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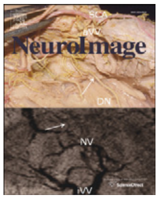

Is 2 + 2 = 4? Meta-analyses of brain areas needed for numbers and calculations

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ABSTRACT

Most of us use numbers daily for counting, estimating quantities or formal mathematics, yet despite their importance our understanding of the brain correlates of these processes is still evolving. A neurofunctional model of mental arithmetic, proposed more than a decade ago, stimulated a substantial body of research in this area. Using quantitative meta-analyses of fMRI studies we identified brain regions concordant among studies that used number and calculation tasks. These tasks elicited activity in a set of common regions such as the inferior parietal lobule; however, the regions in which they differed were most notable, such as distinct areas of prefrontal cortices for specific arithmetic operations. Given the current knowledge, we propose an updated topographical brain atlas of mental arithmetic with improved interpretative power.

Introduction

We use numbers to tell time, report quantities and to estimate how much things cost. Numbers can be represented with words (e.g., three), objects (e.g., ♥ ♥ ♥) or Roman and Arabic numerals (e.g., III or 3). Many functional neuroimaging studies have investigated the brain regions that support numerical processes, e.g., comparing quantities or performing arithmetic operations such as subtraction and multiplication. Extant reviews of numerical processes in the neuroimaging literature are based on qualitative reports (Ansari, 2007, 2008; Dowker, 2006; Neumarker, 2000; Nieder and Dehaene, 2009). As the field of functional neuroimaging has produced a substantial body of data, it is valuable and timely to compile this information using meta-analytical methods to provide a quantitative level of interpretation, which can help guide future studies.

Numbers are basic elements of mathematics which can be used for different operations such as counting, comparing quantities and ranking; number tasks do not involve calculations. In functional magnetic resonance imaging (fMRI) number task studies, stimuli were typically single digits which were later compared to other conditions such as single letters (Eger et al., 2003), arrays of dots that participants judged (e.g., based on size; Ansari et al., 2005, 2007) or a visual stimulus that signalled participants to generate random numbers (Daniels et al., 2003). Campbell (1994) argued that the way numbers are presented (i.e., words, numbers or pictures) plays a key role in the processing or estimating numerical magnitude, whereas other researchers proposed that stimulus format is not a major factor for estimating numerical quantities (Dehaene and Cohen, 1995; McCloskey, 1992). The hypothesis that numerical magnitude estimates are largely unaffected by stimulus format is also supported by neuropsychological models which posit that numerical quantity is expressed in an abstract format in the intraparietal sulcus (Ansari, 2007). The left intraparietal sulcus was shown to activate for quantity estimations independent of stimulus format, whereas the right intraparietal sulcus responded to quantity only when Arabic numerals were used (Ansari, 2007). Thus, in this meta-analysis the intraparietal sulcus, which lies between the superior and inferior parietal lobules, was expected to be a key area among studies that used numbers as stimuli.

Calculation tasks that utilize arithmetic operations, such as subtraction and multiplication, require the subject to identify number quantities and then modify them based on the operational function. Arithmetic decisions pose different cognitive demands based on the number of steps they require (Agostino et al., 2010). Most neuroimaging studies on arithmetic processing used single step arithmetic problems (e.g., $3+4$, $4-3$, 4×3) with one-digit or a combination of one and two-digit numbers (e.g., Fehr et al., 2007). Other arithmetic operations also include manipulating numbers in successive operations (e.g., $4-3+5$; Menon et al., 2000) or even solving integration problems (Krueger et al., 2008). In order to generate an answer, arithmetic operations generally require numbers to be monitored and manipulated. Activity in the prefrontal cortex has been linked to general-purpose cognitive functions such as working memory (Christoff and Gabrieli, 2000; Owen et al., 2005), with considerable emphasis on its role in monitoring or manipulating information, as required in calculation tasks. Researchers who study numerical processing and computations recognize that complex arithmetic tasks require more working memory resources than simple tasks (Fehr et al., 2007; Kong et al., 2005) and also report that training reduces the working memory load on the prefrontal lobes (Ischebeck et al., 2006).

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Theories of numerical cognition differ in their assumptions about the components and mechanisms that underlie mathematical abilities. The 'abstract-code' model represents functionally independent mechanisms for numeral comprehension and numeral production (McCloskey, 1992). In contrast the 'encoding-complex' model predicts that arithmetic operations are not mediated by abstract codes, rather they are influenced primarily by modality-specific processes (e.g., visual and phonological codes; Campbell, 1994). Unlike the 'abstract code' and 'encoding-complex' model, the 'triple-code' model makes specific predictions of the neuroanatomical correlates of functions and mechanisms that underlie mental arithmetic (Dehaene, 1992; Dehaene and Cohen, 1995, 1997). This is likely a major factor why this model is more frequently cited in functional neuroimaging studies, and it was claimed to be more predictive of data (Neumarker, 2000). Thus, we chose the 'triple-code' model as the comparison basis for the findings from the meta-analyses.

Specifically, the 'triple-code' model predicts that numbers are processed in three numerical surface formats: (1) a visual Arabic code represented by strings of digits, (2) an analogic quantity and magnitude code and (3) verbal code represented by words (Dehaene and Cohen, 1997), by distinct brain areas: (1) bilateral activity in inferior ventral occipito-temporal areas underlying visual Arabic code, (2) activity in inferior parietal areas underlying quantity and magnitude judgments and (3) the left perisylvian areas underlying verbal code. Within this framework, simple single-digit calculations can be solved either through a direct route using operands (e.g., 2×5) transcoded into verbal code (two times five), which would elicit the rote memory of this operation (e.g., two times five equals ten), or through an indirect semantic route in which the operands represent quantities on which semantically meaningful manipulations can be performed. The indirect route is typically taken when rote memory for a problem is unavailable, such as in subtraction problems (Dehaene and Cohen, 1997). The direct route is reported to elicit activity in the left cortico-subcortical loop through basal ganglia and thalamus, and the indirect route recruits areas in the inferior parietal cortex and the left perisylvian language network (Dehaene and Cohen, 1997). Thus, within this model, key regions for calculation tasks include bilateral inferior parietal areas responsible for semantic knowledge about numerical quantities, and the cortico-thalamic loop responsible for storing rote sequences of simple-arithmetic facts. Elementary operations applied on numbers rely on rote verbal memory and semantic manipulations associated with magnitudes. Dehaene and Cohen (1997) argued that addition and multiplication rely mostly on rote verbal memory (direct route), whereas subtraction relies mostly on quantitative manipulations (indirect route), and that these two processes are reflected in the brain as two main cortical networks for calculation. The role of the prefrontal cortex in this model was that of strategy choice and planning; hierarchical involvement of prefrontal regions and possible hemispheric asymmetries were not clearly specified.

Using activation likelihood estimation (ALE; Laird et al., 2005; Turkeltaub et al., 2002) we explored the brain areas involved in both number and calculation tasks and provide normative fMRI atlases for these processes in a standard stereotaxic space. In doing so, we first identified what brain structures participated in numerical and computational processes. Secondly we clarified brain structures that participated in processing different types of arithmetic operations (i.e., addition, subtraction and multiplication).

Materials and methods

Literature search and article selection

The literature was searched using the standard search engine of Web of Science (http://www.isiknowledge.com). We looked for keywords (fMRI, number and math) and (fMRI and arithmetic) to identify articles published between January 1st 1990 and January 31st 2009. These articles were also restricted to include human participants and be written in English. This search, which yielded a total of 268 studies, was subjected to two successive criteria to identify articles that used fMRI and number and/or calculation tasks; 155 were neither fMRI studies nor included a number or calculation task, and were excluded. The abstract review also revealed that 14 articles were case studies and 6 were reviews; these were also excluded. The resulting 93 studies were incorporated in a full text review. To preserve data interpretability, we only considered studies that included healthy adult samples with stereotaxic coordinates of whole-brain, within-group results using random effects analysis. Coordinates in these studies also had to be reported in Talairach or Montreal Neurological Institute (MNI) coordinates. Fifty-two studies survived these criteria. One of these studies performed two independent experiments (i.e., with different participants), thus there were a total of 53 datasets considered.

