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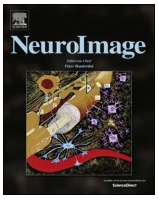

The neural circuits for arithmetic principles

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ABSTRACT

Arithmetic principles are the regularities underlying arithmetic computation. Little is known about how the brain supports the processing of arithmetic principles. The current fMRI study examined neural activation and functional connectivity during the processing of verbalized arithmetic principles, as compared to numerical computation and general language processing. As expected, arithmetic principles elicited stronger activation in bilateral horizontal intraparietal sulcus and right supramarginal gyrus than did language processing, and stronger activation in left middle temporal lobe and left orbital part of inferior frontal gyrus than did computation. In contrast, computation elicited greater activation in bilateral horizontal intraparietal sulcus (extending to posterior superior parietal lobule) than did either arithmetic principles or language processing. Functional connectivity analysis with the psychophysiological interaction approach (PPI) showed that left temporal-parietal (MTG-HIPS) connectivity was stronger during the processing of arithmetic principle and language than during computation, whereas parietal-occipital connectivities were stronger during computation than during the processing of arithmetic principles and language. Additionally, the left fronto-parietal (orbital IFG-HIPS) connectivity was stronger during the processing of arithmetic principles than during computation. The results suggest that verbalized arithmetic principles engage a neural network that overlaps but is distinct from the networks for computation and language processing.

1. Introduction

Arithmetic calculation has three major cognitive components: conceptual knowledge, arithmetic procedural knowledge, and arithmetic facts (Sokol and McCloskey, 1991). The core of arithmetic conceptual knowledge is arithmetic principles, which are the fundamental laws or regularities underlying arithmetic (Prather and Alibali, 2009). Examples of arithmetic laws include the commutative law (3+2=2+3, or 3×2=2×3) and the associative law (e.g., 2×3+3×3=(2+3)×3). Other arithmetic principles include the inverse relation of operations (e.g., 3+4-4=3, 3×4÷4=3), 0- or 1-based computation (e.g., n+0=n, n×1=n, n÷1=n).

Arithmetic principles have been extensively investigated in behavioral studies (e.g., Canobi, 2005; Prather et al., 2009; Rasmussen et al., 2003; Robinson et al., 2006). Researchers have found that even preschoolers can understand and apply arithmetic principles (e.g., Klein and Bisanz, 2000; Rasmussen et al., 2003; Vilette, 2002). For example, Klein et al. (2000) used a nonverbal procedure to present both inversion (e.g., 3+4−4) and standard problems (e.g., 3+5−4) to 4-year-olds. It was found that solutions were faster for inversion than for standard problems. Similar evidence was found among 3-year-old children (Sherman and Bisanz, 2007). However, older children are more likely than younger children apply arithmetic principles to solving arithmetic problems (Canobi, 2005; Robinson et al., 2006). For example, Robinson et al. (2006) reported that the inversion strategy was used significantly more often in grade 8 than in grade 6 when solving addition/subtraction inversion problems and multiplication/division inversion problems. Canobi (2005) also found that when solving computation problems, the percentages of 5- to 7-year-old children who use the inversion strategy increased with age.

A number of behavioral studies have found that participants' knowledge of arithmetic principles is not associated with their performance on computation problems (e.g., Bryant et al., 1999; Rasmussen et al., 2003; Sherman et al., 2007). For example, Rasmussen et al. (2003) found that children's ability to add 9's was not related to their use of the inversion principle for problems involving "+9 − 9". One study (Canobi et al., 1998) nonetheless found that the use of relational properties in computation such as additive composition, commutativ-

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ity, and associativity principles was related to speed and accuracy in solving unrelated problems. These results suggest that the understanding of arithmetic principles and the computational arithmetic ability are two related but independent cognitive components. Consistent with this perspective, neuropsychological studies have shown that these two components can be selectively impaired (e.g., Cappelletti et al., 2001, 2005; Dehaene & Cohen, 1997; Hittmair-Delazer et al., 1994; 1995; McCloskey et al., 1991; Pesenti et al., 2000; Sokol et al., 1991; Warrington, 1982). Specifically, simple computation is impaired but the understanding of arithmetic principles is not, when there are damages to brain regions such as the basal ganglia (patient BE, Hittmair-Delazer et al., 1994), left parietal-occipital cortex (patient DRC, Warrington, 1982), left temporal lobe (patient IH, Cappelletti et al., 2001, 2005), entire white matter (patient DA, Hittmair-Delazer et al., 1995), bilateral temporoparietal areas (patient DF, Pesenti et al., 2000), or right inferior parietal lobule (patient MAR, Deheane & Cohen, 1997). For example, Hittmair-Delazer et al. (1994) reported having a stroke affecting left basal ganglia, patient BE showed impaired simple computation (e.g., 18÷6, 4×9) but could apply arithmetic principles to derive correct answers (e.g., 4×9=9×2+9×2=36).

Researchers have also reported cases for which the processing of arithmetic principles was selectively impaired but arithmetic computation was relatively intact (Delazer and Benke 1997; Sokol et al., 1991). After the surgical removal of a left parietal tumor, Patient JG (Delazer et al., 1997) was reported to have completely lost her arithmetic conceptual knowledge, including basic concepts of the four operations and arithmetic principles (i.e., commutativity law, inverse principle relation), but preserved some ability to solve simple computation problems (multiplications and some additions and subtractions). The patient was unable to answer questions such as “If 13+9 is 22, what is 9+13?”, “if 13+9=22, what is 22−9?”, which required the application of the commutative law and inverse principle, respectively. After suffering from left frontal contusion, Patient GE also showed selective impairment in solving arithmetic problems involving 0 (0-based computational rule) (Sokol et al., 1991). Specifically, for the 0×n problems, he was 0% correct (0/390), but for problems with two non-0 operands, his error rate was 8.8% (156/1763). These studies suggest that the focal brain lesions in left parietal cortex and left frontal cortex can lead to impairment of the understanding of arithmetic principles.

Although the neuropsychological studies reviewed above showed that arithmetic principles’ processing can be dissociated from numerical processing, these studies lacked spatial resolution to pinpoint the neural basis of arithmetic principles. Thus far, there has been only one neuroimaging study of arithmetic principles (Jost et al., 2009). Jost et al. (2009) investigated the neural activation of 0-based problems in multiplication and found that the 0-based multiplication problems solved by rule application elicited greater activation at left caudate nucleus, right inferior frontal gyrus, bilateral middle temporal gyrus, left angular gyrus, and right cuneus extending to the precuneus than those solved by fact retrieval (e.g., 7×8). The current study extended Jost et al. work by including arithmetic principles beyond the 0-based rule in multiplication.

To understand the neural basis of the processing of arithmetic principles, we also need to dissociate it from the processing of general semantic knowledge (e.g., Cappelletti et al., 2012; Julien et al., 2008). Several neuropsychological studies reported dissociation between arithmetic principles and general semantic knowledge (Cappelletti et al., 2005, 2012; Julien et al., 2008; Julien et al., 2010; Sokol et al., 1991; Zamarian et al., 2006). For example, semantic dementia patient IH was reported to have with well-preserved arithmetic conceptual knowledge (including arithmetic principles and operations), but failed in general semantic tasks such as picture naming and word classification (Cappelletti et al., 2005). Semantic dementia patient SG performed well in addition/multiplication arithmetic principles, as well as definitions of operation tasks, but was partially impaired in a comprehensive test of verbal semantic knowledge assessing living and non-living categories (providing 98 incorrect answers out of 480 questions) (Zamarian et al., 2006). Nevertheless, there exists evidence suggesting that arithmetic conceptual knowledge is not totally separated from general semantic knowledge (Cheng et al., 2013; Julien et al., 2008; Julien et al., 2010). For instance, SD patients made procedural errors in a multi-digit calculation task, which suggested a progressive degradation in conceptual understanding of arithmetic (Julien et al., 2008). Patients with severe semantic dementia showed more impairment in judging quantifiers’ (e.g., “many”, “none”) semantic relatedness than the patients with mild semantic dementia, which indicated that quantifier processing is associated with general semantic processing and can be impaired due to temporal lobe damage (Cheng et al., 2013). These observations suggested that the temporal lobes might play an important role in arithmetic conceptual knowledge.

The goal of the current neuroimaging study was to investigate how different brain regions jointly subserve the processing of arithmetic principles as compared to numerical computation and general language processing. Two hypotheses were tested. The first hypothesis is that arithmetic principles involve visualization (or mental models) and hence should activate the bilateral horizontal segments of the intraparietal sulcus (IPS). The mental models integrate the relations of mathematical concepts involved in arithmetic principles. They involve mental imageries of mathematical expressions with spatial information (e.g., “Exchanging the position of operands in addition does not change the result”, “For division, the position of dividend and divider should not be exchanged”). The processing of such spatial information should activate the IPS (e.g., Boccia et al., 2014; Moore and Armstrong, 2003; Szczepanski et al., 2010; Wolbers and Hegarty, 2010).

