Understanding dissociations in dyscalculia
A brain imaging study of the impact of number size on the cerebral networks for exact and approximate calculation

Ruxandra Stanescu-Cosson,[1] Philippe Pinel,[1] Pierre-François van de Moortele,[1] Denis Le Bihan,[1] Laurent Cohen[1,2] and Stanislas Dehaene[1]

[1]*INSERM U334, Service Hospitalier Frédéric Joliot, CEA/ DSV, Orsay and* [2]*Service de Neurologie 1, Hôpital de la Salpêtrière, Paris, France*

Correspondence to: Stanislas Dehaene, Unité INSERM 334, Service Hospitalier Frédéric Joliot, CEA/DSV, 4 Place du Général Leclerc, 91401 Orsay cedex, France E-mail: dehaene@shfj.cea.fr

Summary

Neuropsychological studies have revealed different subtypes of dyscalculia, including dissociations between exact calculation and approximation abilities, and an impact of number size on performance. To understand the origins of these effects, we measured cerebral activity with functional MRI at 3 Tesla and event-related potentials while healthy volunteers performed exact and approximate calculation tasks with small and large numbers. Bilateral intraparietal, precentral, dorsolateral and superior prefrontal regions showed greater activation during approximation, while the left inferior prefrontal cortex and the bilateral angular regions were more activated during exact calculation. Increasing number size during exact calculation led to increased activation in the same bilateral intraparietal regions as during approximation, as well the left inferior and superior frontal gyri. Event-related potentials gave access to the temporal dynamics of calculation processes, showing that effects of task and of number size could be found as early as 200–300 ms following problem presentation. Altogether, the results reveal two cerebral networks for number processing. Rote arithmetic operations with small numbers have a greater reliance on left-lateralized regions, presumably encoding numbers in verbal format. Approximation and exact calculation with large numbers, however, put heavier emphasis on the left and right parietal cortices, which may encode numbers in a non-verbal quantity format. Subtypes of dyscalculia can be explained by lesions disproportionately affecting only one of these networks.

Keywords: parietal cortex; arithmetic; functional MRI; event-related potentials

Abbreviations: ANOVA = analysis of variance; ERP = event-related potential; fMRI = functional MRI

Introduction

Since the work of Henschen and Gerstmann, neuropsychologists have known that the left inferior parietal lobule plays an important role in mental calculation (Henschen, 1919; Gerstmann, 1940). Indeed, lesions of this region can leave the patient totally unable to perform even simple calculations such as 3 – 1 or 8 × 9 (Warrington, 1982; Takayama *et al.*, 1994; Dehaene and Cohen, 1997). Recent work in cognitive neuropsychology has begun to provide a more precise characterization of the functional contribution of inferior parietal cortex within the context of current cognitive models of number processing (Dehaene, 1992; McCloskey, 1992; Dehaene and Cohen, 1995, 1997). In the present study, we used functional MRI (fMRI) and event-related potentials (ERPs) in normal subjects to shed new light on this issue. We used a parametric design to examine the impact of number size on parietal activation and its modulation depending on the emphasis that the task places on quantity processing. A partial report of this work has appeared elsewhere (Dehaene *et al.*, 1999).

Functional imaging studies of arithmetic and the parietal lobe

Roland and Friberg (1985) were the first to observe bilateral inferior parietal and prefrontal blood flow increases during subtraction as opposed to rest using a primitive single-photon imager. These locations were later confirmed with fMRI (Burbaud *et al.*, 1995; Rueckert *et al.*, 1996; Pesenti *et al.*, 2000). The replicability of the parietal activation was

confirmed in a PET study of multiplication and comparison of digit pairs relative to a resting state (Dehaene *et al.*, 1996). Recently, we used fMRI during digit naming, comparison, multiplication and subtraction tasks compared with a letter naming control (Chochon *et al.*, 1999). All three mental calculation tasks, but not digit naming, yielded bilateral inferior parietal activation tightly localized to the banks of the intraparietal sulcus.

Two parametric studies also observed a direct relation between parietal lobe activation and number processing using ERPs. In one, the difficulty of a number comparison task was varied by changing the distance between the numbers to be compared (Dehaene *et al.*, 1996). In the other, the difficulty of a number multiplication task was modified by varying the size of the numbers involved (Kiefer and Dehaene, 1997). In both cases, the numerical parameter was found to modulate ERPs arising from the inferior parietal lobe, with a right-hemispheric bias during number comparison and a strong left-hemispheric lateralization during multiplication.

Despite this converging evidence for bilateral parietal activation, it can still be debated whether this region makes a specific contribution to calculation. In all of the above studies, the tasks requiring mental arithmetic were systematically more difficult than the corresponding control tasks, and were therefore likely to require increased attention and to place a greater load on working memory. Either of those factors, in themselves, could perhaps explain the inferior parietal activation. The first goal of this study, therefore, was to address this methodological criticism by contrasting tasks with similar levels of difficulty and demands on working memory, and to demonstrate that parietal lobe activation is a direct function of the emphasis that the task places on quantity processing.