Meta-analysis

Activation likelihood estimation (ALE) is a quantitative meta-analysis method first proposed by Turkeltaub et al. (2002). This methodology was improved to perform multiple comparison controls and allow for contrasts among meta-analysis datasets (Laird et al., 2005). The resulting programme, GingerALE, is an application freely available for educational and scientific purposes by BrainMap (http://brainmap.org/ale/; Research Imaging Center of the University of Texas in San Antonio). It uses contrast coordinates (i.e. foci) compiled from different studies to generate probabilistic maps of activation related to the targeted domain. Derived values index the likelihood that at least one of the coordinates will fall within a voxel in the template stereotaxic space, thus estimating the degree of spatial overlap among coordinates. MNI coordinates were first transformed into Talairach space using the best-fit MNI-to-Talairach transformation (Lancaster et al., 2007). A typical protocol of smoothing and thresholding was used (Laird et al., 2005): full-width half maximum (FWHM) was set to 10 mm, ALE maps were calculated using 5000 permutations and multiple comparisons were corrected using false discovery rate (FDR) $q=0.05$ (see Laird et al., 2005 for more details on ALE method).

Probabilistic maps of activation were conducted for number tasks and calculation tasks separately, as well as three separate meta-analyses for the arithmetic operations (a) addition, (b) subtraction and (c) multiplication. If the original article reported more than one contrast in the target domain a single contrast was selected, as per the limitations of the statistical analyses. For all analyses there were sufficient foci ($n>100$) to be examined using ALE; this was not the case for division, as there were only two studies that included this operation (Fehr et al., 2007; Ischebeck et al., 2009). The meta-analysis for numerical processing included contrasts that examined distance effects (e.g., small>large) and numerical comparisons (e.g., number comparison>rest; Table 1); no contrasts using numbers in calculation tasks were included. Meta-analyses for addition, subtraction and multiplication included only contrasts that contained the corresponding arithmetic operation (e.g., addition>control task). Meta-analysis for calculation tasks included studies that used more than one calculation type in a single mathematical problem (e.g., $3+4-2$), as well as other operations such as division and integration (Table 1).

A conjunction process was employed to display results from the ALE maps associated with the three arithmetic operations, using AFNI (Cox, 1996). Activity related to each of the three operations was overlaid and displayed – using 3dcalc – such that common regions of activation shared a colour; for instance in red are regions common to addition, subtraction and multiplication.

Arithmetic operations activated regions that are also commonly reported in the working memory literature (e.g., Owen et al., 2005).

Table 1
Descriptive information of studies and contrasts used in the meta-analyses.

		Sample					Selected contrasts	
Author/s	Year	No.	F	Hand	Age	#Con.	Number tasks	Calculation tasks
Dehaene et al.	1999	7	4	R	25.0[a]	3		Exact > approximate
Chochon et al.	1999	8	4	R	25.0[a]	11	Comparison > control	Multiplication > digit naming
Lee	2000	11	5	R	30.0[a]	2		Multiplication > subtraction
Rickard et al.	2000	8	5	R	24	1		Multiplication verification
Le Clec'H et al. St1	2000	5	0	n/r	37	2	Numerals > body parts	
Le Clec'H et al. St2	2000	6	3	n/r	27	2	Numerals > body parts	
Menon et al.	2000	16	8	R	20.3	5		[b]3-s 3-operand > control
Stanescu-Cosson et al.	2000	7	4	R	24.0[a]	9		All calculations > letter matching
Prabhakaran et al.	2001	7	4	R	26	3		One- > 0-operations
Landro et al.	2001	12	n/r	n/r	32.5[a]	3	Respond to #7 > off block	Add until 2 digits = 10 > off block
Pinel et al.	2001	9	n/r	R	n/r	6	Arabic > verbal notation	
Menon et al.	2002	16	8	n/r	19.5[a]	1		Incorrect > correct
Simon et al.	2002	10	7	R	28	6		Subtraction > control
Daniels et al.	2003	8	4	R	25.4	2	Random number generation (rate 1 Hz)	
Delazer et al.	2003	13	6	R	30.5	3		[c]Untrained multiplication > number matching
Molko et al.	2003	14	n/r	n/r	24.3	3		Calculation tasks > rest
Hanakawa et al.	2003	16	8	15 R	28.0[a]	2		Mental operation > verbal rehearsal
Eger et al.	2003	9	5	R	27.9	5	Numbers > colours	
Delazer et al.	2004	13	n/r	R	n/r	2		Multiplication: untrained > trained
Gobel et al.	2004	12	12	R	26.7	2	Number comparison > rest	
Kawashima et al.	2004	8	4	R	44.1	3		Multiplication > control
Pinel et al.	2004	15	9	R	23.7	14	Number comparison > size comparison	
Piazza et al.	2004	12	n/r	R	23	2	Deviations in number of dots	
Audoin et al.	2005	10	7.2	R	26.6	1		Addition > control
Ansari et al.	2005	12	n/r	n/r	19.8	2	Distance effect: small > large	
Cohen Kadosh et al.	2005	15	7	n/r	27.8	9	Numerical > size	
Kaufmann et al.	2005	14	5	R	31.1	3	Numerical comparison > null events	
Kong et al.	2005	16	9	R	28	4		Addition with carrying
Venkatraman et al.	2006	20	n/r	R	n/r	4		[d]Base-7 addition
Ansari et al.	2006	14	8	R	21.3	3	Distance effect: small > large	
Ansari and Dhital	2006	9	3	R	19.8	2	Distance effect: small > large	
Ischebeck et al.	2006	12	8	n/r	26.8	9		Multiplication: untrained > trained
Cantlon et al.	2006	12	5	n/r	25	2	Number > shape	
Piazza et al.	2006	10	3	R	27.0[a]	3	Counting > matching	
Liu et al.	2006	12	7	R	31.5[a]	3	Number comparison tasks > baseline	
DePisapia et al.	2007	20	12	n/r	21.5	4		Mental arithmetic
Fehr et al.	2007	11	6	R	26.8	4		multiplication: complex > simple
Sammer et al.	2007	20	10	R	25.4	1		Addition > reference
Zhou et al.	2007	20	10	R	22.7	4		Multiplication large
Ansari et al.	2007	13	n/r	R	21.5	4	Conjunction: small & large symbolic	
Chen et al.	2007	20	10	R	22.7	1	Unmatched > matched numbers	
Cohen Kadosh et al.	2007	14	9	13 R	25.6	1	Size congruity effect	
Kansaku et al.	2007	13	7	R	31.0[a]	3	Large number counting	
Grabner et al.	2007	25	0	n/r	n/r	1		Multiplication: multi-digit > single-digit
Ischebeck et al.	2007	18	9	R	27.8	5		[e]Novel > repeated
Tan et al.	2007	22	9	R	n/r	7	Size judgment > motor task	[f]Numerical computation (CJ > J)
Piazza et al.	2007	14	n/r	R	n/r	4	Numerical deviants: far > close	
Kuo et al.	2008	12	6	R	25.0[a]	5		Single-addition > baseline
Kaufmann et al.	2008	12	6	R	33.2	4	Nonsymbolic numerical > baseline	
Krueger et al.	2008	18	5	R	25.3	1		Integration problem > font verification
Wood et al.	2008	17	0	R	24.2	1		Multiplicative > non-multiplicative
Zago et al.	2008	14	8	R	23.5[a]	7		Numbers manipulation > maintenance
Ischebeck et al.	2009	17	7	R	25	3		Multiplication: untrained > trained

No., number of participants; F, Female; R, right; #Con., number of reported contrasts; n/r, not reported.