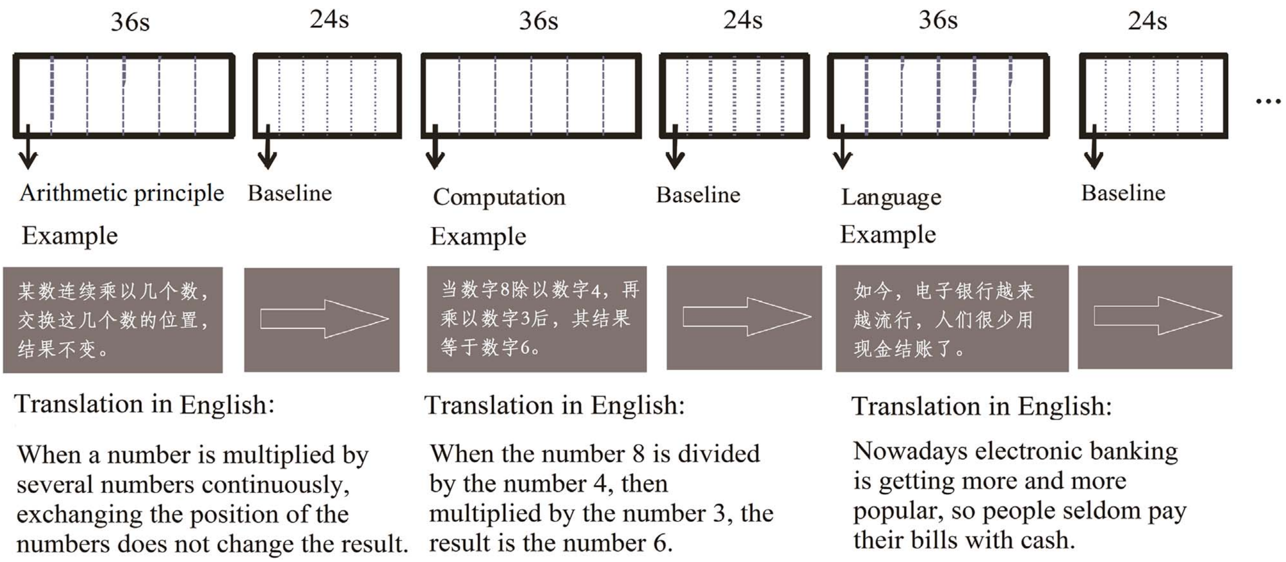
The second hypothesis is that arithmetic principles are a type of conceptual knowledge and are hence processed in the semantic information processing areas including the left middle temporal gyrus (MTG) and left prefrontal cortex. Left MTG is an important semantic hub (e.g., Binder et al., 2009; Wu et al., 2012; Kuperberg et al., 2008). It has been related to mathematical concept processing and quantity processing (Wei et al., 2014; Zhang et al., 2012). Furthermore, damage to left temporal lobe was associated with progressive degradation in conceptual understanding of arithmetic (Julien et al., 2008; Julien et al., 2010). The orbital part of the IFG has also been reported to be responsible for semantic processing (e.g., Kuperberg et al., 2008; Wagner et al., 2001) and specific mathematical semantic processing (Zhang et al., 2012; Wei et al., 2014). For example, Wagner et al. (2001) found that the orbital part of left IFG was involved in controlled semantic retrieval. Finally, left frontal lesion has been linked to impairment in the understanding of arithmetic principles (Delazer and Butterworth, 1997; Sokol et al., 1991).

In the current study, we used sentences rather than symbols to describe arithmetic principles in order to match the format of general semantic processing. For example, the law of additive communativity was expressed as “Exchanging the position of two operands in addition does not change their sum”, rather than its symbolic expression of “a +b=b+a”. A verification paradigm was used for all three tasks. Participants were asked whether a particular statement was correct or incorrect. To match the verbal processing involved in arithmetic principles, the numerical computation verification task was also presented in verbal context (e.g., “When number 8 is first divided by number 4, then multiplied by number 3, the final result is number 12”). For the general language processing task, participants were asked to judge whether descriptions of everyday life were true or not (e.g., “When school starts, new students come one after another and register”).

2. Materials and methods

2.1. Participants

Thirty right-handed undergraduates (15 male; aged 19.1–24.6



某数连续乘以几个数，交换这几个数的位置，结果不变。

When a number is multiplied by several numbers continuously, exchanging the position of the numbers does not change the result.

当数字8除以数字4，再乘以数字3后，其结果等于数字6。

When the number 8 is divided by the number 4, then multiplied by the number 3, the result is the number 6.

如今，电子银行越来越流行，人们很少用现金结账了。

Nowadays electronic banking is getting more and more popular, so people seldom pay their bills with cash.

Fig. 1. Experimental procedure and sample trials. Each run lasted 6 minutes. It contained six experimental blocks (two blocks of six trials for each type of materials) and six blocks of baseline. Each task block lasted for 36 s and each baseline block lasts 24 s. The order of the blocks was arranged in the Latin square design among runs across participants.

years old, and mean age=22.0 years old) were recruited from Southwest University and Peking University, China. These participants reported having no previous history of neurological disorders or head injury. Procedures of the experiment were fully explained to all participants before they gave informed consent. This study was approved by the Institutional Review Board (IRB) of Southwest University and Peking University.

2.2. Materials

The present study used three conditions (arithmetic principles, computation, and general language processing) (See Fig. 1). There were 24 trials/sentences for each condition (see Appendix A). The average length of sentence was controlled to be same among the three types of material. Half of the statements were true and the other half false.

For each task, a Chinese sentence appeared on the screen, which described an arithmetic principle, a computation problem, or a scene in daily life. They were presented in white against a black background (the RGB value was 0, 0, 0).

Stimulus presentation and recording of behavioral data were programmed using E-prime 1.1. Stimuli were projected onto a translucent screen placed at the back of the magnet bore. Participants viewed the screen through a mirror mounted on the head coil, at a distance of ~30 cm from the eyes.

2.3. Procedure

Before scanning, participants received a training session to ensure they understood the instruction of this experiment. After that, participants were required to complete the experimental tasks. The scanning session lasted about 12 min and was organized into two runs, each consisting of six experimental blocks (two 6-trial blocks for each condition) and six baseline blocks (with an arrow at the center of the screen). The balanced Latin square design (Bradley, 1958) was used to counterbalance the order effect of the three conditions. Each run in the experiment lasted 6 min. Each experimental block lasted for 36 s, and the baseline block for 24 s (see the experimental procedure in Fig. 1). There was a 1–2 min rest after each run. In experimental blocks, the response hand was counterbalanced across participants. In the baseline block, participants responded to a leftward or rightward arrow, with left or right index finger, respectively. Both accuracy and speed were emphasized.

2.4. fMRI data acquisition

Imaging was performed on a Siemens (Munich, Germany) 3 T Trio scanner using a standard eight-channel head coil. After automatic shimming of the magnetic field, three-dimensional (3D) high-resolution T1 anatomical images were acquired for coregistration with the functional images. Next, functional volumes were acquired using a multiple slice T2*-weighted echo planar imaging (EPI) sequence with the following parameters: repetition time=2000 ms; echo time =30 ms; flip angle=90°; matrix dimensions=64×64; field of view=200 mm; slice thickness=4 mm. Thirty-two slices covered the entire brain. Twenty participants were scanned at Southwest University's Brain Imaging Center and ten participants were scanned at Peking University's Brain Imaging Center.

2.5. Analysis of the fMRI data

MRI data were analyzed using the SPM12 software (Wellcome Department of Imaging Neurosciences, University College London, UK, http://www.fil.ion.ucl.ac.uk/spm). All volumes were realigned to the first volume and spatially normalized to a common value in order to correct for whole brain differences over time. Images were then smoothed using an isotropic Gaussian kernel of 4 mm and high-pass filtered at a cut-off of 128 s. The functional images were normalized for each individual with a spatial resolution of $3\times3\times3$ mm^3.

2.5.1. Univariate analysis

We first calculated parameter-estimated images for individual participants across the whole brain. Then we conducted group analyses with random effects by applying one-way ANOVA (analysis of variance) in SPM12 on the brain activation maps of all participants, with condition as the independent variable. We first calculated the brain activation for each condition relative to fixation and then did contrasts between conditions. A threshold of $p < .001$, uncorrected, and voxel size of greater than 10 were considered as statistically significant in the univariate analyses. This is an acceptable primary threshold (Carter et al., 2016; Woo et al., 2014) and has thus often been used in previous fMRI studies (e.g., Berteletti et al., 2015; Holloway et al., 2013). In addition, we used cluster-based false discovery rates correction for multiple comparisons at the $p < .05$ threshold.

In order to see whether the effects observed applied to individual items, we also conducted the item-wise analysis, which has been used

Table 1
Loci showing significant univariate activations of the three types of materials.

