# Common and Dissociable Neural Substrates for 2-Digit Simple Addition and Subtraction


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**Abstract.** Although addition and subtraction are the basic operations, in the view of information processing, consensus on the relationship between them has not yet achieved. This study aimed to understand the common points and differences as well as the underlying neural substrates between addition and subtraction through the analysis on the data derived from magnetic resonance imaging measurement. Three kinds of tasks: addition task (AT), subtraction task (ST) and memory task (MT) were solved by seventeen adults. Our results revealed that simple addition also induced the activation in intraparietal sulcus (IPS); activation in hippocampal areas responsible for retrieval was discovered during subtraction calculation; subtraction showed stronger activation in Broca's Area when compared with addition. The findings suggest that calculation strategy is not the key point for distinguishing addition and subtraction, the activation in Broca's Area indicates the differences between the two operations may concern grammar and language expression.


## 1 Introduction

Higher cognitive functions, involving reasoning, learning, computation, problem-solving, and so forth have been considered to be achieved through cooperative activities of multiple brain regions. Brain Informatics (BI) is powerful to reveal the complicated interaction between cortical areas by studying the human information processing system and underlying substrates on basis of systematic methodology [1, 2].

Mental arithmetic is an elemental subject of complex brain science. Many studies have revealed an association between the arithmetic problem-solving and left fronto-parietal cortices [3-5]. The triple-code model of numerical processing put forward by Dehaene and Cohen [6] proposed that numbers are represented in three codes including visual Arabic form, verbal word form and analogue magnitude form, which corresponds to ventral occipitotemporal areas, left perisylvian, and bilateral inferior parietal respectively. Subsequent fMRI studies verified that intraparietal sulcus (IPS) functions as a specific domain for number manipulation, and with increasing


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activation as the task that puts greater emphasis on quantity processing, for instance, in subtraction calculation [7, 8]. On the other hand, multiplication is deemed as an operation in reliance on a multiplication table. The process of multiplication is characterized as direct retrieval of rote arithmetic-facts in the form of verbal word [9]. Neuroimaging studies supported this disassociation of calculation strategies, more activations were found in bilateral inferior parietal lobule during subtraction and in frontal cortex and left perisylvian during multiplication [8].

In contrast, consensus on the relationship between addition and subtraction has not yet achieved. With respect to calculation strategies, addition was considered to be more dependent on retrieval of arithmetic-facts [7]. Dehaene et al. proposed that small exact addition facts and some subtraction problems can be stored in rote verbal memory, but many calculations of subtraction require genuine quantity manipulations [9]. Studies with direct comparison between addition and subtraction are relatively infrequent. One complex 2-digit fMRI research showed more activation in bilateral medial frontal gyrus during addition but more activation in right precentral gyrus, thalamus and left inferior parietal lobule during subtraction [10]. However the results of simple arithmetic were not reported. In brief, both intersection points and discrepancies exist between addition and subtraction, but relationship of the two operations and underlying neural substrates have yet to be explicitly revealed. Therefore, we attempted to clarify this problem with a new-designed fMRI experiment.

Based on the BI methodology, the present study investigated common and different patterns of brain activation of 2-digit addition and subtraction problems without carry and borrow under an intermediate state, which can be seen as a continuum between traditional concept of simple arithmetic binding with 1-digit operators along with no carry and borrow, and complex arithmetic binding with 2-digit operators accompanied by carry and borrow. We assumed that addition and subtraction exploit same calculation strategies by sharing some same brain regions and networks; nonetheless the two operations do have some intrinsic differences.

## 2 Materials and Methods

### 2.1 Subjects

Seventeen healthy undergraduates and postgraduates (7 females, and 17 right-handers) with the mean age of 25.76 ± 3.78 years participated in the experiment who had the normal or corrected-to-normal vision. None of them reported any history of neurological or psychiatric diseases. All the subjects signed the informed consent and this study was approved by the Ethics committee of Xuanwu Hospital, Capital Medical University.

### 2.2 Experimental Design

Four trials with same kind of task were involved in one block which lasted for 24 s. The interval of 24 s between every two blocks with no task (NT) was used as baseline.