Exact and approximate calculation

The second goal of the present study was to examine whether different cerebral networks are active during exact and approximate calculation. A dissociation between preserved approximation and impaired exact calculation was reported by Dehaene and Cohen (1991). Their patient N.A.U. had lost the ability to perform even extremely simple exact calculations, but could still approximate them. For instance, he repeatedly classified $2 + 2 = 3$ as correct, but was able to reject grossly false addition problems (e.g. $2 + 2 = 9$). Because N.A.U. had an extended left posterior lesion, Dehaene and Cohen (1991) tentatively speculated that the right hemisphere might play a special role in number approximation.

More recent theoretical and experimental work, however, suggests that the critical structures distinguishing between exact and approximate calculation might be the bilateral inferior parietal lobules. The triple-code model of number processing (Dehaene, 1992; Dehaene and Cohen, 1995) proposes that the left and right inferior parietal cortices contain an analogical representation of numerical quantity,

which is used to compare numbers and to perform simple quantity manipulations, including approximation. For calculations that call for the manipulation of a verbal representation of numbers, such as retrieving the result of a multiplication in rote verbal memory, the triple-code model proposes that humans rely on the perisylvian language areas of the dominant hemisphere. This rote verbal system would show a relatively greater involvement when an exact calculation result is needed.

Recently, Dehaene and Cohen (1997) have described a double dissociation compatible with this theoretical hypothesis. Two patients with normal number reading and writing, but with severe calculation deficits, were compared. One of them, with an inferior parietal lesion, was impaired in operations taxing quantity manipulation, such as subtraction and bisection of a numerical interval, but showed relative preservation of rote multiplication. Conversely, the other, with a left subcortical lesion and aphasia, was impaired in operations taxing rote verbal memory, particularly simple multiplication, while understanding of numerical quantities was preserved.

In the present brain imaging experiment with normal subjects, we further test this theoretical framework by comparing two numerical tasks with virtually identical input and output requirements, but with differing loads on exact and approximate calculation. We stress that this is a matter of relative emphasis rather than absolute specificity. Although exact calculation is not required during the approximation task, we cannot guarantee that subjects are in fact not occasionally performing it, especially as psychological evidence suggests that activation of addition facts is automatic and cannot be repressed (LeFevre *et al.*, 1988). Nevertheless, the prediction derived from the triple-code model is that the approximation task puts greater emphasis on the internal manipulation of quantities and their inter-relations, and therefore should yield relatively greater bilateral inferior parietal activation relative to the exact calculation task. Conversely, exact calculation should yield greater activation in a widespread left-hemispheric network including language areas.

The number size effect

The third goal of the present study is to identify which brain areas change their activation level when number size is varied. In both the exact and the approximation task, we compared small addition problems (with numbers ranging from 1 to 5) with large addition problems (numbers ranging from 5 to 9). Many, if not all, dyscalculic patients perform much better with operations involving small numbers, such as $3 + 1$ or 2×4, than with operations involving larger ones such as $8 + 7$ or 9×6 (e.g. McCloskey *et al.*, 1991). Number size is also a major determinant of calculation time and error rate in normal subjects (for review see Ashcraft and Stazyk, 1981; Ashcraft, 1992).

Interestingly, number size interacts with type of mental

operation (exact or approximate). Ashcraft and Stazyk asked subjects to verify simple additions (e.g. $2 + 3 = 9$) and systematically varied the size of the operands as well as the distance between the proposed result and the correct one (Ashcraft and Stazyk, 1981). The two factors interacted: as the distance increased, subjects began to reject the false problems by approximation, and the effect of problem size was reduced. At an extreme, for large problems with large distances (e.g. $7 + 8 = 93$), subjects did not compute the correct result and rejection was faster than with the corresponding correct solutions to problems. Ashcraft and Stazyk interpreted those results as indicating the presence of two mental processes: a fast approximation process running in parallel with the slower calculation of the exact result (Ashcraft and Stazyk, 1981).

Our study was designed to replicate the Ashcraft and Stazyk experiment but using a slightly different task. Based on their findings, we predicted that number size should have a strong effect on response times and on brain activation levels when subjects have to compute the exact result, but a significantly smaller effect on response times and brain activation levels when subjects rely on approximation. Brain areas showing such a task by size interaction should constitute the cerebral basis of the size effect in exact calculation.

Methods
Subjects
Seven healthy volunteers (four females, three males; age range 22–26 years) participated in the fMRI study, and twelve (seven females, five males; age range 22–28 years) in the ERP study. This research project was approved by the regional ethical committee, and all subjects gave their written informed consent. The subjects' right-handedness was confirmed by means of the Edinburgh inventory.

Procedure
Cerebral activation was studied for three experimental tasks: exact calculation, approximation and a letter-matching control. Tasks were presented in sequences of alternating blocks of trials, with a resting period inserted between each block (Fig. 1). Four such sequences were presented in semi-random order, two alternating exact calculations with letter matching, and two alternating approximations with letter matching. Each sequence comprised three numerical blocks in alternation with blocks of rest and letters. Within each numerical block, small problems (numbers from 1 to 5) were contrasted with large problems (numbers from 5 to 9). The subjects received instructions before each sequence, and a single word presented on the screen before each block reminded them of the forthcoming block type. They were not warned, however, of the alternation between small and large numbers.