Brain region	BA	Coordinates (X, Y, Z)			Vol.	T
Arithmetic principle						
Occipital cortex						
R. Inferior occipital gyrus	19	36	−87	−6	4574	12.33
(hOc4lp, hOc4v, hOc1)	17	18	−99	−3		
	18	−15	−96	−6		
R. Superior occipital gyrus	7	30	−63	42	170	7.23
	19	33	−66	24		
Frontal cortex						
L. Inferior frontal gyrus (opercular)	44	−39	9	30	2229	10.44
	32	−3	12	51		
	6	−42	3	42		
R. Insula	47	30	27	−3	121	8.72
	48	42	15	12		
R. Precental gyrus	6	36	−3	51	52	5.14
	6	30	−6	45		
		21	0	45		
R. Middle frontal gyrus		54	36	24	26	5.09
		51	36	33		
R. Inferior frontal gyrus (triangular)(45)	48	45	27	24	65	4.37
	48	45	15	27		
Temporal cortex						
L. Hippocampus (Thal)	37	−24	−30	−3	71	8.75
R. Hippocampus (Thal)	37	27	−27	−3	41	5.93
		30	−33	6		
L. Parahippocampal gyrus		−6	−24	−15	23	4.73
Subcortical area and cerebellum						
R. Putamen		21	−6	12	33	4.98
	48	24	3	21		
Computation						
Occipital cortex						
R. Lingual gyrus	18	18	−96	−6	6217	12.79
(hOc3d, hOc3v, hOc1, hOc4lp, hOc4v, hOc2)	17	−18	−99	−3		
	19	36	−87	−6		
Frontal cortex						
L. Inferior frontal gyrus (opercular) (44, Thal)	44	−48	12	27	2003	11.32
	48	−30	24	6		
		−24	−27	−6		
L. Supplementary motor area	6	−3	9	54	428	10.63
	32	9	15	48		
	6	−6	0	63		
R. Insula (45)	47	33	21	−3	604	9.41
	48	45	27	24		
	48	42	15	12		
Subcortical area and cerebellum						
R. Thalamus (Thal)		18	−9	−3	503	7.96
		24	−27	−6		
		21	−3	15		
L. Inferior Cerebellum		−30	−66	−45	81	5.06
		−33	−57	−48		
Language						
Occipital cortex						
L. Inferior occipital gyrus	18	−30	−93	−9	3916	13.38
(hOc3v, hOc4lp, hOc4v, hOc1)	17	18	−99	−3		
		12	−72	−24		
L. Superior occipital gyrus (hIP3)	19	−24	−66	33	102	5.46
	7	−27	−51	45		
	7	−21	−66	45		
Frontal cortex						
L. Supplementary motor area	6	−3	9	54	358	8.42
	32	6	15	51		
	6	−6	3	63		
R. Inferior frontal gyrus (opercular)	44	54	24	33	234	6.37
	45	57	30	27		
	48	45	24	24		
R. Inferior frontal gyrus (orbital)		33	24	−6	89	5.92
	48	39	18	3		
	48	33	18	15		
L. Superior medial frontal gyrus		−6	57	45	18	5.78
	9	−6	51	51		
	9	−9	60	36		
Temporal cortex						
L. Hippocampus (Thal)	27	−21	−30	−6	1995	10.42
	6	−42	0	42		
		−21	3	6		
R. Hippocampus (Thal)	37	27	−27	−3	58	8.75
		24	−15	−6		
R. Parahippocampal gyrus	35	9	−21	−18	25	5.86
Subcortical area and cerebellum						
R. Inferior Cerebellum		21	−36	−45	43	6.37
		−3	−30	−36		
		9	−36	−36		
L. Superior Cerebellum		−9	−30	−15	61	6.07
		−9	−18	−15		
		−3	−36	−3		
R. Thalamus (Thal)		15	−6	−3	64	5.16
		18	0	15		
R. Inferior Cerebellum		3	−33	−51	17	5.04

Note: all the results reported above were significant at $p < .001$, uncorrected at the voxel level, and survived the cluster-level FDR correction at $p < .05$, voxel size > 10. The cytoarchitectonic areas were reported in the brackets, with reported probability higher than 15%, according to www.fz-juelich.de/ime/spm_anatomy_toolbox, the same to the following.

in previous studies (e.g., Bedny et al., 2007; Dodell-Feder et al., 2011).

2.5.2. ROI analysis

We defined ROIs based on results from previous meta-analyses of neural substrates for visuospatial processing and semantic/conceptual processing. For the visuospatial processing hypothesis, we expected that the bilateral horizontal segment of IPS would be activated to a greater extend by arithmetic principles than by general language comprehension. Based on a meta-analysis of visuospatial processing by Boccia et al. (2014), we defined the left horizontal segment of IPS (MNI coordinate [−34, −54, 46]) (hIP3 in cytoarchitectonic maps, according to www.fz-juelich.de/ime/spm_anatomy_toolbox, the same to the following) and right horizontal segment of IPS (MNI coordinate, [32, −56, 52]) (hIP3) as ROIs in the HIPS,

For the semantic/conceptual processing hypothesis, we expected that relative to computation, arithmetic principles would elicit greater activation in left middle temporal gyrus and the orbital part of left inferior frontal gyrus, which are responsible for conceptual knowledge. Based on the meta-analysis of fMRI studies of Chinese processing by Wu et al. (2012) and of fMRI studies of other languages by Binder et al. (2009), we chose 2 locations: left middle temporal gyrus (MNI coordinate [−58, −44, 0]), left orbital part of IFG (MNI coordinate [−46, 28, −4]). These two ROIs are responsible for the memory and retrieval of semantic information. Importantly, these two ROIs have been shown to be involved in the processing of conceptual knowledge in mathematics in an fMRI study on mathematical terminology (Zhang et al., 2012).

Each seed region was a sphere with a radius of 6 mm. These ROIs were used to compare the level of brain activation elicited by the three types of materials. The beta values in the ROIs in the con_*.img files were extracted with our in-house software for brain image data processing written in MATLAB (Math Works Inc., Natick, MA, USA). A repeated measures ANOVA on the beta values was performed to detect the effect of type of materials. Brain maps were visualized using the "bspmview" extension for SPM12 (http://www.bobspunt.com/bspmview/).

2.5.3. Multi-voxel pattern analysis

The goal of the multi-voxel pattern analysis (MVPA) was to examine differences in multivariate activation patterns related to the three

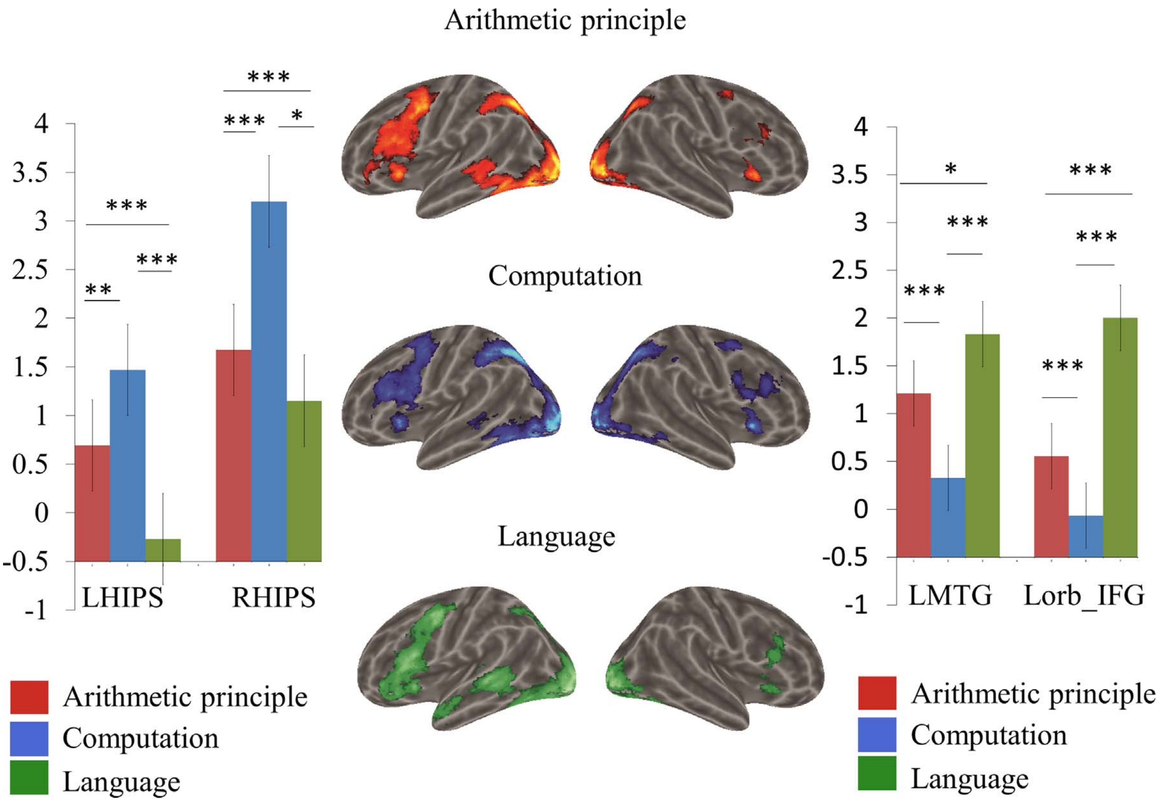


Fig. 2. Activation of each condition ($p < 0.001$, voxel size > 10, uncorrected) and ROI analysis.

experimental conditions. All fMRI data used for classification analyses were preprocessed (including normalization and smoothing) in the same way as described earlier for univariate analyses. We used the decoding toolbox (TDT) implemented in SPM12 (Hebart et al., 2014).The L2-norm support vector machine (SVM) was used for classification. Cross-validation was performed using the leave-one-run-out classification method. Activation patterns were assessed by first training a pattern classifier to discriminate between the three conditions based on the trials of one run. The classifier was then applied to the remaining trials of a given condition. Three separate classifiers were generated to test the brain activation patterns for the three possible pairs (between arithmetic principles and computation, between arithmetic principles and language, and between computation and language). We conducted searchlight analyses on preprocessed data in order to create maps of classification accuracy for each participant. These maps were then used in group-level analyses with one-sample t test.

2.5.4. Functional connectivity analysis

Functional connectivity between a seed region and the rest of the brain was tested using the psychophysiological interaction (PPI) analysis (Friston et al., 1997; Friston et al., 2007). It has been proposed that the left hemisphere plays a key role in both language processing and mental calculation (Chochon et al., 1999; Rivera, Reiss, Eckert, & Menon, 2006; Toga and Thompson, 2003). Seed regions were defined as 6mm spheres around the peak activations of left HIPS based on a conjunction analysis of the three conditions ($p < 0.001$, voxel size > 10, uncorrected). The BOLD time courses within the ROIs were extracted and were adjusted using the F-contrast of all the condition regressors. PPI models were then constructed and the following contrasts between conditions were conducted: arithmetic principles > computation, computation > arithmetic principles, arithmetic principles > language, language > arithmetic principles, computation > language, and language > computation. The PPI term was constructed by taking the product of the deconvolved physiological variable (the BOLD time series) and each psychological variable. The individual contrast images for the PPI parameter estimates were entered into a second-level random effects analysis. A threshold $p < 0.001$(uncorrected) and voxel size > 10 were also used in the above analyses comparing the conditions.