[a] Middle value of age range.

[b] Participants had 3 s to complete 3 operand calculations.

[c] Untrained multiplication refers to multiplication problems on which participants did not receive training.

[d] Base-7 addition refers to addition problems in base-7 numeral system.

[e] Novel > repeated problem solving from the first third of the experiment.

[f] CJ = numerical computation and size judgment task, J = numerical size judgment task.

To examine hemispheric asymmetries we selected Brodmann areas (BA) in parietal and prefrontal regions that showed significant ALE values in all three operations. Anatomical masks in the left and right parietal lobe (BA 7 and BA 40) and left and right middle frontal gyrus (BA 9 and BA 46) were created using the anatomically defined template in AFNI (MNI N27 brain in Talairach space; Eickhoff et al., 2007). The masks were applied to the thresholded ALE maps and voxel-based hemispheric activations in these regions were calculated. The laterality index (LI = [Left − Right] / [Left + Right]) was deemed left dominant when LI > 0.20, and right dominant when LI < −0.20; values in-between were considered bilateral.

Results

Methodological information was extracted from each study. Table 1 shows demographic information of the datasets and selected contrasts of number and calculation tasks. A total of 698 participants took part in these studies. Nine studies did not report gender; of the remaining studies, 47.7% were female participants. The vast majority of the studies that reported handedness (79.25%) tested subjects who were right-handed (99.68%). Six studies did not report the age of the participants. When an age range was given, the median of the age range was used in calculating the average of the whole dataset, which was 26.3 ± 4.57 years. Just over half of the studies (54.7%) reported the education level of participants, of which 70.8% of the participants were reported to have some university education. Half (51%) of the studies reported that their participants received training before performing the task in the scanner. The number of contrasts reported ranged from 1 to 14 with the median being three. Twenty-five studies with 256 foci were included in the number tasks ALE analysis. Thirty-one studies with 403 foci were included in the calculation tasks ALE analysis. The analyses for addition, subtraction and multiplication included 12 studies (185 foci), 9 studies (136 foci) and 13 studies (112 foci), respectively.

ALE maps

Number tasks

Numerical processing was associated with significant ALE values in a set of brain areas, the majority being in the parietal lobes, particularly the inferior and superior parietal lobules (Table 2; Fig. 1a).

Calculation tasks

When performing arithmetic operations, collapsed across addition, subtraction, etc., concordant activity was observed in parietal regions similar to those in number tasks. However, unlike number tasks more prefrontal regions were active for calculation task, such as the middle and superior frontal gyri (Table 3, Fig. 1b).

Table 2
Concordant areas for number tasks.

Hem.	Brain area	BA	x	y	z	ALE	Vol./mm^3
L	Inferior parietal lobule	40	−34	−48	40	0.029	10,952
L	Superior parietal lobule	7	−26	−56	42	0.024	
L	Superior parietal lobule	7	−30	−64	54	0.016	
R	Inferior parietal lobule	40	36	−46	46	0.027	10,464
R	Superior parietal lobule	7	26	−58	42	0.023	
R	Inferior parietal lobule	40	44	−32	46	0.019	
R	Superior parietal lobule	7	32	−56	60	0.010	
R	Superior parietal lobule	7	28	−56	58	0.010	
R	Superior frontal gyrus	6	2	10	48	0.016	3264
L	Cingulate gyrus	24	−8	8	46	0.016	
L	Medial frontal gyrus	6	0	−2	60	0.012	
L	Middle frontal gyrus	6	−50	0	40	0.014	2096
L	Precentral gyrus	6	−42	−2	42	0.014	
L	Precentral gyrus	6	−48	0	32	0.013	
R	Insula	13	34	16	12	0.016	2024
R	Claustrum		28	20	0	0.014	
R	Precentral gyrus	6	48	0	36	0.016	1672
R	Inferior frontal gyrus	9	50	4	28	0.012	
L	Insula	13	−32	12	8	0.015	1336
R	Precentral gyrus	6	28	−14	56	0.019	1328
R	Cerebellum/anterior lobe		24	−56	−28	0.019	1160
L	Middle frontal gyrus	6	−26	−10	54	0.017	1080
R	Middle frontal gyrus	6	28	−4	42	0.013	736
R	Middle frontal gyrus	6	26	0	48	0.012	
R	Cingulate gyrus	32	8	24	40	0.012	640
R	Cingulate gyrus	32	12	18	34	0.011	
L	Fusiform gyrus	37	−38	−56	−10	0.013	520
L	Precentral Gyrus	6	−58	2	20	0.014	504
R	Supramarginal gyrus	40	54	−42	32	0.013	336
L	Lentiform nucleus/putamen		−20	6	14	0.012	272
L	Postcentral gyrus	3	−48	−18	44	0.010	256
L	Postcentral gyrus	3	−50	−18	52	0.008	
L	Cerebellum/pyramis		−26	−64	−28	0.012	184
R	Middle occipital gyrus	18	40	−80	−10	0.012	184
L	Cingulate gyrus	23	0	−20	30	0.012	168

Coordinates (x, y, z) are reported in Talairach convention; Hem., Hemisphere; L, Left; R, Right; BA, Brodmann area; ALE, Activation likelihood estimate; Vol., volume.

Table 3
Concordant areas for calculation tasks.

Hem.	Brain area	BA	x	y	z	ALE	Vol./mm^3
L	Precuneus	7	−28	−68	32	0.033	10,264
L	Superior parietal lobule	7	−26	−60	46	0.027	
L	Inferior parietal lobule	40	−44	−40	42	0.027	
L	Inferior frontal gyrus	9	−42	4	30	0.040	8888
L	Middle frontal gyrus	9	−44	32	28	0.024	
R	Superior parietal lobule	7	30	−62	44	0.037	6424
R	Inferior parietal lobule	40	38	−46	42	0.024	
R	Inferior parietal lobule	40	46	−34	46	0.017	
R	Sub-gyral	39	30	−58	32	0.016	
R	Inferior frontal gyrus	9	46	10	28	0.033	5960
R	Middle frontal gyrus	46	40	34	22	0.022	
R	Middle frontal gyrus	9	42	46	26	0.013	
R	Precentral gyrus	9	38	14	40	0.011	
L	Superior frontal gyrus	6	−6	8	48	0.027	4712
R	Cingulate gyrus	32	4	22	36	0.016	
L	Fusiform gyrus	37	−44	−60	−14	0.022	2960
L	Inferior occipital gyrus	19	−40	−74	−6	0.018	
L	Sub-gyral	6	−28	−2	56	0.026	2304
R	Insula	13	32	22	4	0.025	1600
L	Insula	13	−30	24	2	0.019	1328
L	Middle occipital gyrus	18	−22	−84	−2	0.019	1232
L	Inferior occipital gyrus	18	−28	−90	−10	0.014	
R	Caudate body		10	6	6	0.020	824
R	Cerebellum/declive		36	−58	−20	0.015	624
R	Middle frontal gyrus	6	30	−4	54	0.016	392
L	Superior frontal gyrus	10	−34	50	22	0.013	280
L	Cerebellum/posterior lobe		−38	−64	−36	0.013	264
L	Cerebellum/tuber		−38	−58	−28	0.012	
R	Thalamus		20	−28	8	0.013	112
R	Inferior occipital gyrus	18	32	−88	−6	0.013	104

Coordinates (x, y, z) are reported in Talairach convention; Hem., Hemisphere; L, Left; R, Right; BA, Brodmann area; ALE, Activation likelihood estimate; Vol., volume.