Experimental tasks
Subjects fixated continuously on a small square. In each trial, an addition problem was flashed for 200 ms, with the plus sign centred and the operands 2° left and right of fixation. After another 200 ms fixation interval, two numerical choices were projected at the same location (see Fig. 1). The subjects held a button in each hand. For exact calculation, they had to select the correct sum for the addition by depressing the corresponding button as quickly as possible. They were told that, because the two choices were numerically very similar, they had to compute the exact addition result in order to respond correctly. For approximation, they had to select the most plausible number amongst two false results. Subjects were told that because one of the two choices was grossly false, they did not have to compute the exact addition result, but could rely on a coarse estimation. In the control letter-matching task, subjects were presented with letters instead of numbers and were asked to press the button on the side where a letter was repeated (Fig. 1). During the final rest periods, only the central fixation square appeared on screen.

Stimuli
For small problems, operands ranged from 1 to 5, and for large problems they ranged from 5 to 9 (see Appendix). Problems involving ties (e.g. $2 + 2$, $6 + 6$) were avoided because they show a smaller problem size effect (Ashcraft, 1992). For the exact task, the two alternatives proposed to the subjects were the correct result and a result that was off by at most two units. In 90% of exact problems, the wrong result was of the same parity as the correct result, thus preventing the use of a short-cut based on parity checking (Krueger and Hallford, 1984). For the approximation task, the two alternatives were a number off by one unit, and a number off by a larger amount (4.7 units on average). Note that the alternatives were always two single digits (range 2–9) for the small problems and two teen numbers (range 10–19) for the large problems. The spatial location of the larger operand of the addition, as well as the spatial location of the correct response, were randomly varied.

Control stimuli were designed by replacing each digit in the small problems by the corresponding letter in the alphabet (from A to J; letter I was excluded because of its similarity to digit 1), and replacing one of the alternatives with a letter repeated from the problem. Stimuli were presented visually using a video projector and a translucent screen (fMRI) or a standard PC screen (ERPs). The experiment was programmed using Expe5 software (Pallier *et al.*, 1997).

Imaging parameters
The fMRI experiment was performed on a 3T MRI system (Bruker, Germany). Functional images sensitive to blood oxygen level dependent contrast were obtained with a T_2^*-weighted gradient echo-planar imaging sequence [TR
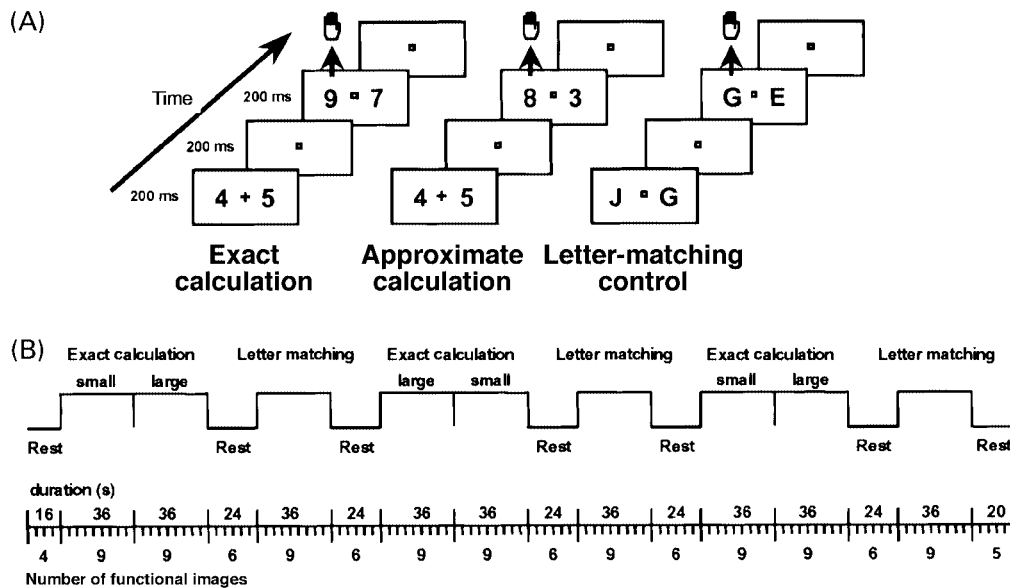
Fig. 1 (**A**) Examples of stimulus displays used in the three tasks (only problems with small numbers are shown). (**B**) Sample sequence of blocks used. Four such sequences were presented in semi-random order: two sequences alternating exact calculation with letter matching, and two sequences alternating approximation with letter matching, with additional counter-balancing of the ordering of blocks with small and large numbers.

(repetition time) = 4 s, TE (echo time) = 40 ms, angle = 90°, FOV (field of view) 192 × 256 mm, matrix = 64 × 64]. Thirty 5-mm thick axial cuts, covering the whole brain, were obtained every 4 s. In each sequence, 124 volumes were collected. The first four images of each sequence were excluded from the analysis. High-resolution images [3D gradient echo inversion-recovery sequence, TI (inversion time) = 700 ms, TR = 1600 ms, FOV = 192 × 256 × 256 mm, matrix = 256 × 128 × 256, slice thickness = 1 mm) were also acquired for anatomical localization.

