem difficulty. However, because addition and multiplication in the present study did not differ in difficulty level, working memory load would not have accounted for the operation effect we found in the IPS. Therefore, this effect was likely due to arithmetic operations' differences in visuospatial processing.

It is worth mentioning that mental representations of numbers have been found to involve the "mental number line." Such a number line has obvious spatial properties as shown by the SNARC effect (i.e., subjects respond more quickly to smaller numbers with the left hand, and more quickly to larger numbers with the right hand on number-processing tasks) (Dehaene et al., 1993). Future research should test the dissociation between addition and multiplication by comparing the magnitude of the SNARC effect for addition vs. multiplication.

Verbal processing

Relative to addition, multiplication had more activation in the precentral gyrus, supplementary motor area, and posterior and anterior superior temporal gyrus at the left hemisphere. The left posterior temporal gyrus corresponds to Wernicke's area. These brain regions are associated with verbal production, such as, planning and executing of throat and tongue movement (e.g., Cowell et al., 2000; Hanakawa et al., 2003; Hickok et al., 2000; Paus et al., 1996; Riecker et al., 2002; Wildgruber et al., 1996; Zhou et al., 2006b; Ziegler et al., 1997). Previous research has also demonstrated significant left lateralization in the precentral gyrus for covert speech (Bohland and Guenther, 2006; Riecker et al., 2002; Wildgruber et al., 1996). Also consistent with our conclusion is the finding of greater left lateralization for

multiplication than for addition at the left precentral gyrus, which suggested more verbal processing for the former. These findings of more activation in verbal areas by multiplication agree with previous neuropsychological findings (e.g., Delazer and Benke, 1997; Lemer et al., 2003, van Harskamp et al., 2002) and an fMRI study (Richard et al., 2000). We found differences between brain activations for addition and multiplication only at the left side of brain, which also generally consistent with the result from one of our previous ERP studies that multiplication generated greater negative potentials at the electrodes over the left anterior brain (Zhou et al., 2006a).

However, we did not find the operation effect (i.e., greater activation for multiplication than for addition) in the left inferior frontal gyrus and insula (corresponding to Broca's area). One of plausible explanations is that the inferior frontal gyrus might be more sensitive to the general task difficulty rather than the demand on verbal processing. Thus, we found the problem-size effect in the left inferior frontal gyrus and insula. This interpretation was further supported by the result from our previous fMRI study in which backward recitation of number and alphabetic sequences elicited more activation in the left inferior frontal gyrus than did forward recitation (Zhou et al., 2006b). Backward recitation was more difficult than forward recitation, although forward recitation had more verbal production.

The angular gyrus, more precisely the parietal-temporal-occipital association area in the present study, is believed to be associated with verbal codes in number processing (see a review by Dehaene et al., 2003). For example, the angular gyrus could be activated by single-digit multiplication relative to number comparison or subtraction (Chochon et al., 1999; Lee, 2000), by exact addition relative to approximation (Dehaene et al., 1999), by small-size single-digit addition to large-size one (Stanescu-Cosson et al., 2000), and by arithmetic problems previously trained relative to arithmetic problems not trained (Delazer et al., 2003, 2004, 2005). Relative to fixation and addition, multiplication in the present study did not significantly activate the angular gyrus. This result was consistent with the finding that forward recitation of numerical and alphabetic sequences relative to fixation or to backward recitation did not have significant activation in the angular gyrus (Zhou et al., 2006b). Some neuropsychological studies have found that injuries to the angular gyrus or even the removal of these brain regions did not affect subjects' language production or multiplication (e.g., Delazer and Benke, 1997; van Harskamp et al., 2002; Tucha et al., 1997). Additionally, we indeed found the reversed problem-size effect in the left angular gyrus for addition and multiplication, as found by Stanescu-Cosson et al.'s (2000) study on addition. The reversed problem-size effect was also present in the left superior frontal gyrus and left medial superior frontal gyrus, also consistent with Stanescu-Cosson et al.'s finding. This reversed problem-size effect is difficult to interpret in terms of verbal processing because Stanescu-Cosson et al. also found the same effect for approximate addition, which is presumably performed via non-verbal quantity codes of numbers. Further studies are required to clarify the precise role of angular gyrus and related areas in numerical and non-numerical cognition.

Acquisition of arithmetic facts

As mentioned in the Introduction, two different types of strategies (i.e., procedural strategies and verbal memory strategy) are taught in school to learn arithmetic facts. In China, the

differential use of these two strategies for different arithmetic facts is especially clear. For addition and subtraction, varieties of procedures (e.g., transforming “ $4+7=3+7+1=11$ ”) were used, but for multiplication, Chinese children are required to use exclusively the rote verbal strategy (Zhou and Dong, 2003). Multiplication facts (with only smaller-operand-first entries) are organized as pithy mnemonic formulas, expressed with simple Chinese number words (一一得一, means “one one is one”). Chinese children start to memorize the multiplication table during the second semester of the first grade or the first semester of the second grade (as compared to the third grade in the U.S.). It takes about 4 months for students to learn all multiplication facts.

Because of this emphasis on rote memory, Chinese children and adults are very efficient in reciting multiplication facts. For example, previous studies by Campbell and Xue (2001) and LeFevre and Liu (1997) found that, although a substantial number of American and Canadian adults (up to 29%) used procedural strategies to solve single-digit addition and multiplication problems, Chinese subjects rarely used procedural strategies for either addition or multiplication (e.g., Campbell and Xue, 2001; Geary, 1996; LeFevre and Liu, 1997). Instead, they use direct retrieval for both tasks (perhaps due to the relative simplicity of addition and the proficient recitation of the multiplication table). Consequently, as shown in the present and other studies (e.g., Campbell et al., 1999; Zhou and Dong, 2003), Chinese subjects showed similar reaction times for single-digit addition and multiplication.

Summary

Previous neuropsychological studies have shown that injuries in the posterior part of the brain (e.g., intraparietal cortex) affect addition more than multiplication. In contrast, lesions in the left perisylvian language region result in more difficulty in single-digit multiplication than in addition and subtraction (e.g., Cohen et al., 2000; Dehaene and Cohen, 1997; Delazer and Benke, 1997; Lemer et al., 2003; Pesenti et al., 1994; van Harskamp et al., 2002, 2005). A recent ERP study (Zhou et al., 2006a) also provided evidence of neural dissociation between addition and multiplication (with the latter possibly relying more on verbal processing). Relying on the better spatial resolution of fMRI and overcoming several weaknesses of the previous fMRI studies on this topic (see Introduction), the present fMRI study of Chinese adults' simple arithmetic showed that single-digit addition and multiplication elicited differential brain activations. Our results support the notion that the retrieval of addition facts has greater reliance on visuospatial processing, and the retrieval of multiplication facts on verbal processing. Such differences are likely to have resulted from different acquisition experiences of simple arithmetic facts.

Acknowledgments

This study was supported by the National 973 Project (2003CB716803), the Natural Science Fund for Distinguished Young Scholars of China (30625024), the programs for NCET in University (04-0866), SFRDP (20060610073) and SRF from ROCS from SEM (2005385-10-5), the Distinguished Young Scholars of Sichuan (05ZQ026-031), the (UK) Royal Society International Joint Project with NSFC, and the National Pandeng Project (95).

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