As shown in Table 1, three kinds of tasks in the same form of presentation were employed in the experiment: addition task (AT), subtraction task (ST) and memory task (MT). Experimental materials containing 2-digit numbers and operation signs were displayed visually, in sequence of "first operand", "second operand", "operation sign", and "reference answer" within each trial. The first operand was always greater than the second one, subjects were required to compute "first operand plus second operand" in AT or "first operand minus second operand" in ST. Neither carry nor borrow were involved in the calculations. Subjects were required to make a true or false judgment by pressing buttons when the reference answer was presented, left hand for the true and right hand for the false. The ranges of false reference answers were "true answers ± 1 or ± 10"; the rate of false questions was 50% across all the trials. The mark of "#" was used as the operation sign for MT which means subjects should judge whether the reference answer was same as one of the two previous operands or not. As another baseline, the MT includes cognitive process of basic visual coding, information maintaining, judging and button pressing, so the calculation components can be extracted by comparing AT and ST with MT. To avoid automatic visual-spatial processing, presentation of the equations disaccorded with writing order, and all the stimuli were displayed separately in a flashing pattern with a short exposure time. As shown in Fig. 1, the exposure time for the first operand, second operand, operation sign and reference answer is 250 ms, 250 ms, 500 ms and 2000 ms respectively. Every two stimuli were separated by a 500 ms pause (only black background), and the inter-trial interval was 1500 ms.

### 2.3 MR Data Acquisition

A 3.0 T MRI system (Siemens Trio Tim; Siemens Medical System, Erlanger, Germany) and a 12-channel phased array head coil were employed for the scanning. Foam padding and headphone were used to limit head motion and reduce scanning noise. 192 slices of structural images with a thickness of 1 mm were acquired by using a T1 weighted 3D MPRAGE sequence (TR = 1600 ms, TE = 3.28 ms, TI = 800 ms, FOV = 256 × 256 $mm^2$, flip angle = 9°, voxel size = 1 × 1 × 1 $mm^3$). Functional images were collected through a T2 gradient-echo EPI sequence (TR = 2000 ms, TE = 31 ms, flip angle = 90°, FOV = 240 × 240 $mm^2$, matrix size = 64 × 64). Thirty axial slices with a thickness of 4 mm and an interslice gap of 0.8 mm were acquired. The scanner was synchronized with the presentation of every trial.

### 2.4 Data Preprocessing

The preprocessing of fMRI data was implemented with SPM8 software (Wellcome Department of Cognitive Neurology, London, UK, http://www.fil.ion.ucl. ac.uk). The first two images were removed to allow the magnetization to approach dynamic equilibrium. A format convertion was conducted in order to make the fMRI data available for the SPM software, then a series of stages followed: realignment that aimed at identifying and correcting redundant body motions, coregister that merged the high resolution structural image with the mean image of the EPI series,

**Table 1.** Example of experimental tasks

| Task | Sequence of Presentation | | | | Button Pressing |
|---|---|---|---|---|---|
| AT | 46 | 32 | + | 78 | Left Hand (True) |
| ST | 46 | 32 | - | 13 | Right Hand (False) |
| MT | 46 | 32 | # | 46 | Left Hand (True) |