Statistical analysis of fMRI data

All fMRI analyses were performed with Statistical Parametric Mapping, version 96 (SPM96). To correct for motion, the scans from each subject were realigned using as a reference, the image whose aquisition time was nearest to that of anatomical images. The images were then spatially normalized to Talairach space using the reference template of the Montreal Neurological Institute. A spatial smoothing of 5 mm (full-width at half maximum) was applied to the individual functional images (15 mm for the group analysis). The normalized functional images had voxels of $4 \times 4 \times 4$ mm^3.

Within each sequence, each type of block was modelled by two temporal basis functions for early and late activations. The time course of each voxel was thus modelled by a linear combination of 32 variables of interest (eight functions for each sequence). Twelve variables of non-interest implemented a high-pass filter set at 320 s. Statistical parametric mapping contrasts were used to examine the effects of task, number

size, and their interaction. Because each numerical task was acquired in a distinct block, between-task contrasts were defined as interaction terms. For example, to compare exact calculation with approximation we used the following interaction term: (exact calculation – its letter control) – (approximation – its letter control). Both individual and group analyses were performed. For the group analysis, data were averaged across subjects for each time point in each of the four experimental sequences, thus creating an 'average subject' data set which was then submitted to the same statistical analysis as an individual subject. The voxelwise threshold was fixed at $P < 0.001$, while the clusterwise threshold was $P < 0.05$ corrected for multiple comparisons across the brain volume. We report the results of the group analysis, together with the number of subjects showing a given effect.

Acquisition and analysis of ERPs

ERPs were sampled at 125 Hz with a 128-electrode geodesic sensor net referenced to the vertex (Tucker, 1993). We rejected trials with incorrect responses, voltages exceeding ±100 µV, transients exceeding ±50 µV, electro-oculogram activity exceeding ±70 µV, or response times outside a 200–2500 ms interval. The remaining trials were averaged in synchrony with stimulus onset, digitally transformed to an average reference, band-pass filtered (0.5–20 Hz), and corrected for baseline over a 200-ms window prior to stimulus onset.

We restricted the statistical analysis to a window of 450 ms following presentation of the operands, during which ERPs could only reflect processes associated with the computation
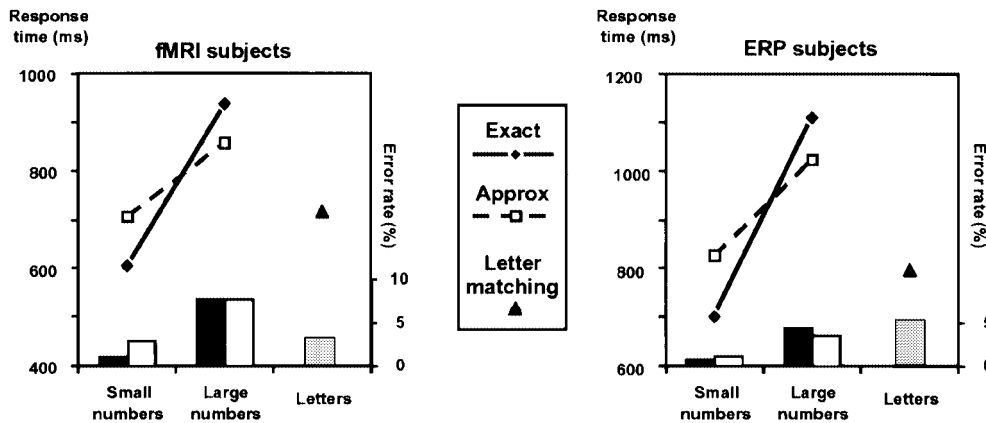
Fig. 2 Behavioural results during fMRI (left) and ERP recordings (right). Bars show error rates during exact calculation (filled), approximate calculation (open) and letter matching (grey).

Table 1 *Results of ANOVAs performed on reaction times*

Effect	fMRI study		ERP study	
	$F(1,6)$	P	$F(1,11)$	P
Task (exact versus approximation)	<1	–	<1	–
Number size	54.3	0.0003	26.7	0.0003
Task–size interaction	27.6	0.0019	18.9	0.0012
Size effect in approximation	19.7	0.044	13.3	0.004
Size effect in exact	69.8	0.0002	31.4	0.0002
Approx. with large numbers versus control	7.70	0.032	21.0	0.0004
Exact with large numbers versus control	18.8	0.0049	16.3	0.0019
Approx. with small numbers versus control	<1	–	<1	–
Exact with small numbers versus control	7.01	0.027	6.01	0.032

of the operation, but not with the proposed results. ERPs beyond 450 ms were not analysed because the stimuli were not as well matched (number size being confounded with the number of digits of the stimuli) and because differences in response time resulted in large differences in P3 latencies, which obscured other effects of interest. To identify periods with significant differences, experimental conditions were initially compared using sample-by-sample Kolmogorov-Smirnov tests, with a criterion of $P < 0.05$ for five consecutive samples on at least eight electrodes simultaneously. This allowed us to select pairs of symmetrical left and right electrodes where a given effect was maximal. Voltages from these electrodes, averaged over five consecutive samples (40 ms), were entered into a repeated-measures analysis of variance (ANOVA) with task, number size and hemisphere as within-subject factors.