3. Results

3.1. Behavioral performance

The mean reaction times (RTs) were 3038ms, 3000ms, and 3039ms for the conditions of arithmetic principles, computation, and general language processing, respectively. The corresponding mean accuracy rates were 89%, 88%, and 87%. Repeated measures ANOVA showed that the main effect of stimulus type (condition) was not significant for either RTs, $F(1,29)=0.33$, $p > 0.05$, or the accuracy, $F(1, 29)=0.39$, $p > 0.05$.

3.2. Univariate analysis: subject-wise analysis

The brain activation data for each condition relative to baseline are displayed in Table 1. Arithmetic principles activated bilateral IPS (including bilateral horizontal segment of IPS and bilateral posterior superior parietal lobe), extending to right inferior and superior occipital cortex, as well as bilateral inferior frontal gyrus, right middle frontal gyrus, and bilateral hippocampus. Similar areas were activated by computation. In contrast, language processing activated a large number of areas including bilateral hippocampus and parahippocampal gyrus in left temporal lobe; right inferior frontal gyrus, left superior frontal gyrus in the prefrontal cortex; and left inferior and superior occipital cortex extending to left posterior superior parietal lobule (Fig. 2).

Table 2 and Fig. 3 show the task differences in brain activation based on direct contrasts. Arithmetic principles elicited greater activation than did computation in the left middle temporal gyrus and left

Table 2

Loci showing significant activations based on contrasts between the three conditions in subject-wise analysis.

Brain region	BA	Coordinates (X, Y, Z)			Vol.	T
Arithmetic principle > Computation						
Frontal cortex						
L. inferior frontal gyrus (Orbital)	47	−48	27	−3	67	5.14
	45	−54	24	6		
Temporal cortex						
L. Middle temporal gyrus	21	−57	−39	0	81	5.05
	21	−57	−27	−3		
	20	−60	−30	−12		
Arithmetic principle > Language						
Parietal cortex						
L. Precuneus	7	−9	−72	39	872	6.38
(hIP3, hIP1, 7PC, hIP2)	40	−39	−48	48		
	7	12	−66	36		
L. Posterior cingulate gyrus	23	−6	−36	27	110	5.84
	23	6	−33	27		
	23	−3	−27	30		
R. Anterior cingulate gyrus	32	12	30	24	73	5.35
	48	27	27	27		
	32	15	33	33		
R. Supramarginal gyrus	40	51	−36	42	81	5.28
(PF, PFm, hIP2, hIP3, hIP1, PFt, PF)	40	39	−39	42		
	40	57	−36	48		
Frontal cortex						
L. Inferior frontal gyrus (Triangular)	45	−39	33	12	269	5.53
	9	−33	36	36		
	45	−45	33	24		
L. Middle frontal gyrus		−24	6	48	105	5.45
	6	−18	9	60		
L. Precental gyrus		−27	0	33	23	5.41
	48	−33	−3	27		
	48	−27	3	24		
L. Precental gyrus (44)	6	−45	3	21	35	5.29
	48	−39	−3	21		
R. Middle frontal gyrus	45	45	45	18	57	5.22
	45	36	42	12		
	46	39	51	6		
R. Middle frontal gyrus	8	30	15	51	73	4.62
	8	27	15	66		
	6	21	3	57		
Computation > Arithmetic principle						
Parietal cortex						
R. Inferior parietal lobule (hIP3)	40	33	−48	48	682	7.75
	7	27	−69	39		
	39	36	−75	21		
Occipital cortex						
L. Middle occipital gyrus	19	−36	−81	27	526	7.02
	19	−27	−78	27		
	18	−24	−63	18		
Frontal cortex						
R. Inferior frontal gyrus (opercular)	44	51	9	12	105	7.34
	44	48	9	24		
	48	39	0	27		
R. Precental gyrus	6	−48	3	27	30	5.33
	44	−51	9	33		
R. Middle frontal gyrus	46	33	39	33	30	4.05
	46	39	33	36		
	46	39	42	27		
Computation > Language						
Parietal cortex						
L. Inferior parietal lobule	7	−27	−57	42	4169	9.41
(hIP3, PF, PFt, hIP1, hIP2)	40	−60	−33	42		
	40	−36	−48	45		
R. Median cingulate (33)	24	9	9	36	33	4.80
		9	3	30		
L. Median cingulate (5 Ci, 5 M)		−12	−33	39	32	4.74
		−6	−42	48		
		−15	−42	48		
Frontal cortex						
L. Precental gyrus (44)	6	−48	3	21	471	7.99
	8	−24	6	51		
	6	−27	−3	60		
L. Inferior frontal gyrus (triangular) (45)	45	−45	33	21	613	7.86
	48	−33	33	18		
	45	−36	45	18		
R. Middle frontal gyrus	45	42	45	21	722	7.62
	45	45	39	12		
	46	39	45	33		
R. Inferior frontal gyrus (opercular) (44)	6	51	6	24	115	7.47
	44	51	9	12		
	48	30	0	30		
Temporal cortex						
L. Inferior temporal gyrus (FG4)	30	−54	−51	−15	27	4.89
	37	−54	−60	−12		
Subcortical area and cerebellum						
L. Inferior Cerebellum		−39	−48	−42	22	6.28
		−36	−51	−54		
L. Inferior Cerebellum		−24	−75	−51	40	5.79
		−24	−63	−42		
L. Inferior Cerebellum		18	−75	−48	17	4.95
L. Superior Cerebellum		−27	−69	−24	25	4.76
		−24	−57	−33		
L. Inferior Cerebellum		−33	−66	−45	37	4.68
		−36	−72	−30		
		−36	−60	−39		
Language > Arithmetic principle						
Parietal cortex						
L. Precuneus	30	−9	−51	9	66	5.67
	30	−3	−57	15		
		−6	−48	0		
Frontal cortex						
L. Superior medial frontal gyrus	9	−3	51	33	552	7.49
	9	−6	45	48		
		−9	39	60		
L. Middle frontal gyrus (orbital)	11	−6	33	−12	184	5.45
(s32, s24, Fo1, Fo2)	11	−6	42	−15		
	11	0	33	−24		
Temporal cortex						
L. Middle temporal gyrus (TE3)	21	−60	−6	−15	1239	8.41
	20	−45	9	−39		
	20	−33	−27	−21		
R. middle temporal pole (Fo3)	38	48	18	−36	332	6.38
	47	30	36	−12		
	38	45	21	−24		
R. Parahippocampal gyrus	28	24	0	−24	113	5.76
(Amygdala (LB), FG3)	34	18	3	−15		
	20	33	−30	−21		
Subcortical area and cerebellum						
R. Superior Cerebellum		27	−84	−30	84	6.00
		18	−84	−39		
		12	−87	−33		
Language > Computation						
Frontal cortex						
L. Superior medial frontal gyrus	8	−6	42	51	573	8.22
		−9	39	60		
		−6	54	48		
R. Inferior frontal gyrus (orbital)(45, Fo3)	47	39	33	−15	89	6.18
	47	30	36	−12		
	47	48	30	−3		
Temporal cortex						
L. Middle temporal gyrus (TE3)	21	−60	−6	−15	1688	9.32
	38	−45	15	−24		
	20	−51	−9	−18		
R. middle temporal pole	20	36	18	−36	316	6.42
	38	45	15	−24		
	20	51	−12	−18		
R. Hippocampus	36	30	−6	−24	62	5.40
(CA1, Amygdala (LB), DG)	20	33	−15	−21		
	34	21	3	−18		
R. Middle temporal gyrus (PF)	21	66	−36	0	33	4.26
	21	48	−36	−3		
R. Parahippocampal gyrus	35	21	−18	−21	19	4.02

(continued on next page)

Table 2 *(continued)*

Brain region	BA	Coordinates (X, Y, Z)			Vol.	T
(CA3, Subiculum, DG)	30	24	−27	−21		
	20	33	−30	−21		
Subcortical area and cerebellum						
R. Superior Cerebellum		27	−75	−33	184	7.70
		30	−87	−36		
		18	−87	−36		
L. Inferior Cerebellum		−15	−84	−33	54	5.05
		−15	−87	−24		
		−30	−87	−33		
L. Rectus	11	3	42	−21	33	4.17
(Fo1, Fp2, Fo2)	11	−3	51	−12		
	11	0	33	−24		

Note: all the results reported above were significant at $p < .001$, uncorrected at the voxel level, and survived the cluster-level FDR correction at $p < .05$, voxel size > 10.

orbital part of inferior frontal gyrus (BA 47), whereas computation elicited greater activation in right inferior parietal lobule (hIP3), left middle occipital gyrus, right inferior and middle frontal gyrus, and left precentral gyrus. Arithmetic principles elicited greater activation than language processing in left inferior parietal lobule (including hIP3, hIP1, 7PC, hIP2), right inferior parietal lobule, bilateral precuneus, right supramarginal gyrus (including PF, PFm, hIP2, hIP3, hIP1, PFt, PF), left triangularis part of inferior frontal gyrus, right middle frontal gyrus and left precentral gyrus, but language processing elicited greater activation than arithmetic principles in left precuneus, left superior frontal gyrus, left middle temporal gyrus, right middle temporal pole, and right parahippocampal gyrus. Computation elicited greater activation than language processing in left inferior parietal lobule (including hIP3, PF, PFt, hIP1, hIP2), bilateral median cingulate, left precentral gyrus, left triangular and right opercular part of inferior frontal gyrus, right middle frontal gyrus and left inferior temporal gyrus, but language elicited greater activation in left superior medial frontal gyrus, right orbital part of inferior frontal gyrus, bilateral middle temporal gyrus, and right hippocampus.