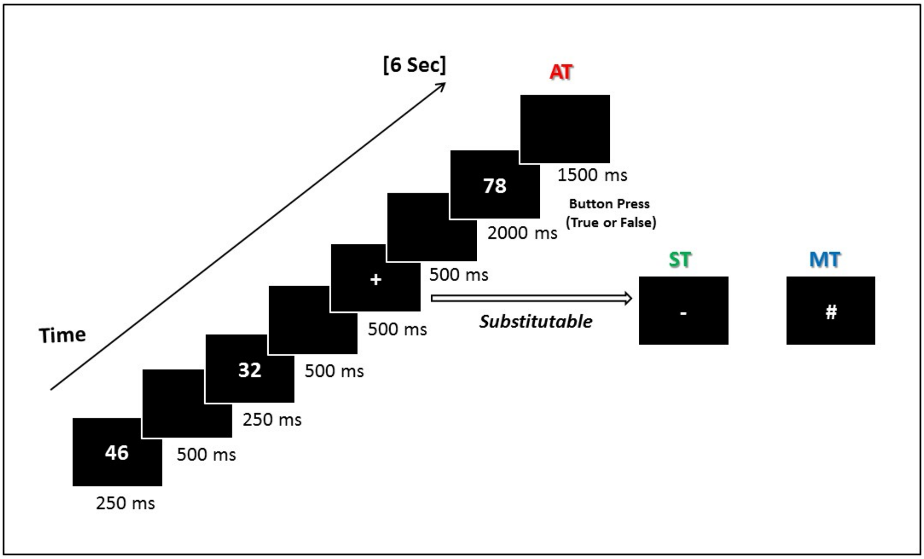


**Fig. 1.** Paradigm of stimuli presentation. Subjects should make a true or false judgment during the 2000 ms emergence of reference answer presented after the operation sign. Both accuracy (ACC) and reaction time (RT) would be recorded when subjects pressing the buttons. One trial lasted 6 seconds (3TR), 4 continuous trials with same kind of task constituted one block. The only difference among presentations of the 3 tasks is the operation signs.

normalization that adjusted the structural image to the MNI template and applied normalization parameters to EPI images, smoothing that had fMRI data smoothed with an 8 mm FWHM isotropic Gaussian kernel. After normalization, all volumes were resampled into 3×3×3 $mm^3$ voxels. Head movement was < 2 mm in all cases.

## 2.5 fMRI Analysis

Statistical analysis was performed on individual and group data using a general linear model as implemented in SPM8. Contrast images of individual subjects were firstly constructed based on the general linear model. In the level of group analysis, one-sample t-tests were performed for each voxel of the contrast images. Some responses irrelevant to the cognitive activities during tasks caused by body motion, breathing or heartbeats would be eliminated by the comparison with the baseline "NT". Regions common to the calculation across addition and subtraction were revealed by contrast of AT > NT in conjunction with ST > NT. More independent components of calculation were acquired by the comparison of AT > MT and ST > MT. A threshold of $p < 0.05$ with false discovery rate (FDR) corrected and minimum cluster size of $k > 10$ voxels was used to identify common regions and independent components for calculation. Finally, differences between addition and subtraction were shown by ST > AT (activations reported survived an uncorrected voxel-level intensity threshold of $p < 0.001$ with minimum cluster size of $k > 10$ voxels). Regions of activation originally obtained in MNI coordinates were converted into Talairach coordinates with the GingerALE and labeled with Talairach Daemon (BrainMap Project, Research Imaging Center of the University of Texas Health Science Center, San Antonio, USA, http://brainmap.org).

# 3 Results

## 3.1 Behavioral Results

One-way ANOVA was performed on the accuracy (ACC) and reaction time (RT) among the three tasks of AT, ST and MT for all trials. The average ACC for the AT was 94.9 ± 4.57 % (Mean ± SD), for the ST was 93.42 ± 5.79 %, and for the MT was 95.71 ± 3.79 %. The main effect of conditions was not significant, $F(2, 54) = 1.12$, $p = 0.334$. The average RT was 687.34 ± 96.71 ms for the AT, 714.61 ± 127.75 ms for the ST, and 725.67 ± 105.19 ms for the MT. The main effect of conditions was not significant either with $F(2, 54) = 0.604$, $p = 0.55$.

## 3.2 fMRI Results

**Common Regions of Activation.** All task conditions (addition task, subtraction task, and memory task) were compared to no task (NT) condition, and then a conjunction analysis was implemented on the comparison of AT > NT and ST > NT, to obtain the common regions of activation between addition and subtraction (see Table 2). Significant brain activation with threshold of $p < 0.05$ (FDR corrected) and $k > 10$ was observed in visual cortex and frontoparietal network including bilateral cuneus and fusiform, lingual gyrus on the right hemisphere; bilateral inferior parietal lobule, right superior parietal lobule, bilateral insula and superior frontal gyrus, precentral gyrus, inferior frontal gyrus, and medial frontal gyrus on the left hemisphere. Only increased activation was found. (see Figure 2).