Scalp topographies were visualized using 2D maps constructed by spherical spline interpolation (Perrin *et al.*, 1989). To aid in the spatial localization of sources, dipole models were generated with BESA99 for Windows (Scherg and Berg, 1990). In an earlier short report (Dehaene *et al.*,

1999), we used the earlier DOS version of BESA, which limited us to analyses of 60 electrodes only; the new version allowed us to analyse the full topography derived from 128 electrodes, hence the small differences with our previous results. To constrain the models, three fixed dipoles were placed at locations where the most important fMRI effects were observed during calculation tasks: the left inferior frontal region and the bilateral parietal region. The programme then selected the dipole orientation and strength to match the scalp topography on a five-sample window (40 ms) surrounding the time point of interest. We then attempted to simplify this model by keeping only dipoles with the strongest contribution. In only one case (modelling of an early visual effect contemporaneous with the visual N1) did this approach appear inappropriate, and a single dipole model was used instead. We stress that dipole models, which are based on a spherical four-shell approximation of the head, can only represent coarse and indicative estimates of brain activity.

Results
Behavioural results
The subjects' individual error rates did not exceed 5.4% in fMRI and 3.6% in ERPs. A 2 × 2 ANOVA was performed on the mean correct response times, with operation (approximation or exact calculation) and number size as within-subject factors (see Fig. 2 and Table 1). There was no main effect of operation, indicating that the two tasks were matched for difficulty. A main effect of number size indicated that subjects were slower with large numbers than with small numbers (242 ms in fMRI, 309 ms in ERPs). Importantly, the two factors showed interaction. Although the number size factor reached significance in both the approximation and the exact calculation tasks, it had a significantly larger effect in exact calculation than in approximation. A similar ANOVA on error rates revealed only a main effect of number size, with no difference between operations and no interaction.

Next, we compared performance in the four numerical

Table 2 *Activation loci during all calculation tasks relative to letter matching*

Cortical area	Talairach coordinates			Z	No. of voxels	No. of subjects
	x	*y*	*z*			
L dorsolateral prefrontal cortex	–52	12	24	7.51	90	6
	–48	16	48	4.42		
R intraparietal sulcus	32	–64	44	7.35	181	7
	48	–36	48	7.29		
	32	–60	28	5.45		
R dorsolateral prefrontal cortex	48	44	24	7.20	427	6
	40	16	40	7.07		
R inferior frontal gyrus	44	32	–4	6.95		6
L intraparietal sulcus	–40	–56	48	6.44	47	5
	–60	–44	48	4.41		
L inferior frontal gyrus	–52	44	0	5.63	72	5
	–60	40	16	4.07		
	–52	44	28	4		
L cingulate gyrus	–8	32	52	5.47	50	6
	–4	24	56	4.8		
R cuneus	4	–76	8	4.33	47	2

L = left; R = right

tasks with the letter-matching control. The two blocks with large numbers tended to be more difficult than the control. This was significant for response times (Table 1), and non-significant differences were found in the same direction for error rates. With small numbers, however, approximation did not differ from the control on response time, and if anything tended to be easier than the control, when error rate was used as a measure [$F(1,6) < 1$ in fMRI; $F(1,11) = 10.5$, $P = 0.008$ in ERPs]. Finally, exact calculation with small numbers was easier than the control, as measured by response time as well as by error rate [$F(1,6) = 6.25$, $P = 0.047$ in fMRI; $F(1,11) = 16.4$, $P = 0.0019$ in ERPs].

These behavioural results imply that in the functional imaging analysis, two comparisons were unaffected by task difficulty confounds: either comparing exact calculation with approximation directly, or comparing the tasks with small numbers with the letter control.

fMRI results

Number versus letter processing

In a comparison of all number processing tasks with letter matching, the activated areas were the banks of the left and right intraparietal sulci, the bilateral dorsolateral and inferior frontal gyri, the left cingulate gyrus, and the right cuneus (Fig. 3 and Table 2). All of these areas, except the right cuneus, were also significantly activated in letter matching relative to rest ($P < 0.001$). During tasks with small numbers relative to the letter control, we found significant activations of the right dorsolateral and inferior frontal gyri, right intraparietal sulcus and right precuneus (Fig. 3 and Table 3).

Exact versus approximate calculation

In exact calculation versus approximation (Table 4 and Fig. 4), significant activations were in the left anterior inferior

frontal region, left precuneus, right parieto-occipital gyrus, bilateral angular gyri and right middle temporal gyrus. All of these peaks remained significant when only the blocks of exact calculation with small numbers were contrasted with the letter matching control ($P < 0.05$). In approximation versus exact calculation (Table 5), activation was found in the left and right intraparietal sulci, the right precuneus, left and right precentral sulci, left dorsolateral prefrontal cortex, left superior prefrontal gyrus, left cerebellum, and left and right thalami. Again, all of these peaks were activated even when only the approximation blocks with small numbers were compared with letter matching ($P < 0.05$).