3.3. Univariate analysis: item-wise analysis

Item-wise analysis showed similar results in activation patterns and contrasts between conditions as those from the subject-wise analysis. Table 3 and Fig. 4 show the task differences in brain activation based on direct contrasts. Arithmetic principles elicited greater activation than did computation in the left middle temporal gyrus, and left orbital part and triangular part of inferior frontal gyrus as well as left angular gyrus, whereas computation elicited greater activation in right superior parietal lobule (including hIP3,7A, 7PC, hIP1) and left middle frontal gyrus. Arithmetic principles elicited greater activation than language processing in left precuneus (including hIP1, hIP2), left posterior cingulate gyrus, left rolandic operculum, left superior frontal gyrus, right postcentral gyrus, left inferior temporal gyrus and right superior temporal gyrus, but language processing elicited greater activation than arithmetic principle in left precuneus, left superior frontal gyrus, and bilateral middle temporal gyrus. Computation elicited greater activation than did language in the left inferior parietal lobule (hIP3, hIP2, hIP1), but language elicited greater than did computation in left precuneus, right angular, left superior medial frontal gyrus, left middle frontal gyrus, bilateral middle temporal gyrus.

3.4. ROI analysis

Compared to language processing, arithmetic principles elicited significantly higher activation in left HIPS, $t(29)=4.19$, $p < .001$, and right HIPS, $t(29)=2.69$, $p < .05$, but lower activation in left middle temporal gyrus, $t(29)=2.64$, $p < .05$, and left orbital part of IFG, $t(29)=5.42$, $p < .001$. Compared to computation, arithmetic principles elicited significantly lower activation around left HIPS, $t(29)=2.96$, $p < .01$, right HIPS, $t(29)=5.42$, $p < .001$, and significantly higher activation in left middle temporal gyrus, $t(29)=4.52$, $p < .001$, and left orbital part of IFG, $t(29)=3.76$, $p < .001$. (see Fig. 2).

3.5. Multi-voxel pattern analysis

MVPA identified several cortical regions whose activity patterns

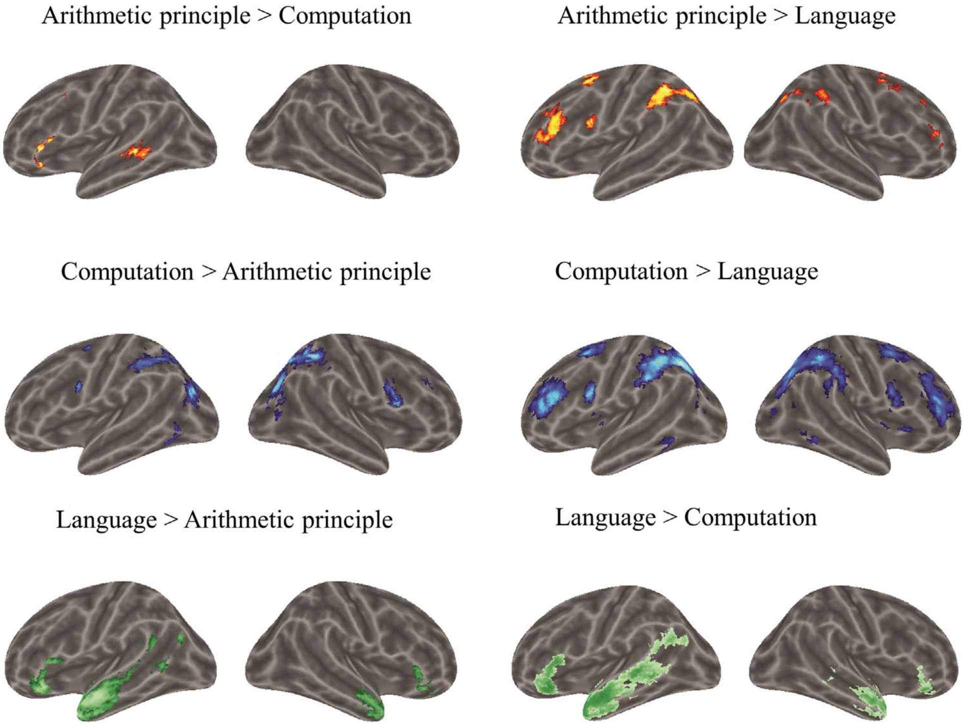


Fig. 3. Univariate activation contrast among conditions based on subject-wise analysis ($p < 0.001$, voxel size > 10, uncorrected).

Table 3
Loci showing significant activations based on contrasts between the three conditions in item-wise analysis.

Brain region	BA	Coordinates (X, Y, Z)			Vol.	T
Arithmetic principle > Computation						
Parietal cortex						
L. Angular gyrus (PGa, PFm, PGp)	39	−42	−57	33	228	6.67
	39	−51	−63	42		
		−45	−72	45		
Frontal cortex						
L. Precental gyrus	9	−36	12	45	86	7.08
L. Inferior frontal gyrus (triangular) (45)	45	−51	30	3	317	6.82
L. Inferior frontal gyrus (orbital)	47	−45	30	−12		
	47	−45	39	−9		
L. Superior medial frontal gyrus	8	−9	27	57	231	5.74
	8	−6	27	66		
		−12	54	42		
Temporal cortex						
L. Middle temporal gyrus	21	−60	−42	0	183	5.54
	21	−60	−33	−3		
	20	−60	−33	−12		
L. Middle temporal gyrus	20	−48	−15	−12	78	4.96
	21	−54	−3	−21		
	20	−45	0	−30		
Arithmetic principles > Language						
Parietal cortex						
L. Precuneus (hIP1, hIP2)	7	−12	−63	39	4737	9.28
	40	−48	−45	60		
	40	−33	−45	39		
L. Posterior cingulate gyrus (5 Ci)	23	−6	−36	27	287	8.62
	23	6	−36	27		
		12	−30	39		
Frontal cortex						
L. Rolandic operculum (44)	6	−48	3	18	358	8.45
	44	−51	6	27		
	48	−39	−3	3		
R. Middle frontal gyrus (44)	6	27	6	45	1386	6.94
	32	12	33	24		
	6	51	3	15		
L. Superior dorsolateral frontal gyrus	6	−15	−9	72	81	5.98
	4	−12	−21	60		
		−12	−15	54		
R. Postcentral gyrus (4a)		12	−30	81	13	3.92
	4	6	−24	69		
Temporal cortex						
L. Inferior temporal gyrus	37	−57	−54	−12	89	6.90
	20	−54	−45	−15		
R. Superior temporal gyrus (OP1, OP4, TE3)	42	57	−24	15	42	4.70
	22	66	−21	15		
	22	66	−12	9		
Subcortical area and cerebellum						
R. Inferior Cerebellum		30	−69	−45	107	6.32
		36	−60	−45		
		15	−72	−39		
R. Superior Cerebellum		30	−60	−30	120	5.58
	19	21	−69	−24		
		39	−60	−33		
L. Inferior Cerebellum		−15	−72	−45	175	5.30
		−33	−60	−36		
		−36	−45	−39		
Computation > Arithmetic principle						
Parietal cortex						
R. Superior parietal lobule (hIP3,7A, 7PC, Hip1)	7	27	−63	51	2099	8.77
	7	33	−54	66		
	40	30	−51	39		
Frontal cortex						
L. Middle frontal gyrus	9	−36	39	39	70	5.23
	46	−30	48	24		
	46	−39	45	27		
Subcortical area and cerebellum						
L. Inferior Cerebellum		−21	−69	−42	75	5.60
		−15	−54	−48		
		−30	−66	−54		
		15	−63	−45		
Computation > Language						
Parietal cortex						
L. Inferior parietal lobule (hIP3, hIP2, hIP1)	40	−45	−42	39	18058	19.92
	7	−27	−60	42		
	7	−24	−69	45		
Subcortical area and cerebellum						
R. Thalamus		18	−9	−6	50	6.50
		24	−15	−9		
Language > Arithmetic principle						
Parietal cortex						
L. Precuneus		−30	−51	6	39	5.94
		−24	−45	12		
Frontal cortex						
L. Superior medial frontal gyrus	9	−3	48	48	564	9.47
	9	−3	51	36		
	9	−9	48	54		
Temporal cortex						
L. Middle temporal gyrus	21	−54	3	−18	1409	12.55
	20	−51	−15	−18		
	20	−45	12	−33		
R. Middle temporal pole	38	45	18	−36	629	9.21
	38	45	21	−27		
	20	45	−6	−24		
Subcortical area and cerebellum						
R. Inferior Cerebellum		21	−87	−33	91	7.20
		30	−84	−36		
L. Calcarine	30	−9	−51	6	119	6.73
		−3	−39	−6		
L. Rectus (Fo1, Fo2, Fp2, s24)	11	0	33	−27	122	6.17
	11	3	45	−18		
	11	−3	33	−6		
L. Inferior Cerebellum	25	−24	−87	−30	53	5.65
Language > Computation						
Parietal cortex						
L. Precuneus	30	−6	−54	12	147	6.69
	30	−3	−51	21		5.64
		−9	−48	36		3.94
R. Angular gyrus (PGp, PGa)		57	−63	33	48	5.39
	39	57	−63	24		4.83
	37	60	−63	15		3.90
Frontal cortex						
L. Superior medial frontal gyrus	9	−9	57	39	1096	12.89
	8	−9	27	60		12.67
	9	−9	48	54		12.36
L. Middle frontal gyrus	9	−36	12	45	53	6.56
	9	−39	21	54		4.82
Temporal cortex						
L. Middle temporal gyrus	20	−51	−9	−15	2481	16.32
	47	−45	24	−3		15.91
	47	−42	30	−12		15.65
R. Middle temporal gyrus (Fo3)	21	48	−3	−24	1173	12.47
	47	36	33	−18		11.62
	20	39	18	−36		11.59
Subcortical area and cerebellum						
R. Inferior Cerebellum		21	−84	−36	193	10.26
L. Rectus (Fp2, Fo1, s32)		0	51	−15	91	7.59
	11	0	36	−24		6.95
	11	−6	30	−15		3.51
L. Inferior Cerebellum		−18	−90	−33	80	5.56
		−27	−81	−36		4.75
L. Caudate nucleus		−12	9	12	22	4.11