**Components Specified for Calculation.** After the conjunction analysis, we focused on components specified for computing addition and subtraction respectively. Similarities between calculation processing of the two operations may uncover not only common regions of activation, but also close patterns or strategies for calculation. In order to extract and retain the cognitive components of calculation, redundant components (e.g. visual coding, information maintaining, button pressing, and so forth) were excluded by comparing AT and ST with MT (see Table 3).

**Table 2.** Common activation to addition and subtraction. The results were revealed by contrast of AT > NT in conjunction with ST > NT ($p < 0.05$, FDR corrected; $k > 10$). Loci of maxima are in Talairach coordinates in millimeters. LinG, lingual gyrus; FuG, fusiform gyrus; IPL, inferior parietal lobule; PrecG, precentral gyrus; IFG, inferior frontal gyrus; SPL, superior parietal lobule; mFG, medial frontal gyrus; SFG, superior frontal gyrus; L, left; R, right.

| Region | BA | Cluster | Talairach Coordinates | | | T-score |
|---|---|---|---|---|---|---|
| | | | x | y | z | |
| R. Cuneus | 17 | 624 | 18 | -93 | -1 | 8.66 |
| R. LinG | 17 | | 21 | -84 | 0 | 7.78 |
| R. FuG | 19 | | 27 | -83 | -10 | 6.61 |
| L. IPL | 40 | 250 | -43 | -45 | 38 | 6.85 |
| | | | -49 | -41 | 46 | 5.98 |
| L. Cuneus | 17 | 601 | -15 | -95 | -1 | 5.79 |
| L. FuG | 19 | | -23 | -86 | -11 | 5.75 |
| L. PrecG | 6 | 38 | -51 | 3 | 37 | 4.57 |
| | | | -46 | 0 | 31 | 4.01 |
| L. IFG | 9 | | -54 | 6 | 29 | 4.08 |
| R. IPL | 40 | 33 | 48 | -41 | 48 | 4.49 |
| | | | 40 | -49 | 47 | 3.60 |
| R. SPL | 7 | | 34 | -55 | 52 | 3.31 |
| L. Insula | 13 | 18 | -32 | 14 | 9 | 3.71 |
| R. Insula | 13 | 17 | 30 | 16 | 13 | 3.57 |
| L. mFG | 6 | 17 | -4 | 1 | 48 | 3.49 |
| L. SFG | 6 | | -2 | 10 | 49 | 3.31 |
| R. SFG | 6 | | 7 | 10 | 52 | 3.23 |

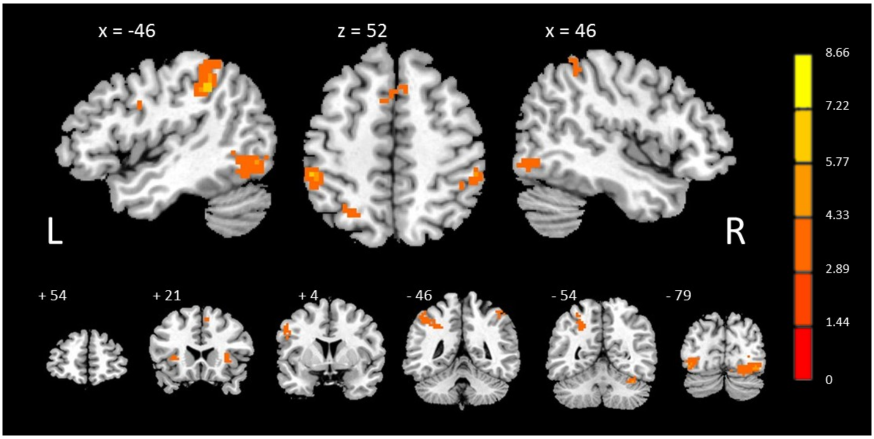


**Fig. 2.** Common activation to addition and subtraction revealed in MNI coordinates by conjunction analysis with the threshold of $p < 0.05$ (FDR corrected) and $k > 10$. Only increased activation was identified. Color bar indicates the t-score.