The left basal ganglia have been tentatively implicated in the rote verbal retrieval of exact arithmetic facts (Dehaene and Cohen, 1995). Although no basal ganglia activations were found in the above tasks, this could be due to the significance threshold, which required 35 contiguous active voxels. We therefore searched the basal ganglia for activation at $P < 0.001$, uncorrected, with a threshold of only three contiguous voxels. Only a small cluster of three voxels in the left putamen showed greater activation during exact rather than during approximate calculation ($-24, 4, -4; Z = 3.27$). No subcortical activation was observed in the converse contrast.

Problem size effect in exact and approximate calculation

We first compared large versus small numbers in the exact calculation task (Table 6 and Fig. 5). The activated areas were the left and right intraparietal sulci, left inferior frontal gyrus (in its posterior sector, close to Broca's area), left precentral sulcus, right dorsolateral prefrontal cortex and bilateral cingulate gyri. This network overlapped considerably with the one observed during approximation relative to exact calculation. The bilateral intraparietal and left precentral
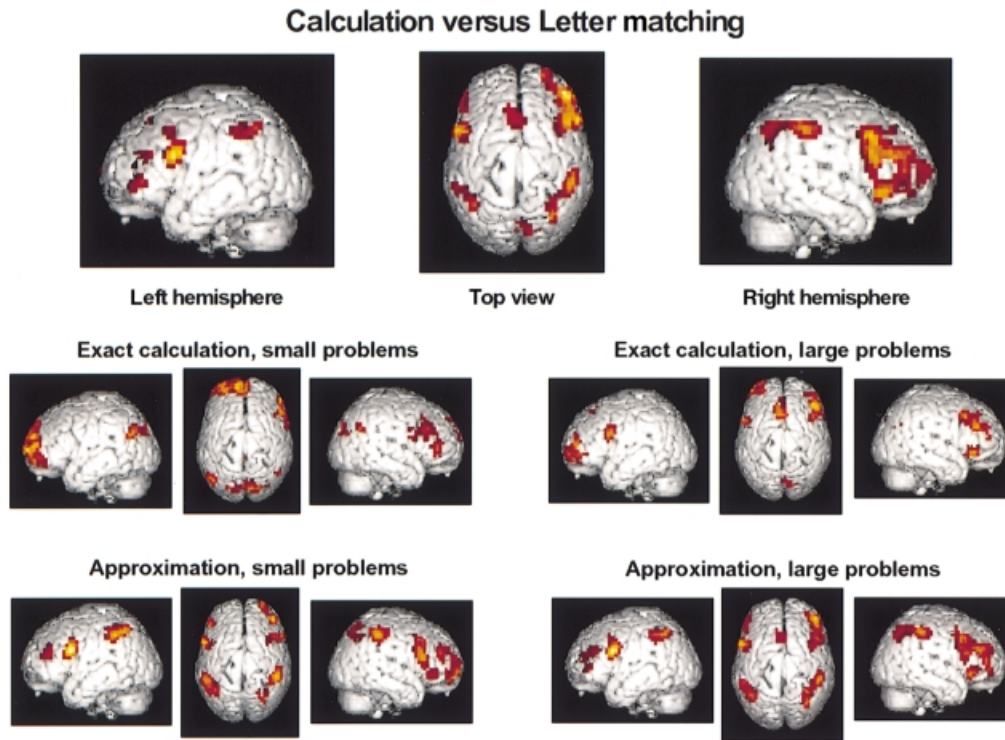
Calculation versus Letter matching

Left hemisphere   Top view   Right hemisphere

Exact calculation, small problems   Exact calculation, large problems

Approximation, small problems   Approximation, large problems

Fig. 3 Areas showing greater activation during calculation than during the letter-matching control. The top images show the global contrast of all calculation tasks relative to control. The smaller images show this contrast separately for each task and number size.
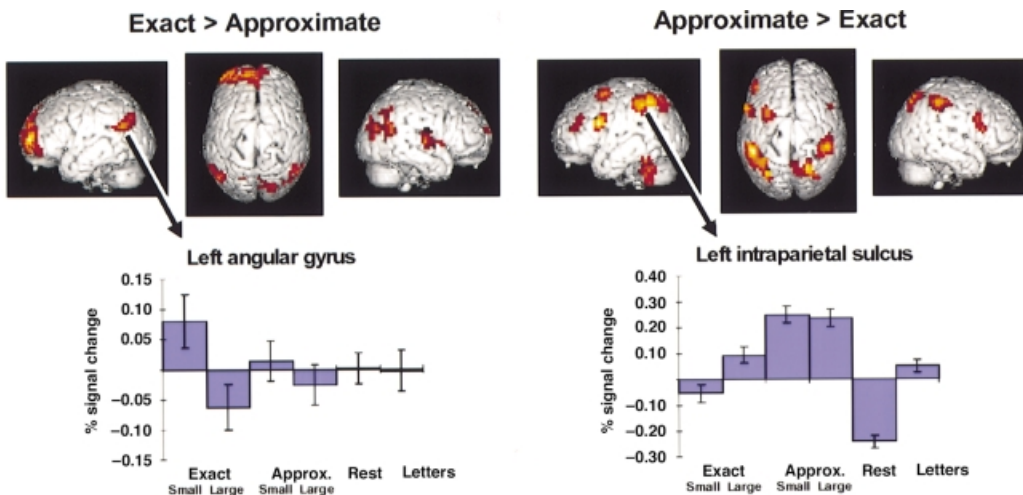

Exact > Approximate   Approximate > Exact

Left angular gyrus   Left intraparietal sulcus

Fig. 4 fMRI differences between exact and approximate calculation. Histograms indicate percentage signal change in the different conditions relative to the grand mean over the entire experiment in two neighbouring regions of the left parietal lobe with distinct profiles.

activations coincided exactly in both comparisons at $P = 0.001$, and all the peaks in which a problem size effect was observed during exact calculation also showed significantly greater activation during approximate than during exact calculation at $P = 0.05$. Hence, although different networks are used for exact and approximate calculation, increasing number size during exact calculation recruits the cerebral areas implicated in approximation.