Addition

Solving addition problems specifically elicited significant ALE values in visual areas, parietal areas, frontal and prefrontal regions, as well as bilateral thalamus, right insula (BA 13), right claustrum and bilateral cerebellum (Table 4, Fig. 1c).

Subtraction

Completing subtraction tasks was also associated with ALE values in areas in occipito-temporal visual regions, parietal areas, frontal and prefrontal regions. Additionally, significant ALE values were observed in bilateral insula (BA 13) and right cerebellum (see Table 5, Fig. 1c).

Multiplication

Multiplication problems were associated with activity in occipito-temporal visual regions, parietal areas, temporal regions, frontal and prefrontal regions. Concordant activations across studies were also seen in bilateral cingulate gyrus (BA 32), bilateral thalamus, left claustrum, right insula, right caudate body and right cerebellum (Table 6, Fig. 1c).

Laterality indices

Laterality indices are presented in Fig. 2. When performing addition problems laterality indices for BA 7, BA 40, BA 9 and BA 46 were 0.43, 0.64, 0.31 and 0.55, respectively. Thus, all indices were positive and greater than 0.20 for addition, suggesting that the left hemisphere is dominant for solving addition problems. Subtraction problems were associated with laterality indices of 0.44, 0.44, 0.01, and 0.04 for BA 40, BA 9, BA 7, and BA 46, respectively; thus BA 40 and BA 9 were left hemisphere dominant, BA 7 and BA 46 were bilaterally activated, suggesting mixed hemispheric dominance for subtraction. Laterality indices for multiplication, however, were primarily right hemisphere dominant with BA 7, BA 40 and BA 46 sources yielding

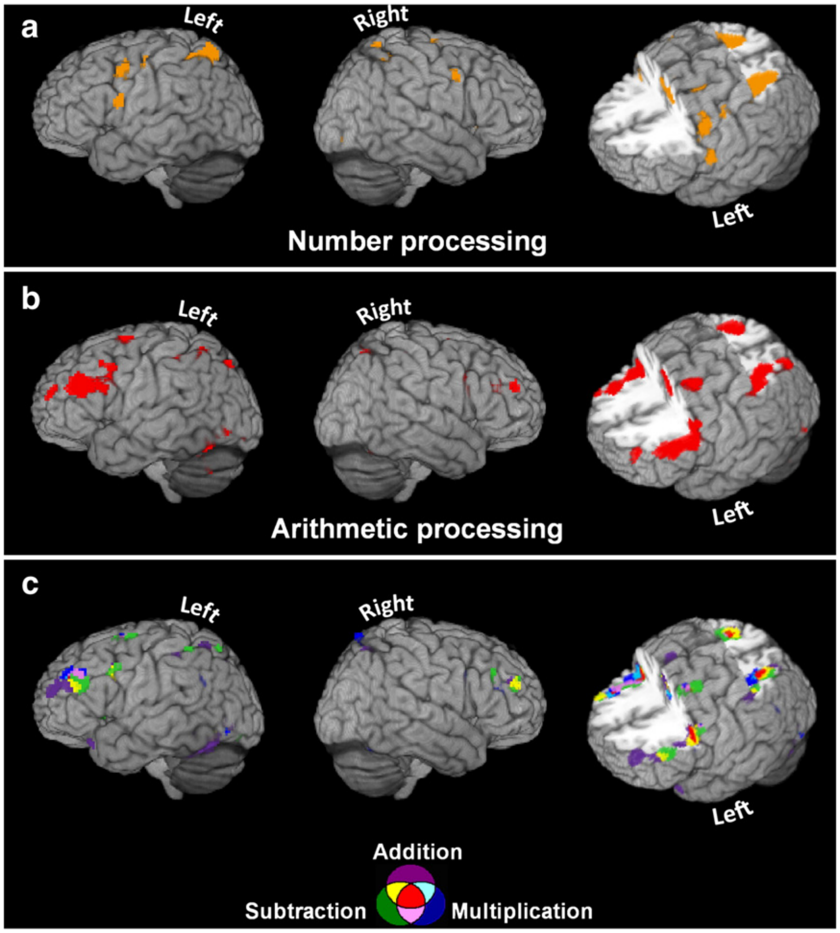

Fig. 1. Rendered ALE activation maps. (a) Brain areas activated during number tasks (brain areas listed in Table 2). (b) Brain areas activated during calculation tasks (brain areas listed in Table 3). (c) Conjunction display of brain areas activated separately by addition (purple), subtraction (green) and multiplication (blue) (brain areas listed in Tables 4, 5 and 6). Red signifies brain regions common to the three arithmetic operations; yellow signifies brain regions common to addition and subtraction; light blue signifies regions common to addition and multiplication; pink signifies brain regions common to subtraction and multiplication.

laterality indices of −0.42, −0.49 and −1, respectively; only BA 9 was left lateralized (0.29).

Discussion

Neurofunctional activity associated with number and calculation tasks was examined using quantitative ALE meta-analyses. There were three main findings from these meta-analyses:

(a) Although a large overlap existed among areas with significant ALE values during number and calculation tasks, the regions in which they differed were most notable, such as distinct areas of prefrontal cortices.
(b) Solving calculation tasks elicited ALE values in more prefrontal areas than solving number tasks. This difference suggests that solving calculations implicates more cognitive resources, such as working memory, than number tasks.
(c) Addition, subtraction and multiplication differentially recruited prefrontal and parietal regions in the left and right hemispheres: Activity was dominant in the left hemisphere for addition, it was either bilateral or left dominant for subtraction and was primarily right hemisphere dominant for multiplication.

In order to create a more complete normative atlas for mental arithmetic, we propose an update to a major model of mathematical processes, based on the findings of these meta-analyses.

Common areas to number and calculation tasks

Areas common to number and calculation tasks included core visual and oculomotor areas, fusiform gyri, inferior frontal gyri, cingulate gyrus, insula, cerebellum, superior parietal lobule and inferior parietal lobule (Figs. 1a and b). The core visual areas (e.g., inferior and middle occipital gyri, BA 18/19) were common across tasks (Tables 2 and 3), as in most of the paradigms the stimuli were visually presented. Similarly, eye movements present during visual tasks generate saccades (Anderson et al., 2007; Corbetta et al., 1998), which would elicit concordant activity in middle and superior frontal and precentral gyri (BA 6). This significant accord among studies on core visual and oculomotor regions was expected and served as a calibration measure of the technique and demonstrated the effectiveness of the meta-analytical method.

The left fusiform gyrus was also common to number and calculation tasks (Figs. 1a and b; Tables 2 and 3). As part of the occipito-temporal network, the fusiform gyrus is associated with encoding object properties such as colour, shape and texture (e.g., Allison et al., 1994; Ungerleider and Mishkin, 1982; Zeki and Marini, 1998) and object categorization (Martin, 2007). Previous studies showed that the left fusiform gyrus is responsive to orthographic structure during visual word recognition (Binder et al., 2006), leading researchers to suggest that the role of the left fusiform is to integrate features into elaborate schemes that represent whole words or objects (Starrfelt and Gerlach, 2007). The triple-code

Table 4
Concordant areas for addition.