**Table 3.** Components for addition and subtraction identified by AT > MT and ST > MT ($p < 0.05$, FDR corrected; $k > 10$). VLPFC, ventral lateral prefrontal cortex; MFG, middle frontal gyrus; PCC, posterior cingulate cortex; Parahip, parahippocampal gyrus.

| Comparison | Region | BA | Cluster | Talairach Coordinates | | | T-score |
|---|---|---|---|---|---|---|---|
| | | | | x | y | z | |
| *AT > MT* | L. PrecG | 6 | 104 | -43 | -5 | 26 | 7.00 |
| | L. Insula | 13 | 79 | -26 | 16 | 12 | 6.64 |
| | L. Hippocampus | | 27 | -29 | -37 | 7 | 6.24 |
| | R. Caudate tail | | 165 | 24 | -40 | 13 | 6.09 |
| | R. Cingulate | 31 | | 24 | -47 | 23 | 5.78 |
| | R. Precuneus | 7 | | 26 | -67 | 29 | 4.80 |
| | R. Putamen | | 46 | 24 | 19 | 13 | 5.75 |
| | R. VLPFC | 13/ 47 | | 32 | 15 | -1 | 4.66 |
| | R. Insula | 13 | | 32 | 20 | 5 | 4.36 |
| | L. Precuneus | 7 | 82 | -24 | -52 | 43 | 5.43 |
| | R. Caudate | | 11 | 15 | -16 | 28 | 4.67 |
| *ST > MT* | R. Putamen | | 7049 | 24 | 19 | 13 | 9.08 |
| | L. MFG/ IFG | 46/ 45 | | -48 | 27 | 23 | 7.28 |
| | L. Insula | 13 | | -43 | 5 | 18 | 7.23 |
| | L. Precuneus | 7 | 1034 | -24 | -59 | 37 | 6.36 |
| | L. PCC | 30 | | -29 | -74 | 11 | 5.86 |
| | L. IPL | 40 | | -43 | -43 | 38 | 5.74 |
| | L. FuG | 37 | 66 | -45 | -52 | -11 | 4.29 |
| | R.Parahip | 30 | 27 | 21 | -40 | 7 | 3.78 |
| | R. LinG | 18 | 33 | 13 | -71 | 7 | 3.55 |

Addition components were revealed by contrast of AT > MT, including precentral gyrus and hippocampus on the left hemisphere, caudate tail, cingulate, putamen, ventral lateral prefrontal cortex, and caudate on the right hemisphere, and bilateral insula and precuneus. Similarly, subtraction components were revealed by contrast of ST > MT, including putamen, hippocampal areas, and lingual gyrus on the right side, and left insula extending to left middle frontal gyrus and inferior gyrus, in addition to precuneus, posterior cingulate, inferior parietal lobule, and fusiform gyrus on the left. Only increased activation was found (see Figure 3).

**T-Test between Addition and Subtraction.** In consideration of the possible complexity contained in subtraction relative to addition, one-sample t-test of ST > AT was implemented to investigate differences between the two operations (see Table 4). Subtraction showed stronger activation in the left inferior frontal gyrus (both BA44 and BA45), left precentral gyrus and bilateral insula; no decreased activation was found, which means the activation induced by addition was weaker all over the brain (see Figure 4). The threshold was adjusted into $p < 0.001$ (uncorrected) and $k > 10$ due to the tiny voxels survived through the comparison between AT and ST.