To clarify the functional roles of the elements of this

network, we examined in what areas the problem size effect was larger during exact calculation than during approximation, as found in the behavioural response times analysis. In three areas, the appropriate interaction term was found to be significant: left intraparietal sulcus (–36, –44, 44; $Z = 4.27$), left precentral sulcus (–52, 8, 28; $Z = 4.75$), and left inferior frontal gyrus, again close to Broca's area (–40, 28, 4; $Z = 3.69$). These areas, which form only a left-lateralized subset of those showing a size effect during exact

Table 3 *Activation loci during calculation with small numbers relative to letter matching*

Cortical area	Talairach coordinates			Z	No. of voxels	No. of subjects
	x	*y*	*z*			
R dorsolateral prefrontal cortex	56	20	28	6.06	204	5
	48	44	24	5.7		
	44	20	40	5.34		
R intraparietal sulcus	48	−36	48	5.73	37	4
R precuneus	4	−68	32	4.56	48	1
	12	−80	36	4.35		
	20	−76	28	4.29		

R = right.

Table 4 *Sites of greater activation during exact calculation than during approximation*

Cortical area	Talairach coordinates			Z	No. of voxels	No. of subjects
	x	y	z			
L middle frontal gyrus	−32	64	4	7.53	329	4
(inferior part)	−40	60	−4	7.06		
L antero-mesial prefrontal cortex	−8	60	16	6.14		5
L precuneus	−8	−56	20	5.64	353	3
R parieto-occipital sulcus	20	−80	28	5.27		2
R angular gyrus	40	−76	20	5.07		2
L angular gyrus	−44	−72	36	4.99	99	4
	−44	−64	24	4.98		
	−60	−64	−28	4.65		
R middle temporal gyrus	48	−16	8	4.68	106	1
	56	−12	8	4.57		
	68	−12	0	4.06		

L = left; R = right.

Table 5 *Sites of greater activation during approximation than during exact calculation*

| Cortical area	Talairach coordinates			Z	No. of voxels	No. of subjects
	x	*y*	*z*			
R intraparietal sulcus	44	−36	52	6.37	134	3
	36	−36	44	6.34		2
R superior parietal lobule	20	−60	60	6.03	114	4
	28	−72	52	5.08		
R precuneus	4	−60	52	4.99		3
L intraparietal sulcus	−56	−44	52	5.96	215	5
	−48	−40	44	5.71		
L superior parietal lobule	−32	−68	56	5.1		3
L precentral sulcus	−56	12	24	5.81	86	5
R precentral sulcus	48	16	20	4.8	51	4
	48	12	28	4.74		
L superior frontal gyrus	−32	8	64	4.75	45	2
L cerebellum	−48	−48	−28	4.74	95	5
	−48	−56	−40	4.56		
	−40	−52	−52	4.12		
L dorsolateral prefrontal cortex	−44	64	12	4.46	57	4
	−36	68	16	4.43		
	−48	36	32	4.12		
R thalamus	12	−16	16	4.43	45	1
L thalamus	−20	−8	16	4.04		1