Note: all the results reported above were significant at $p < .001$, uncorrected at the voxel level, and survived the cluster-level FDR correction at $p < .05$, voxel size > 10.

could be used to classify the experimental conditions with high accuracy (70% and above). The results are displayed in Table 4 and Fig. 5. Arithmetic principles and computation could be successfully classified by activation patterns in left and right frontal cortex such as left inferior frontal gyrus, right superior frontal gyrus, left insula and left SMA, as well as those in the occipital cortex such as left lingual gyrus and right calcarine, the parietal cortex such as right superior

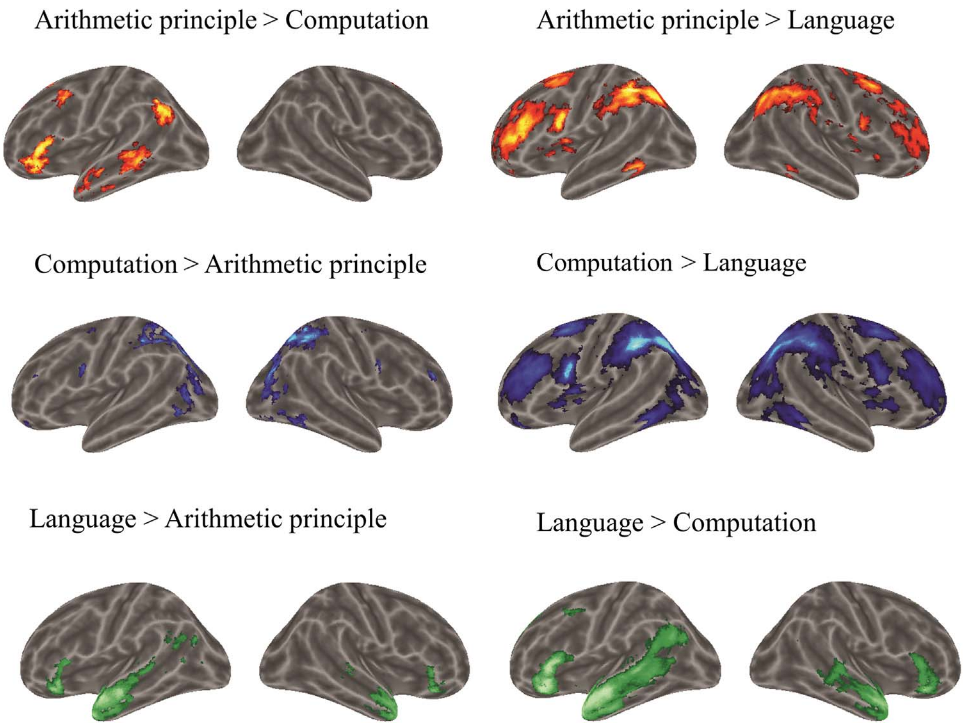


Fig. 4. Univariate activation contrast among conditions based on item-wise analysis ($p < 0.001$, voxel size > 10, uncorrected).

parietal lobule (including 7A, hIP3) and left superior parietal lobule, and the temporal cortex such as left middle temporal gyrus. Arithmetic principles and language processing could be classified by activation patterns in left opercular part of inferior frontal gyrus, right triangular part of inferior frontal gyrus, bilateral middle temporal gyrus, and left superior parietal lobule and right superior parietal lobule. Finally, computation and language processing could be classified by activation patterns in left inferior frontal gyrus, right middle temporal lobe, and cerebellum. The results from the MVPA were similar to those from univariate results reported in the two sections above.

3.6. Functional connectivity analysis

The conjunction analysis identified a region in the left HIPS (peak at MNI coordinates [−27, −54, 45], hIP3). This region served as the candidate seed region for the subsequent PPI analysis. We used six separate PPI models to test our primary hypothesis, that is, arithmetic principles > computation, arithmetic principles > language processing, computation > arithmetic principles, language processing > arithmetic principles, computation > language processing, and language processing > computation. Regions that showed stronger connectivity with the left HIPS are shown in Table 5 and Fig. 6.

3.6.1. The contrast between arithmetic principles and computation

In line with our hypothesis, PPI parameter estimates of the connectivity from left HIPS to left MTG and left orbital part of IFG were larger for arithmetic principles than those for computation. In contrast, left HIPS's connectivity with left middle occipital gyrus was greater for computation than for arithmetic principles.

3.6.2. The contrast between arithmetic principles and language processing

The arithmetic principles > language processing contrast did not show any significant results. The language > arithmetic principles contrast showed significant results in brain regions such as left cingulate gyrus and right precuneus, left middle occipital gyrus, right orbital part of inferior frontal gyrus, bilateral middle temporal gyrus and bilateral fusiform gyrus.

3.6.3. The contrast between computation and language processing

Functional connectivity between the seed region and left IPS, right angular gyrus, and right middle occipital gyrus were greater for computation than for language processing. In contrast, left HIPS's connectivity with bilateral middle temporal gyrus, left superior medial frontal gyrus, left middle frontal gyrus and left precuneus were stronger for language processing than for computation.

All univariate and functional connectivity results reported above survived cluster-level FDR correction at $p < .05$, suggesting that the observed effects were stable across different analyses.

4. Discussion

In this study, we tested two hypotheses: (1) the processing of arithmetic principles relies on visuospatial processing and (2) it relies on semantic/conceptual processing. Based on both univariate and multi-voxel pattern analyses, we found that arithmetic principles elicited greater activation than did language processing in bilateral HIPS, and greater activation than did computation in left middle temporal gyrus and left orbital part of IFG. Based on functional connectivity analysis, we found that left HIPS's connectivities with left MTG and left orbital part of IFG were stronger for arithmetic principles than for computation. These results suggested that neural substrates of arithmetic principles were a distributed system that requires cooperation of brain areas such as left middle temporal gyrus, left orbital part of inferior frontal gyrus, and bilateral HIPS.

4.1. The role of HIPS for the processing of arithmetic principles

As expected, the processing of arithmetic principles had greater activation than general language processing (i.e., sentence reading) in bilateral HIPS (e.g., hIP1, hIP2, hIP3 in cytoarchitechtonic maps). The finding is consistent with the important role of the HIPS in numerical and arithmetic processing (Cantlon et al., 2009; Dehaene et al. 1999; Ischebeck et al., 2006; Piazza et al. 2006, 2007; Santens et al. 2010; Zhang et al., 2012), but extends the role of the HIPS to the processing of arithmetic principles. Previous neuroimaging studies did not directly compare the processing of arithmetic principles and the non-mathe-

Table 4
Brain areas that showed significant differences in multivariate activation patterns between the three conditions (Cluster size > 10, accuracy > 70%).

Brain region	BA	Peak coordinates			Vol.	Accuary		
		(X, Y, Z)				*Whole*	*Label 1*	*Label 2*
Arithmetic principles vs. Computation								
Parietal cortex								
R. Supeior parietal lobule (7A, hIP3)	7	24	−57	57	511	78	80	77
L. Supeior parietal lobule (5L, 2)		−21	−45	72	104	76	82	70
Occipital cortex								
L. Lingual (hOc1, hOc3v)	17	−12	−87	−3	87	77	80	73
R. Calcarine (hOc1)	17	15	−87	3	46	73	80	67
Frontal cortex								
L. Inferior frontal gyrus	48	−36	15	30	140	74	67	75
R. Superior frontal gyrus	6	15	−15	66	33	75	80	70
L. Supplementary motor area	8	−6	21	51	95	75	78	77
L. Insula	48	−33	12	−9	33	72	73	70
R. Postcentral gyrus (2, 1)	2	45	−36	57	13	72	78	65
Temporal cortex								
L. Middle temporal gyrus	21	−57	−39	−3	74	74	67	82
Subcortical area and cerebellum								
R. Cerebellum		−18	−69	−51	47	74	78	70
R. Cerebrum		18	−75	−39	300	75	78	72
L. Sub-lobar		−27	−39	18	2126	87	90	83
Arithmetic principles vs. Language								
Parietal cortex								
L. Supeior parietal lobule (7PC, 2, 5 L, 1)	2	−36	−45	60	2019	82	87	77
R. Supeior parietal lobule (7PC)	7	33	−54	69	21	74	87	62
Frontal cortex								
L. Inferior frontal gyrus (44)	48	−51	15	21	3081	84	83	85
R. Inferior frontal gyrus (45)	45	48	36	12	121	75	78	72
R. Middle frontal gyrus	44	33	9	42	63	75	82	68
Temporal cortex								
R. Middle temporal gyrus	21	51	0	−21	461	78	78	78
L. Inferior temporal gyrus (FG4)(	20	−45	−45	−15	134	77	87	67
Subcortical area								
R. Cerebellum		33	−54	−45	27	74	75	73
L. Cerebellum		−6	−57	−51	169	76	87	70
R. Cerebellum		18	−78	−45	131	76	87	70
R. Cerebrum		48	−42	−9	267	80	83	77
L. Rectus (Fo1)	11	−12	39	−18	35	73	72	72
L. Cerebrum (PFm)		−63	−57	15	22	72	77	67
R. Cerebrum		33	−42	21	14	75	75	75
R. Cerebrum		15	−30	24	27	75	76	73
R. Cerebrum		18	9	72	88	76	75	77
Computation vs. Language								
Frontal cortex								
L. Inferior frontal lobe (44, 45)	48	−51	18	15	11044	90	92	88
Temporal cortex								
R. Middle temporal gyrus	20	51	−9	−21	940	78	73	83
Subcortical area and cerebellum								
R. Cerebellum		18	−78	−39	371	78	80	77
R. Rectus (Fo1)	11	3	39	−24	109	76	80	72
L. Caudate		−3	6	−3	68	75	75	75
R. Cerebrum		45	−45	−9	179	77	82	72
R. Cerebrum		21	−24	27	182	78	80	75
R. Cerebrum		30	21	33	128	78	78	78