Hem.	Brain area	BA	x	y	z	ALE	Vol./mm^3
L	Precuneus	19	−26	−70	32	0.023	5240
L	Superior parietal lobule	7	−28	−60	50	0.023	
L	Cerebellum/declive		−44	−62	−18	0.018	5128
L	Inferior occipital gyrus	19	−40	−76	−4	0.015	
L	Cerebellum/culmen		−36	−48	−26	0.012	
L	Sub-gyral	37	−50	−44	−8	0.010	
L	Inferior frontal gyrus	9	−42	6	30	0.020	3792
L	Middle frontal gyrus	46	−40	22	20	0.012	
L	Superior frontal gyrus	6	−6	10	48	0.020	3304
R	Superior frontal gyrus	6	4	−2	66	0.013	
R	Superior parietal lobule	7	34	−62	48	0.015	2600
R	Superior parietal lobule	7	28	−64	42	0.014	
R	Precuneus	7	28	−66	34	0.014	
R	Inferior frontal gyrus	9	46	8	28	0.019	1904
L	Inferior parietal lobule	40	−44	−40	42	0.020	1704
L	Sub-gyral	6	−24	−2	52	0.013	1512
L	Middle frontal gyrus	46	−46	38	24	0.014	1200
L	Superior frontal gyrus	10	−34	50	22	0.013	
R	Thalamus/ventral lateral nucleus		14	−12	16	0.011	1168
R	Thalamus		8	0	8	0.010	
R	Insula	13	34	20	4	0.013	992
R	Claustrum		32	8	10	0.012	
R	Middle frontal gyrus	9	42	44	26	0.013	648
L	Lingual gyrus	17	−20	−90	0	0.010	584
L	Lingual gyrus	18	−22	−80	−4	0.010	
R	Lingual gyrus	17	18	−88	−4	0.012	568
R	Middle frontal gyrus	6	30	−4	52	0.013	416
L	Inferior frontal gyrus	47	−32	26	2	0.010	408
R	Inferior parietal lobule	40	40	−44	40	0.012	296
L	Thalamus/ventral lateral nucleus		−18	−14	18	0.011	216
R	Cerebellum/culmen		38	−52	−26	0.010	160
L	Inferior frontal gyrus	47	−36	24	−16	0.008	136
L	Inferior frontal gyrus	47	−40	22	−20	0.008	

Coordinates (x, y, z) are reported in Talairach convention; Hem., Hemisphere; L, Left; R, Right; BA, Brodmann area; ALE, Activation likelihood estimate; Vol., volume.

model (Dehaene and Cohen, 1997) claims that the fusiform gyri, in both hemispheres, underlie visual number form. The current results suggest that this is the case only for the left fusiform. We propose that in both number and calculation tasks, the left fusiform plays a role in the visual recognition of the stimuli, assimilating features. The fact that the right fusiform gyrus did not show comparable activity may be attributed to the suggestion that right visual regions are biased towards global rather than local processing (Fink et al., 1997; Han et al., 2002). Thus, the right fusiform gyrus may process the apparent whole rather than features, which may explain its affinity for processing faces (Le Grand et al., 2003; McCarthy et al., 1997; Puce et al., 1995; Rhodes, 1993), but not for numbers that need to be processed locally.

Table 5
Concordant areas for subtraction.

Hem.	Brain area	BA	x	y	z	ALE	Vol./mm^3
L	Precuneus	19	−28	−64	40	0.018	5480
L	Inferior parietal lobule	40	−42	−48	48	0.012	
R	Superior parietal lobule	7	30	−58	42	0.027	4480
R	Inferior frontal gyrus	9	42	8	30	0.013	3344
R	Precentral gyrus	6	44	0	34	0.012	
R	Middle frontal gyrus	46	42	18	24	0.011	
R	Middle frontal gyrus	9	42	28	26	0.011	
L	Inferior frontal gyrus	9	−44	8	28	0.022	2440
L	Insula	13	−32	22	4	0.016	2384
L	Middle frontal gyrus	9	−44	32	28	0.019	1784
L	Superior frontal gyrus	8	0	16	52	0.016	1616
L	Cingulate gyrus	24	−8	6	44	0.007	
R	Insula	13	30	22	6	0.015	1584
L	Sub-gyral	6	−26	2	56	0.014	1504
L	Inferior occipital gyrus	18	−28	−90	−8	0.012	648
L	Inferior occipital gyrus	18	−34	−84	−14	0.007	
R	Middle frontal gyrus	10	42	44	24	0.011	576
R	Cingulate gyrus	32	4	22	32	0.012	456
L	Precuneus	7	−12	−70	50	0.012	448
R	Caudate body		14	8	6	0.011	432

Coordinates (x, y, z) are reported in Talairach convention; Hem., Hemisphere; L, Left; R, Right; BA, Brodmann area; ALE, Activation likelihood estimate; Vol., volume.

Table 6
Concordant areas for multiplication.

Hem.	Brain area	BA	x	y	z	ALE	Vol./mm^3
R	Inferior frontal gyrus	9	46	10	28	0.019	3784
R	Middle frontal gyrus	46	42	32	22	0.016	
L	Inferior frontal gyrus	9	−44	4	30	0.016	1704
L	Inferior frontal gyrus	44	−50	8	20	0.007	
L	Superior parietal lobule	7	−24	−60	44	0.013	1632
L	Superior parietal lobule	7	−30	−50	42	0.012	
R	Superior parietal lobule	7	20	−66	54	0.011	1504
R	Superior parietal lobule	7	30	−60	46	0.009	
L	Superior occipital gyrus	19	−30	−70	28	0.014	1392
L	Claustrum		−26	22	2	0.011	944
L	Middle frontal gyrus	9	−42	30	32	0.010	928
L	Middle frontal gyrus	9	−36	42	34	0.010	
L	Cingulate gyrus	32	−8	8	42	0.009	728
L	Medial frontal gyrus	6	−4	2	54	0.009	
R	Cingulate gyrus	32	6	20	38	0.011	672
R	Medial frontal gyrus	8	2	18	46	0.007	
L	Thalamus/medial dorsal nucleus		−8	−22	12	0.009	624
L	Sub-gyral	6	−28	0	56	0.010	600
R	Thalamus/pulvinar		22	−30	8	0.012	536
R	Cerebellum/culmen		34	−60	−24	0.010	496
R	Cerebellum/declive		28	−64	−16	0.007	
R	Inferior parietal lobule	40	36	−48	40	0.011	480
L	Fusiform gyrus	19	−38	−70	−8	0.008	440
L	Middle occipital gyrus	18	−46	−76	−10	0.007	
L	Thalamus		−16	−8	16	0.010	368
R	Insula	13	26	26	8	0.009	360
L	Superior temporal gyrus	39	−50	−58	28	0.009	344
R	Caudate body		14	0	20	0.008	272
R	Postcentral gyrus		46	−32	48	0.008	232
R	Inferior parietal lobule	40	44	−36	48	0.008	
R	Inferior occipital gyrus	18	32	−86	−4	0.007	104

Coordinates (x, y, z) are reported in Talairach convention; Hem., Hemisphere; L, Left; R, Right; BA, Brodmann area; ALE, Activation likelihood estimate; Vol., volume.

The inferior frontal gyri (BA 9) responded bilaterally to calculation tasks, whereas number tasks elicited concordance only in the right inferior frontal gyrus (Tables 2 and 3). Previous research showed that the inferior frontal lobes are active in visual working memory tasks (Song and Jiang, 2006) and regulate activity of the posterior cortices during visual input (Barcelo et al., 2000; Ranganath et al., 2003). BA 9 has been associated with higher cognitive monitoring and manipulation of information (Christoff and Gabrieli, 2000). Inferior frontal activity has also been associated with working memory, attention (Ischebeck et al., 2009; Zago et al., 2008) and task difficulty (Zhou et al., 2007) in calculation tasks. The triple-code model proposed that the frontal lobes underlie strategy choice and planning in mathematical processes (Dehaene and Cohen, 1997), but the model did not explain why these or other prefrontal regions would be preferentially activated for calculation tasks over number tasks. Consistent with previous reviews (Christoff and Gabrieli, 2000; Owen et al., 2005), we propose that the inferior prefrontal cortices are involved in processing information that requires simple cognitive operations (i.e., rules) or the processing of a few items in order to attain task solution.