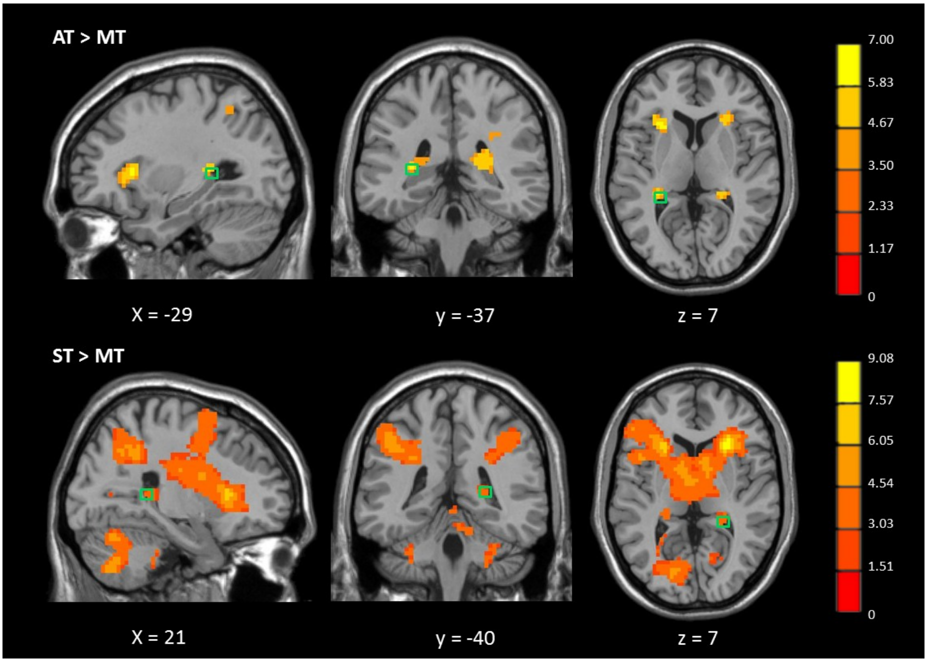


**Fig. 3.** Components for addition and subtraction respectively revealed by contrast of AT > MT and ST > MT with the threshold of $p < 0.05$ (FDR corrected) and $k > 10$ in Talairach coordinates. Only increased activation was identified. The top panel showed regions specified for addition calculation; bottom panel showed regions specified for subtraction calculation. The activation in hippocampal areas was highlighted with squares located at (-29, -37, 7) for addition and (21, -40, 7) for subtraction. Color bar indicates the t-score.

**Table 4.** Regions of activation revealed by contrast of ST > AT. Activations reported survived an uncorrected threshold of $p < 0.001$ with a minimum cluster size of 10 contiguous voxels.

| Region | BA | Cluster | Talairach Coordinates | | | T-score |
|---|---|---|---|---|---|---|
| | | | x | y | z | |
| L. IFG | 44/ 45 | 228 | -48 | 22 | 17 | 5.81 |
| L. Insula | 13 | | -40 | 24 | 18 | 5.4 |
| | | | -42 | 7 | 18 | 4.91 |
| R. Insula | 13 | 41 | 27 | 22 | 10 | 4.34 |
| L. PrecG | 6 | 13 | -49 | -1 | 42 | 3.99 |

## 4 Discussion

The regions activated in the present study corroborate some parts of results in relevant researches [3-6]. In general, the frontoparietal network is critical for both subtraction and addition. Furthermore, subcortical regions play an important part as well. The relationship between the two operations is complex because both the similarities and differences can be identified in the mean time.