Note: The cytoarchitectonic areas were reported in the brackets, according to www.fz-juelich.de/ime/spm_anatomy_toolbox.

matical processing in the brain (i.e., Jost et al., 2009). Our finding of the involvement of the HIPS for arithmetic principles supports the visuospatial processing hypothesis–the HIPS is responsible for the spatial information from the visualization (or mental models) of arithmetic principles. It is worth noting that single mathematical concepts expressed with mathematical terminologies would not elicit

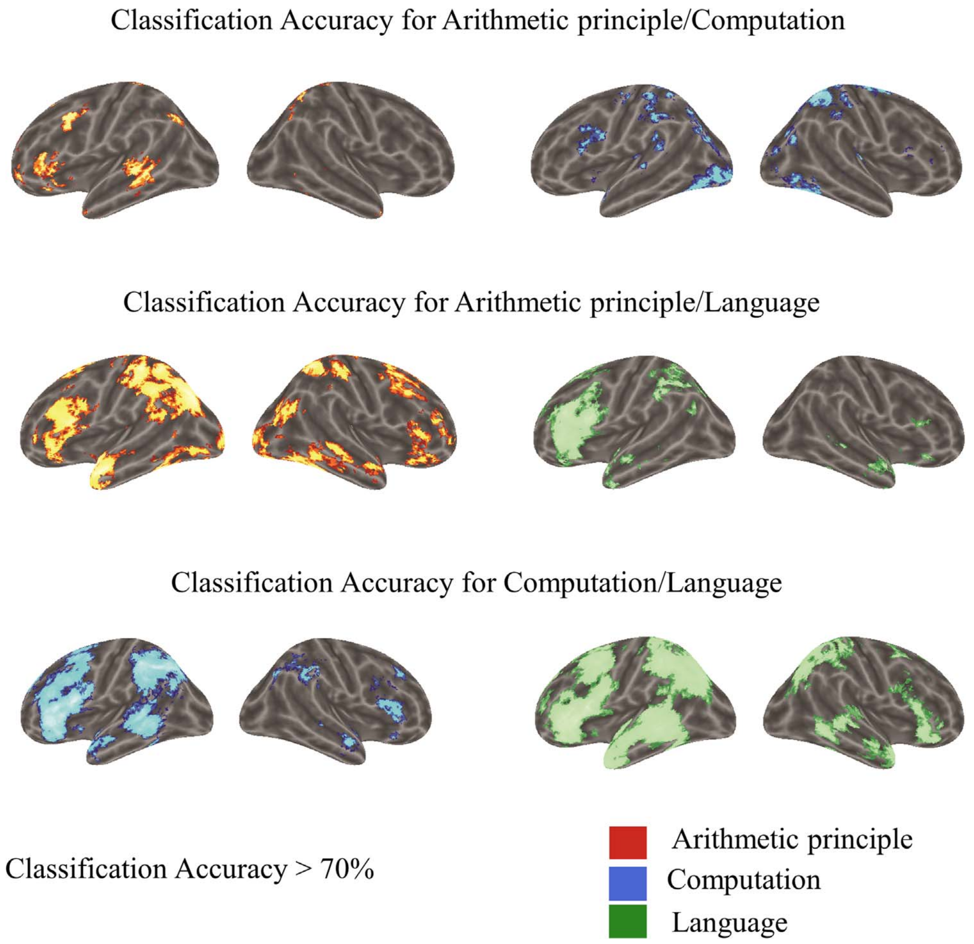


Fig. 5. The brain maps of classification accuracy based on three MVPA classifiers: arithmetic principles vs. computation (top panel), arithmetic principles vs. language processing (middle panel), and computation vs. language processing (bottom panel). The accuracy in maps is larger than 70%.

greater HIPS activation than would ordinary words (Zhang et al., 2012). Thus, the involvement of the HIPS may be specific to mental models involving (spatial) relations among multiple mathematical concepts. Of course, such relations are likely to involve less spatial processing than computation as found in this study. The finding of HIPS's involvement in arithmetic principles was in line with previous visuospatial studies (e.g., Boccia et al., 2014; Tomasino and Gremese et al., 2015; Wolbers et al., 2010).

Aside from the visuospatial processing explanation for the involvement of HIPS in the processing of arithmetic principles, we need to acknowledge the alternative explanation of quantity processing. The HIPS is typically activated by number-related processes, and is assumed to have a core quantity system (e.g., Ansari et al., 2006; Eger et al., 2003; Pinel et al., 2001; Cohen Kadosh et al., 2005; Cantlon et al., 2009; Nieder and Dehaene, 2009; see a review by Dehaene et al., 2003). For example, numerical processing has been shown to activate HIPS to a greater extent than language-related processing (e.g., Eger et al., 2003; Wei et al., 2014; Zhang et al., 2012). The number-related activation in HIPS has been explained as the result of quantity processing for numbers (see a review by Dehaene et al., 2003). Although arithmetic principles do not involve any numbers directly, they involve the quantity relations among numbers after computations. Thus, it is also possible that the activation in HIPS for the processing of arithmetic principles may be due to the numerical quantity processing. Indeed, the visuospatial hypothesis and numerical quantity hypothesis for the arithmetic principle-elicited HIPS activation could be compatible. First, both share similar brain regions. Functional MRI studies have shown that bilateral parietal lobes are responsible for both spatial and quantity processing (e.g., Bulthé et al., 2015; Colby et al., 1999; Riemer et al., 2016; see a review by Hubbard et al., 2005). Second, spatial and numerical quantity representations have been found to be closely related (Bulf et al., 2015; Dehaene et al., 1993; Fischer et al., 2003; Schuller et al., 2015; Viarouge et al., 2014; Yu et al., 2016). For example, numbers can automatically elicit spatial representations, as evidenced by the spatial-numerical association of response codes (SNARC) effect (i.e., the left hand responds faster to small numbers, whereas the right hand responds faster to large numbers, Dehaene et al., 1993; Viarouge et al., 2014). Attention can be automatically biased towards the left or right space by the quantity expressed by digits (Fischer et al., 2003).

4.2. The role of the left MTG and left orbital part of IFG in the processing of arithmetic principles

The current study also found that the processing of arithmetic principles elicited more activation in left middle temporal gyrus and left orbital part of inferior frontal gyrus than did computation. We further found that the HIPS had stronger connectivity with left MTG and left orbital part of IFG during the processing of arithmetic principles than during computation. Jost et al. (2009) also found that left MTG was activated to a greater extent by 0-based than simple non-rule-based multiplication problems. Previous studies have shown these brain regions are important for the representation of abstract conceptual knowledge (e.g., Hoffman et al., 2015; Skipper-Kallal et al., 2015; Zhang et al., 2012). For example, the neural circuits for the processing of arithmetic principles are similar to those for mathematical terminology (Zhang et al., 2012). Zhang et al. showed that the judgment of semantic relation among mathematical terms (e.g.,

Table 5
Loci showing significant activations based on contrasts of functional connectivities between the conditions.

Brain region	BA	Coordinates (X, Y, Z)			Vol.	T
Arithmetic principle > Computation						
Frontal cortex						
L. Inferior frontal gyrus (orbital)	38	−45	27	−12	34	5.11
	45	−51	27	0		
	47	−45	33	−6		
Temporal cortex						
L. Middle temporal gyrus	22	−54	−39	3	39	5.00
	21	−60	−39	−6		
	21	−60	−30	3		
Arithmetic principle > Language						
No brain regions found						
Computation > Arithmetic principle						
Occipital cortex						
L. Middle occipital gyrus	19	−33	−81	24	32	5.35
(PGp, hOc4la)	39	−42	−75	18		
Computation > Language						
Parietal cortex						
L. Inferior parietal lobule	40	−48	−48	51	21	4.65
(hIP2, PF, PFt, 1)	40	−51	−36	48		
R. Angular gyrus	7	30	−63	45	21	4.52
	7	33	−63	36		
Occipital cortex						
L. Middle occipital gyrus	7	−27	−63	39	55	5.83
(hIP3, hIP1)		−21	−57	36		
Language > Arithmetic principle						
Parietal cortex						
L. Anterior cingulate gyrus	32	−3	48	18	1614	8.37
	32	−6	51	27		
	8	−6	39	54		
L. Median cingulate gyrus	23	0	−15	39	66	5.64
L. Median cingulate gyrus		−9	−45	36	52	4.74
		−12	−54	48		
		−6	−57	39		
R. Precuneus		9	−51	45	19	4.07
		15	−57	42		
Occipital cortex						
L. Middle occipital gyrus (PGp, PFm)	39	−42	−75	30	136	4.88
	39	−54	−69	21		
	39	−48	−57	24		
Frontal cortex						
R. Inferior frontal gyrus (orbital)(Fo3)	47	33	33	−12	61	4.70
	47	39	30	−18		
	38	39	24	−24		
Temporal cortex						
L. Middle temporal gyrus	21	−57	−6	−24	307	6.27
	21	−51	0	−21		
	20	−51	−21	−15		
L. Fusiform gyrus (FG3)	37	−30	−39	−18	66	6.11
R. Middle temporal gyrus (TE3)		57	−6	−15	97	5.63
	20	48	−6	−24		
	20	54	−12	−27		
R. Middle temporal gyrus (PGa, PGp)	21	54	−54	21	92	5.10
	39	51	−66	24		
	39	45	−51	24		
L. Middle temporal gyrus (PGa)	21	−63	−51	9	50	4.81
	22	−54	−51	18		
	37	−60	−60	9		
R. Middle temporal gyrus (TE3)	21	63	−21	−6	32	4.80
R. Fusiform gyrus	37	33	−36	−12	27	4.73
Subcortical area						
L. Calcarine	17	0	−63	12	318	7.97
	30	−12	−51	9		
	23	−3	−54	21		
Language > Computation						
Parietal cortex						
L. Precuneus	30	−3	−51	21	341	5.22
	29	−6	−48	9		
	27	9	−42	3		
Frontal cortex						
L. Superior medial frontal gyrus	10	−3	51	30	494	6.50
	9	−9	48	45		
	8	−3	39	51		
L. Middle frontal gyrus	9	−39	24	48	22	4.66
Temporal cortex						
L. Middle temporal gyrus	21	−63	−42	−3	380	7.53
(PGa, PGp)	39	−42	−54	24		
	39	−45	−66	30		
L. Middle temporal gyrus	22	−57	−12	−9	743	7.37
	38	−48	24	−9		
	21	−54	−6	−24		
R. Middle temporal gyrus	22	60	−42	6	225	6.21
(PGa, PGp)	39	54	−63	24		
	37	60	−60	9		
R. Middle temporal gyrus	22	54	−12	−12	320	6.18
	38	45	21	−27		
	21	54	−3	−24		
Subcortical area and cerebellum						
L. Rectus		0	39	−21	88	5.36
(Fo1, Fp2)	11	6	45	−12		
	11	−6	39	−6		
L. Superior Cerebellum		−18	−78	−30	31	4.59
		−12	−87	−36		
R. Cuneus		12	−69	27	60	4.23
(hOc3d, hOc4d, 7M)		−18	−96	30		
		0	−72	27		