The right cingulate gyrus (BA 32) was activated during number tasks (Table 2) and bilaterally activated for calculation tasks (Table 3). The cingulate gyri have been related to error monitoring (Taylor et al., 2007), integration of information (Devue et al., 2007) and resolving interference such as that present in a Stroop task (Peterson et al., 1999). Perhaps due to its functional topography – as it wraps around the corpus callosum – the cingulate gyrus' role is often interpreted as coordinating and integrating activity of multiple attentional systems (Peterson et al., 1999) and setting goals in multimodal functions (Turak et al., 2002). Within the current context, we suggest that the cingulate gyri implement cognitive goals by integrating available information.

The insula were active bilaterally for both number and calculation tasks (Tables 2 and 3). The insular cortices are located deep within the lateral fissure linking the temporal and frontal lobes and are known for their involvement in emotional processes (Britton et al., 2006; Calder et al., 2000; Gorno-Tempini et al., 2001; Heinzel et al., 2005; Paulus and Stein, 2006). The insula are also associated with execution of responses (Huettel et al., 2001), error processing (Hester et al., 2004) and were proposed to be part of a network hub (i.e., salience network) responsible for switching between other competing brain networks (i.e., executive-control network and the default-mode network) during information processing (Sridharan et al., 2008; Uddin and Menon, 2009). With the anterior cingulate gyrus, the insula can initiate motivated behaviours (Uddin and Menon, 2009). As their role may not be linked directly to the task at hand but rather to the experimental situation, where the participant must toggle between goal-directed and default-mode processes, insular contributions may be considered more generic.

Bilateral regions of the cerebellum were concordantly active during number and calculation tasks (Tables 2 and 3). The cerebellum is known historically for its involvement in motor functions. The cerebellum is associated with action sequencing (Buhusi and Meck, 2005) and is now implicated in a wide range of cognitive functions; in a recent ALE meta-analysis the cerebellum was concordantly activated by tasks that target language, spatial processing, working memory and executive function (Stoodley and Schmahmann, 2009). Studies on mathematics have reported cerebellar activity (Dehaene et al., 1999; Fehr et al., 2007; Grabner et al., 2007; Kong et al., 2005; Kuo et al., 2008; Piazza et al., 2007; Wood et al., 2008; Zago et al., 2008); however, its contribution was not systematically discussed. We suggest that the cerebellum, influenced by a prescribed plan of action or task goal, is involved in the coordination of visual motor sequencing particularly under conditions with time constrains, as are often required in number and calculation tasks.

Finally, our meta-analyses revealed concordant bilateral activity for numbers and calculations in the inferior and superior parietal lobules. Although, parietal activity is involved in a range of functions, it is an established finding in fMRI studies of mathematical cognition. Dehaene et al. (2003) distinguished three parietal circuits for number processing, (a) the bilateral intraparietal system associated with quantity representation, (b) the left angular gyrus associated with verbal processing of numbers, and (c) the posterior superior parietal lobule associated with attentional processes. The first, they describe as being almost 'category-specific' to number-related processes, the second and third were not specific to the number domain but part of verbal fact retrieval and attention systems, respectively, associated with calculations (Dehaene et al., 2003). Results from our meta-analyses cannot speak to these distinctions; however, activation likelihood scores related to inferior and superior parietal regions were the highest for number tasks (Table 2) and one of the highest for the calculation tasks (Table 3). Thus, the current data are consistent with the hypothesis (Dehaene et al., 2003; Dehaene and Cohen, 1997) that in number and calculation tasks, parietal regions may represent amounts symbolically or quantitatively.

Areas concordant only to number tasks

Activity in the left putamen was observed exclusively when processing number tasks (Table 2). The putamen, part of the basal ganglia, has been implicated in tasks of motor control (Marchand et al., 2008; Menon et al., 1998) and learning of stimulus–response associations (Packard and Knowlton, 2002). Furthermore, thalamo–cortico–striatal circuits have been characterized as a general-purpose seconds-to-minutes timing mechanism (Buhusi and Meck, 2005). The triple-code model places the putamen under the cortico-subcortical loop that includes the basal ganglia and the thalamus, in the left hemisphere. Our results also show that the significant contributions of left putamen occur in number tasks, whereas the caudate and the thalamus were involved in calculation tasks. Although our proposal needs further targeted experimentation, we suggest that the putamen's involvement in number tasks is to integrate information by pacing the coordination of top-down and bottom-up items.

The claustrum, a thin structure medial to the insular cortex, was active in the right hemisphere for number tasks (Table 2). Although not concordant among all calculation tasks, activity in this region was found in the right and left hemisphere for addition and multiplication, respectively (Tables 4 and 6). Although evidence on the functional contributions of the claustrum is lacking, the claustrum is linked to sequencing of inputs across different modalities and data types in order to elicit integrated conscious precepts (Crick and Koch, 2005), which could likely be its role in number tasks.

The left postcentral gyrus was concordant only among studies that used number tasks (Table 2). The traditional view of the postcentral gyrus function is its involvement in touch and kinesthesia. More recently, this cortical region has been associated with encoding by performing an action (Russ et al., 2003) and changes in visual percept in the absence of real or imagined motor response (Vanni et al., 1999). As this area was only active during number tasks, it may be that participants engaged in a kinesthetic representation of the stimuli to facilitate problem solution, or alternatively that the largely right-handed participants systematically engaged in subtle right hand or motor movement that aided their problem solving.

Areas concordant only to calculation tasks

Activity in the right caudate body was only observed in calculation tasks (Table 3). The caudate is part of the basal ganglia, implicated in higher-order motor control (Menon et al., 1998); recent evidence showed that the caudate also plays a key role in learning and memory (Graybiel, 2005; Nomura and Reber, 2008). The triple-code model suggests that the left caudate is involved in the retrieval of rote arithmetic facts (Dehaene and Cohen, 1995, 1997). The function of the right caudate in mathematical tasks has not been elucidated, although it has been implicated in early practice effects in mathematics (Ischebeck et al., 2007). We propose that the right caudate may play a role in assigning the priority values or sequence to information that needs to be processed; a similar role taken by the putamen in number tasks.

The right thalamus was also significantly concordant only among calculation tasks. The thalamus, located between the midbrain and the cortex, is known as the gateway to the cerebral cortex (Pinault, 2004), acting as a relay station between cortical and subcortical regions (Nadeau, 2008), being implicated in execution of responses (Huettel et al., 2001) and executive-control (Marzinzik et al., 2008). It has been suggested that thalamic gating affects cortico–thalamo–cortical (Nadeau, 2008) and cortico-cortical communications (Sherman and Guillery, 2002), a hypothesis that is in agreement with the notion that an *a priori* goal can influence the function of subcortical regions such as the basal ganglia and the thalamus. The anatomical and functional properties of the thalami are such that they allow communications among structures along temporal and spatial scales, as driven by neuronal attention-related demands (Pinault, 2004). According to the triple-code model, the thalamus is a critical component of a left cortico-subcortical loop that underlies visuo-verbal retrieval of arithmetic facts; however, the activity we observed was in the right hemisphere. We propose that the right thalamus, together with its subcortical neighbour, the caudate, may assign the priority value of the gateway for converging information.

Sub-gyral activity in BA 39, which encompasses the angular gyrus, was observed in the right hemisphere for calculation tasks as part of a larger cluster in parietal cortex (Table 3). There is general agreement that the left angular gyrus is involved in verbally-mediated processes (Price, 1998, 2000 for reviews), which also contribute to numerical cognition (Dehaene et al., 2003). Specifically, it is suggested to be involved in the verbal retrieval of numbers (Dehaene et al., 2003). Although right angular gyrus was found active in language tasks (Price, 2000) it has not received as much attention. For instance, a transcranial magnetic resonance study suggested that both left and right angular gyri are important for number representation, although the left hemisphere showed a larger effect (Gobel et al., 2001). Damage to the right angular gyrus was associated with hemispatial neglect (e.g., Hillis et al., 2005) and imaging studies showed that this same region was active for saccade production (Mort et al., 2003), as well as goal-directed salience representations (Zenon et al., 2010). Thus, in the case of calculation tasks, the right angular gyrus may be involved in visual–spatial attending processes required during problem solving which may also contribute to visual–spatial fact retrieval.