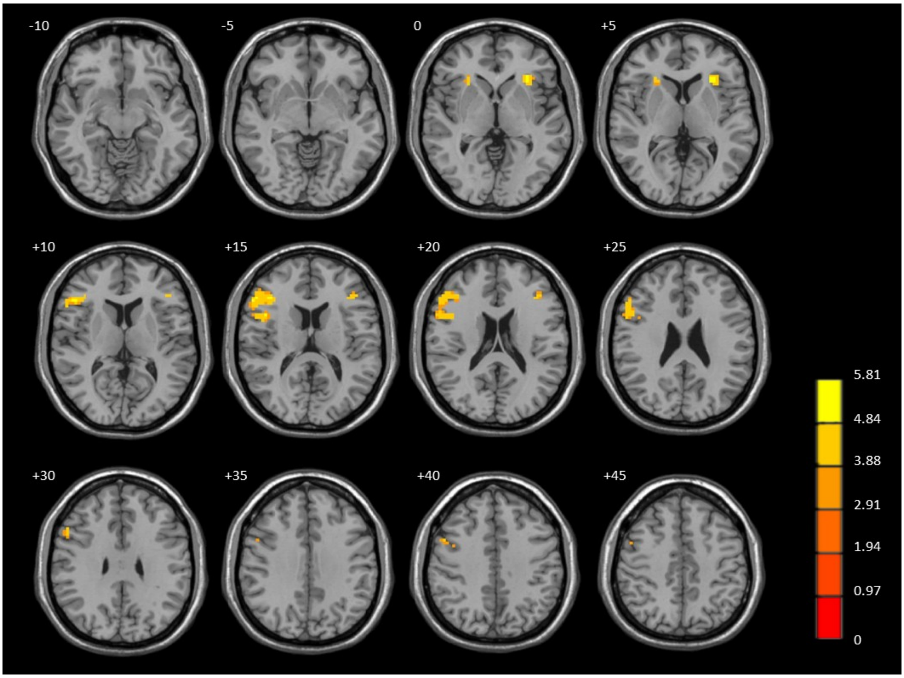


**Fig. 4.** Differences between addition and subtraction presented in the axial view. Subtraction showed significantly stronger activation in the regions of BA44 and 45 revealed by contrast of ST > AT with the threshold of $p < 0.001$ (uncorrected) and $k > 10$ in MNI coordinates. Color bar indicates the t-score.

### 4.1 Activation of IPS in Addition and Subtraction

Although researchers have come to an agreement on the participation of IPS in calculation tasks, conflicts still exist on whether addition calculation would activate the IPS. For instance, Rosenberg-Lee et al. reported no activation in parietal cortex during addition calculation when they compared the four basic operations [7]. Whereas Fehr and colleagues claimed the activation of left inferior parietal lobule during addition in a similar situation where they compared the common brain regions of the four operations [8]. One difference between the two studies is the form for presenting visual stimuli. The paradigm in the former experiment is to present the whole arithmetic equation and last for a period of time. The later experiment showed the stimuli separately like sequential series so that subjects had to retain each stimulus after interpreting it into verbal form rather than calculating automatically on basis of visual Arabic form depending on visual-spatial processing. Based on BI methodology that advocates systematic investigation on human information processing, strategies of problem-solving can also be referred. Subjects will be inclined to pick the easier and faster approach and avoid the regular number manipulation with IPS if conditions permit. Thus the current study that also required subjects to calculate on basis of information in verbal form obtained activation in the surface of bilateral parietal areas as well as the intra part of left parietal sulcus (IPS) as shown in Fig. 2 during calculating addition and subtraction. Of course, approaches to solve problems can be influenced by the circumstances. It is possible that subjects confined themselves to make real calculations on no matter addition or subtraction in the fMRI experiment.

### 4.2 Retrieval of Arithmetic-Facts in Addition and Subtraction

In the present study, subjects showed activation in the hippocampal areas even during the subtraction calculation indicating the retrieval strategy is not specialized for multiplication and addition, but also for subtraction. Cho et al. proposed the engagement of hippocampal-prefrontal network in children's fact retrieval during addition calculation [11]. Vincent et al. raised that hippocampal-cortical memory system was associated with recollection memory based on past experiences to make prospectively oriented decisions [12]. Taking the connection between direct retrieval and hippocampus into account, evident activation induced by subtraction in hippocampal areas when dealing with 2-digit (not 1-digit) simple problems in this study implies the application of retrieval strategy in subtraction may be more frequent than anticipated.

### 4.3 Differences between Addition and Subtraction

The Broca's Area (BA44, 45) was found activated significantly when conducting the contrast of ST > AT. It may be more an issue of connection than difference between addition and subtraction because no stronger activation found in addition than subtraction may suggest addition and subtraction share the fundamental neural substrates. And subtraction made something extra over the common base, which can be reflected into the activation of Broca's Area. In that way, what is the role of Broca's Area when the extra parts are processed in subtraction? It is likely that there is a close connection between subtraction and grammar as well as language expression [13, 14].

## 5 Conclusion

The activation of IPS in addition when visual-spatial processing is unavailable and the more frequent utilization of retrieval of arithmetic-facts in subtraction implies the calculation strategy is not the key point for distinguishing addition and subtraction. The two operations may share a common neural substrate; on the other hand, the dis-association appeared in Broca's Area indicates the differences between the two operations may concern grammar and language expression.

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