Note: all the results reported above were significant at $p < .001$, uncorrected at the voxel level, and survived the cluster-level FDR correction at $p < .05$, voxel size > 10.

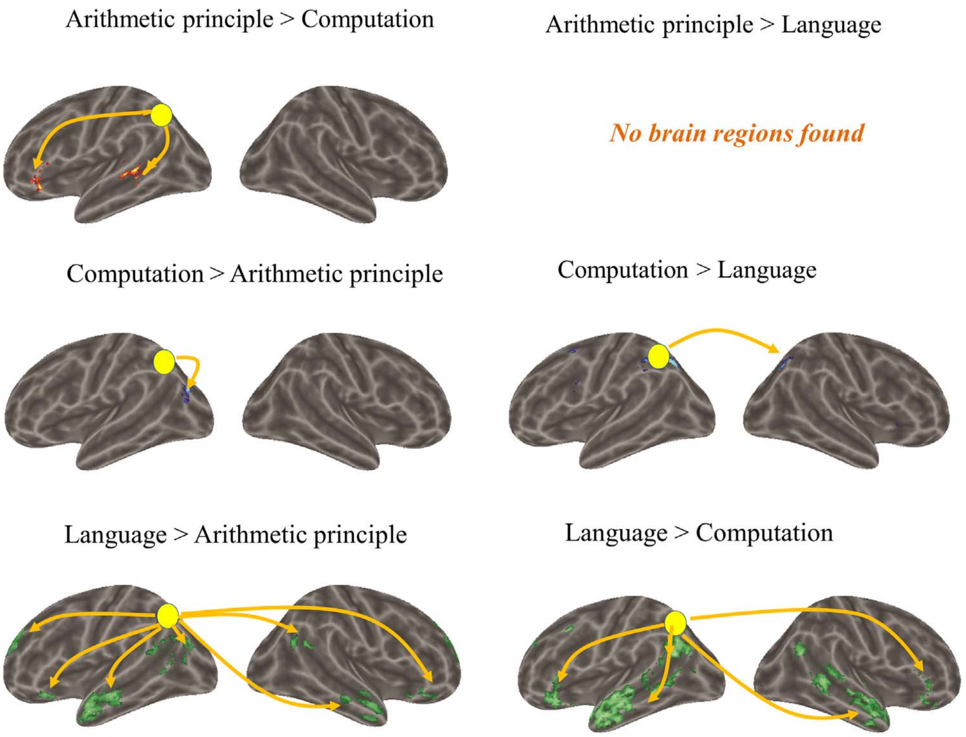
"Between integer and fraction, which is semantically closer to decimal?") had greater activation in left MTG and left IFG than the judgment of semantic relation among numbers (e.g., "Between 37 and 86, which number is semantically closer to 54?"). These results could account, at least partially, for some neuropsychological findings. Left frontal lesion was found to lead to selective impairment of the processing of arithmetic principles (Delazer et al., 1997; Sokol et al., 1991). Frontotemporal dementia patients also showed impaired calculation skills, which might be due to a damage to left MTG and left orbital part of IFG, two areas that play critical roles in arithmetic knowledge (Cappelletti et al., 2012). Atrophy of left temporal gyrus, on the other hand, would not lead to impaired performance in arithmetic principles relative to general semantic processing (e.g., Cappelletti et al., 2005).

A number of previous studies have shown that the orbital part of IFG is responsible for semantic/conceptual processing (e.g., Devlin et al., 2003; Kuperberg et al., 2008; Nosarti et al., 2010; Wagner et al., 2001). Devlin et al. (2003) applied transcranial magnetic stimulation (TMS) to the orbital part of IFG in 8 healthy participants while they performed semantic decision and perceptual (size) decision tasks. TMS slowed participants' reaction time during the semantic task but not during the size decision task. Wagner et al. (2001) found that the orbital part of left IFG was involved in controlled semantic retrieval. Kuperberg et al. (2008) found that semantic violations in sentences led to increased activity within the orbital part of left IFG, reflecting participants' increased and prolonged efforts to retrieve semantic knowledge about the likelihood of events occurring in the real world.

Taken together the above results, the processing of arithmetic principles seems to be supported by the left MTG and left orbital part of IFG as well as the bilateral HIPS.

4.3. The role of the bilateral IPS and left inferior occipital cortex in computation

Univariate analyses showed that computation elicited greater activation in the bilateral IPS (including hIP3, PF, PFt, hIP1, hIP2) than did arithmetic principles and language processing. This finding is consistent with previous research (Rosenberg-Lee et al., 2011; Prado


Arithmetic principle > Computation

Arithmetic principle > Language

Computation > Arithmetic principle

Computation > Language

Language > Arithmetic principle

Language > Computation

Fig. 6. Comparisons of functional connectivities between the three conditions based on PPI ($p < 0.001$, voxel size >10, uncorrected).

et al., 2011), and it has been interpreted as the IPS's role in quantity processing or spatial processing during computation.

We found greater activation in the occipital cortex and stronger parieto-occipital connectivity for computation than for the processing of language processing, perhaps due to the greater involvement of visual processing in computation. Indeed, previous behavioral studies have shown a close relation between visual processing and arithmetic performance (e.g., Anobile et al., 2013; Rosner, 1973; Rourke and Finlayson, 1978; Sigmundsson et al., 2010; Tibber et al., 2012). For example, Rosner (1973) showed that compared to auditory perception, visual perception explained more variance in arithmetic performance. Anobile et al. (2013) and Tibber et al. (2012) also found that visual perception made a unique contribution to arithmetic performance. In a longitudinal study, Kurdek and Sinclair (2001) found that visuo-motor integration performance as well as verbal skills during kindergarten predicted mathematical achievement in fourth grade. Clinical studies showed impaired visual-perceptual and visual-spatial performance in dyscalculic children (e.g., Rourke et al., 1978; Sigmundsson et al., 2010). Recently, Zhou et al. (Zhou et al., 2015; Zhou and Cheng, 2015) found that the visual perception could account for the close relation between arithmetic computation and numerosity processing (e.g., which of two dot arrays has more dots?). All these studies suggest that visual perception is fundamental to arithmetic computation.

One limitation of the current study was that some of our arithmetic computation problems contained simple computation (e.g., n×1) in one of the two steps for each problem. We did that because we wanted to reduce the difficulty level of numerical computation to match the difficulty level and sentence length of the other two tasks (the processing of verbalized arithmetic principles and general language processing). Consequently, participants could use the 1-based computational principles to solve one step of the problems. The application of arithmetic principles in simple computation task could attenuate the contrast effects between the processing of arithmetic principles and numerical computation. However, the effect of this problem should be limited because (1) there were two steps (e.g., When the number 4 is subtracted by the number 2, then multiplied by the number 1, the result is the number 2) for each problem and only the second step involved the n×1 or n÷1 computation, and (2) there were 13 problems with the n×1 or n÷1 computation, and 11 problems without the n×1 or n÷1, which showed similar results in a separate analysis (for both types of problems, arithmetic principles had greater activation in the left middle temporal cortex and left inferior frontal gyrus in both contrasts.).

4.4. Summary

Both univariate and multi-voxel pattern analysis in the current fMRI study showed that the left MTG and left orbital part of IFG were more involved during the processing of the arithmetic principles than during computation, and that the HIPS was more involved in the processing of arithmetic principles than general language processing. Furthermore, left parieto-frontal and parieto-temporal connectivities were stronger for the processing of arithmetic principles than for computation. These results suggest that verbalized arithmetic principles involve both semantic/conceptual processing and numerical quantity processing. In contrast, compared to the processing of arithmetic principles, computation elicited stronger bilateral IPS and inferior occipital gyrus activation and stronger parieto-occipital connectivity.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.neuroimage.2016.12.035.

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