Activity in the middle frontal gyri (BA 9/46) were observed bilaterally only during calculation tasks (Table 3). These areas correspond roughly to the dorsolateral prefrontal cortex that is associated with attention and working memory (Arsalidou, 2008; Christoff and Gabrieli, 2000; Curtis and D'Esposito, 2003; Owen et al., 2005), particularly when externally generated information needs to be monitored and manipulated (Christoff and Gabrieli, 2000). In comparison to inferior frontal regions, the dorsolateral prefrontal cortices are involved when more coordination and cognitive control needs to be applied (Rypma et al., 1999). For instance, studies using calculation tasks demonstrated activity in the middle frontal gyri, which was attributed to working memory and procedural complexity (Delazer et al., 2003; Fehr et al., 2007; Kong et al., 2005; Simon et al., 2002; Zhou et al., 2007). It appears that the middle frontal gyri (BA 9/46) underlie general cognitive resources and are activated during tasks of increased complexity (i.e., calculation tasks compared to number tasks). In calculation tasks the numbers to be acted upon need to be held in mind and the operation applied on them. We propose that the application of operations (i.e., executive steps to be taken) occurs in the frontopolar cortex (discussed below), whereas holding and monitoring task-relevant information is controlled by the dorsolateral areas of the prefrontal cortex.

The left superior frontal gyrus (BA 10), part of the lateral frontopolar cortex, was also concordant only during calculation tasks (Table 3). As with other areas of the prefrontal cortex, frontopolar regions are reported to play a part in multiple cognitive functions. For instance, they are involved in voluntary decision making (Boorman et al., 2009), variable dimension-based attention (Pollmann et al., 2007), abstract relational integration (Green et al., 2006), attentional switching processes (Pollmann, 2001) and monitoring primary and secondary goals (Dreher et al., 2008). A common characteristic of these functions is the control of internally generated information (Christoff and Gabrieli, 2000), such as plans and goals. In a review, Ramnani and Owen (2004) described this region as coordinating outcomes of different cognitive operations in pursuit of a goal. Computing mental calculations fits with this interpretation, as typically more than one cognitive operation is needed to produce an outcome in calculation tasks (Furst and Hitch, 2000), whereas number tasks have fewer steps to arrive at a solution. Studies which utilize calculation tasks attribute frontopolar activity to goal and sub-goal coordination and its involvement in working memory (Audoin et al., 2005; DePisapia et al., 2007; Tan et al., 2007). Based on these previous reports that represent the frontopolar cortex as a region were executive goals are generated, we propose that for calculation tasks it generates sub-steps that can lead to the calculated solution.

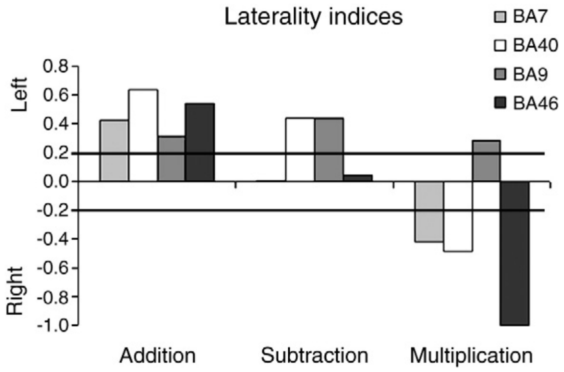

Fig. 2. Laterality indices for regions in the parietal and prefrontal cortex. Brodmann areas (BA) 7 and 40 lie in the parietal cortex, and BA 9 and 46 lie in the prefrontal cortex. For each arithmetic operation, a laterality index ($LI = [Left - Right]/[Left + Right]$) of activated voxels was calculated for each region. Black horizontal lines represent the criteria of laterality, whereby $LI > 0.20$ is deemed left dominant and $LI < -0.20$ as right dominant, values in-between were considered bilateral.

Laterality indices

Addition, subtraction and multiplication are well established operations in the repertoire of a typical adult. Parietal and prefrontal cortices play a key role in calculation tasks. Laterality indices showed hemispheric asymmetries in parietal (BA 7, BA 40) and prefrontal (BA 9, BA 46) regions, which were driven by mathematical operations (Fig. 2). Addition was left lateralized in the regions we examined, subtraction was bilateral (BA 40, BA 46) or left lateralized (BA 7, BA 9), whereas multiplication was right lateralized with the exception of BA 9.

Historically, the right hemisphere has been associated with spatial processing and the left hemisphere with verbal processing; however the picture is more complex than this. A recent hypothesis, particular to the prefrontal cortex, states that the prefrontal asymmetries are not merely domain-specific or material-specific, but instead vary on two distinct, continuous dimensions of verbalizability and imaginability (Casasanto, 2003). An alternative hypothesis states that hemispheric involvement is task driven such that left and right hemispheres process symbolic (i.e., mental) and signalic (i.e., perceptual-motor or automatized) information, respectively (Pascual-Leone, 1987, 1995). A similar interpretation in number processing was given by Piazza et al. (2007). The triple-code model (Dehaene and Cohen, 1995, 1997) claims that bilateral inferior parietal sulci are responsible for quantity manipulations (subtraction) and verbal arithmetic facts (addition and multiplication) are represented in the left hemisphere. Although, partially supported by our results, these interpretations do not fully explain our observations.

With the exception of BA 9, we observed a distinct pattern that shifted from left to right as we considered addition, subtraction and multiplication, in that order (Fig. 2). For instance, BA 7 activation was left lateralized for addition, bilateral for subtraction and right lateralized for multiplication. BA 40 was left dominant for addition and subtraction; albeit subtraction had a lower laterality index value. BA 46 also followed this left-bilateral–right pattern for addition–subtraction–multiplication. Thus, parietal regions appear to be following the same laterality trend with the left being the dominant hemisphere for addition and for subtraction at a lesser extent, and the right being the dominant hemisphere for multiplication. Prefrontal regions, however, reveal different results, driven by laterality indices of multiplication. For example, BA 46 exhibited a similar pattern to the parietal regions, while BA 9 was left-lateralised regardless of the arithmetic operation. Behavioural research shows that adults do not always use retrieval of simple-arithmetic facts (e.g., LeFevre et al., 1996a,b). For instance, apart from direct retrieval, arithmetic operations can also be solved using counting (e.g., $5 + 4 = \ldots 6, 7, 8, 9$)

and transformation (e.g., $5+4=5+5-1=10-1=9$; Imbo and Vandierendonck, 2007). Thus, this leads us to suggest that BA 9 may underlie a common process in the three operations, whereas BA 46 and the parietal regions were differentially affected and may be more influenced by the strategy adopted for solving each operation. Although, this may not be the case for more complex mathematical operations, for simple calculations, multiplication appears to be mostly automatized (right hemisphere), whereas addition and subtraction may entertain strategies such as counting and transformation.

Recommended update to the triple-code model

The triple-code model has stimulated substantial research in number and mathematical processes; however, the model needs to be updated. It has been more than a decade since the initial conception of the model, and the considerable increase in neuroimaging evidence should be considered. An update is primarily needed to account for regions that are concordant among studies, most of which are part of the working memory network (Fig. 3). Working memory is the ability to temporarily hold and manipulate relevant information in mind. Executive functions such as attention control and working memory play an important role in mathematical processing. Considerable behavioural evidence has demonstrated that working memory is correlated with mathematical performance (LeFevre et al., 2005; Raghubar et al., 2010, reviews) and is sustained by prefrontal cortex activity (Arsalidou, 2008; Christoff and Gabrieli, 2000; Owen et al., 2005). Working memory and relevant processes within working memory (e.g., storage and procedures) are not accounted for by the triple-code model. We suggest that such a revision to the model would greatly improve its interpretative power.

According to our meta-analyses, prefrontal activity is also readily observed during number and calculation tasks; however, their contributions can be differentiated. The prefrontal cortices act as a general resource to cognitive functions and their involvement is hierarchically organized (Christoff and Gabrieli, 2000; Owen et al., 2005). Using this hierarchical involvement hypothesis we propose a distinction for processing arithmetical information in the prefrontal cortex. We propose that prefrontal contributions are based on the difficulty of the task, which also generates testable hypotheses. The inferior frontal gyri are involved in processing simple numerical tasks that have only few storage or procedural requirements. If the task requires several cognitive procedural steps (e.g., carrying a number in 2-digit addition) or increased storage time or load, the middle frontal gyri (BA 46) are involved. Lastly, the medial and superior frontal gyri (BA 10) are involved in generating strategies for solving multi-step problems. For instance more activity should be elicited in this region by $(6\times12+8)$ than $(72+8)$.

Other concordant areas we suggest be included in the model are the dorsal cingulate gyri, the precentral gyri, the right angular gyrus, the insula and the cerebellum. The cingulate gyri play a key role in working memory processes (Arsalidou, 2008; Owen et al., 2005); particularly the dorsal subdivision was found to underlie cognitive rather than emotional processes (Bush et al., 2000). In visual tasks, as are typical in mathematics, the precentral gyri are critically involved in eye movements (Anderson et al., 2007). The right angular gyrus (BA 39) is involved in goal-directed salience representations (Zenon et al., 2010) and damage to this region leads to hemispatial neglect (Hillis et al., 2005). The insula is implicated in switching between working memory and default states during problem solving (Sridharan et al., 2008; Uddin and Menon, 2009), while the cerebellum is involved in

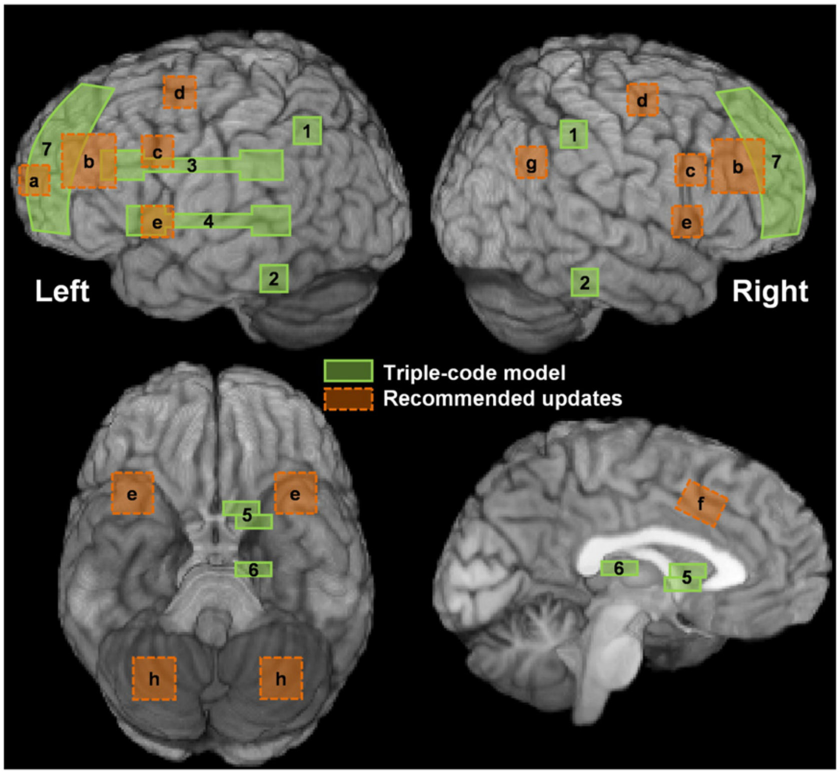

Fig. 3. Recommended updates to the triple-code model. We illustrate in green the schematized cortical locations of the triple-code model proposed by Dehaene and Cohen (1995, 1997); (1) Inferior parietal cortex: quantity representation, (2) Temporal cortex: visual number form, (3) Articulatory loop, (4) Verbal system, (5) Basal ganglia: arithmetic facts, (6) Thalamus: arithmetic facts, and (7) Prefrontal cortex: strategy choice and planning. In orange are additional schematic locations of areas concordant among studies, as demonstrated by these meta-analyses; (a) Superior frontal BA 10: goal, sub-goal creation, (b) Middle frontal BA 46: monitor more than a few items, (c) Inferior frontal BA 9: monitor simple rules or a few items, (d) Precentral gyrus: eye movements, (e) Insula: toggle goal-directed and default-mode processes, (f) Cingulate gyrus: implement cognitive goals, (g) Right angular gyrus: visual – spatial fact retrieval, and (h) Cerebellum: goal-directed, visual motor sequencing. Subcortical regions specific to meta-analyses of number or calculation tasks are not depicted.

multiple cognitive tasks including working memory (Stoodley and Schmahmann, 2009).

Limitations

The present paper focuses on brain regions that underlie solving number and calculation tasks via quantitative meta-analyses of results reported in the literature. We highlight that the data represent concordance across common domains (e.g., number tasks) that were derived within these categories over a range of contrasts. Optimally, results generated over identical contrasts should be analysed, as they would be less influenced by methodological factors. However, not enough studies report the same contrasts to accumulate adequate foci ($n > 100$) for sufficient statistical power for such specific meta-analyses. Also because of an insufficient number of foci, we could not investigate division as a fourth operation in the meta-analyses. Limitations specific to the ALE methodology include unaccounted differences in statistical approaches (e.g., statistical threshold) adopted by the original articles and spatial extent and magnitude of activation associated with each activation focus. These limitations are discussed in more detail elsewhere (Christ et al., 2009; DiMartino et al., 2009; Ellison-Wright et al., 2008). Despite these drawbacks, ALE has a number of advantages as a neurofunctional review method. With computational steps that are automatised, ALE allows for the quantification of locations of common activations among studies that may vary significantly in methodologies such as presentation intervals of the stimuli and whether they were block or event-related designs. The foci are thus reported by independent research groups using common domains (e.g., addition, multiplication) but different methodologies. It is common to observe diversity in methodology of functional imaging studies that leads to the diversity of findings. ALE provides a valuable alternative to traditional approaches for meta-analysis, and creates new avenues of revealing over-arching patterns and integrating large amounts of scientific information.

Conclusions

The ability to process numbers and perform computations relies on a large number of brain regions. For many years the triple-code model (Dehaene and Cohen, 1995, 1997) has provided a framework for research in mental arithmetic. We have demonstrated that mathematical performance emerges from areas extensively discussed and studied under this model; however, we also show that another set of areas, not part of this framework, demonstrate significant probabilities of being detected in number and calculation tasks, namely the cingulate gyri, the insula and the cerebellum. Another unaccounted part of this model is the hierarchical contribution of the prefrontal cortices as represented by working memory processes that appear essential in number and computation tasks. Our meta-analyses indicated that dorsolateral (BA 9, BA 46) and frontopolar (BA 10) areas of the prefrontal cortices are affected by the difficulty of the task. Although the function of these regions seems to be generic, their contributions to mental arithmetic need to be represented in a neurofunctional model of arithmetic, which we propose as an update to the triple-code model. There were also lateral asymmetries in the frontal activations that were process-specific; this will be an intriguing area of further research. We believe that the field of numerical and mathematical processes will benefit from this updated review and foundation, with a topographical atlas for mathematical processes in the healthy adult brain in standard stereotaxic space.

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