R = right; L = left.
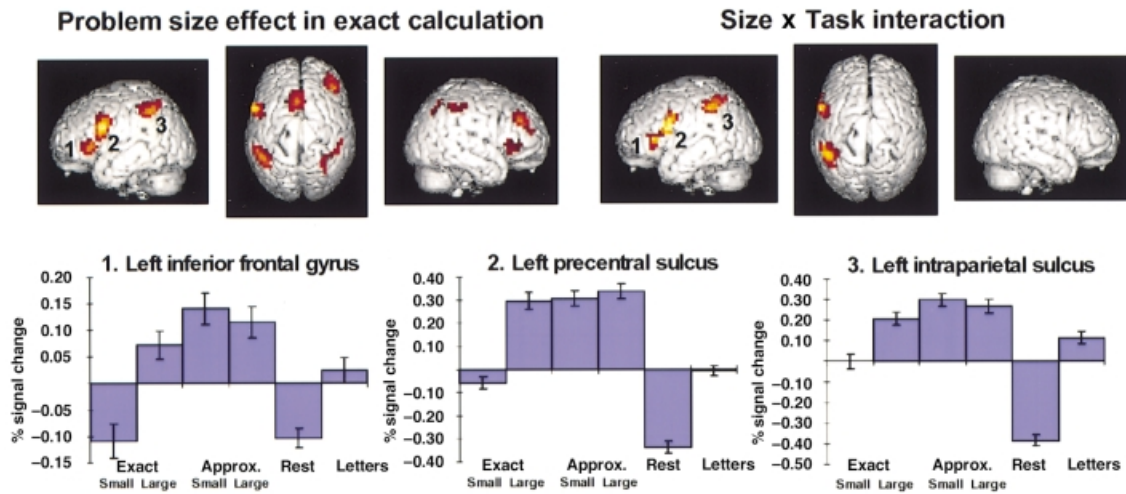
Fig. 5 Effect of problem size on brain activation patterns. *Top row*: areas showing greater activation in response to large than to small numbers during exact calculation. *Bottom row*: interaction of size and task, showing areas where a greater problem size effect was found in exact than in approximate calculation, paralleling behavioural results.
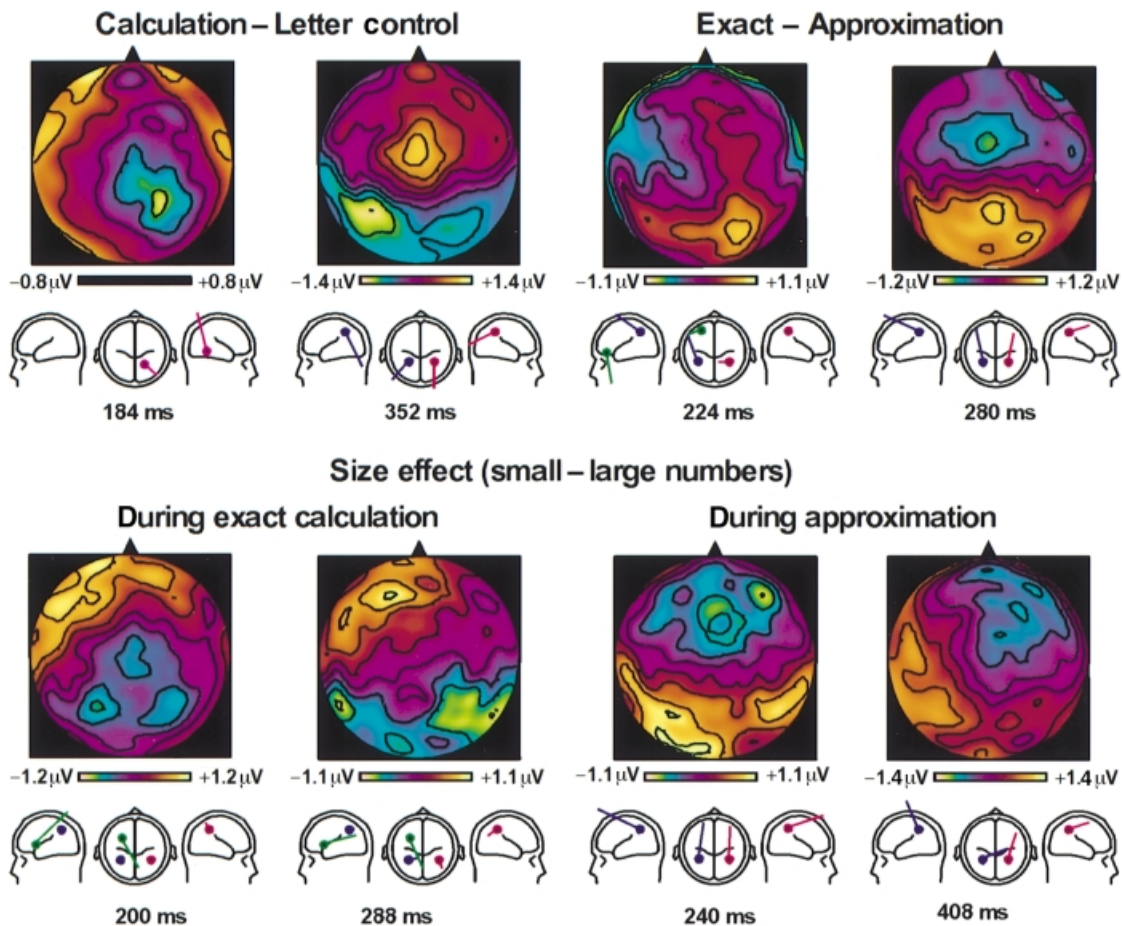

Fig. 6 Main effects observed in ERP recordings during a 0–450 ms time window following stimulus presentation. For each effect, a voltage map in spherical coordinates is presented, with contours spaced every 0.25 µV. The best dipole model that was found for this topography is presented below (dipoles are colour-coded arbitrarily)

calculation, thus constitute the cerebral bases of the problem size effect (Fig. 5).

What about the other areas? A conjunction analysis showed that most of them showed a number size effect irrespective of the nature of task: the left cingulate gyrus (–8, 20, 56; $Z = 6.70$), the right intraparietal sulcus (32, –60, 52; $Z =$

Table 6 *Sites showing a problem size effect during exact calculation*

Cortical area	Talairach coordinates			Z	No. of voxels	No. of subjects
	x	*y*	*z*			
L precentral sulcus	–52	8	28	7.33	116	6
	–56	12	20	6.89		
L intraparietal sulcus	–44	–52	48	6.75	92	6
	–56	–36	52	4.66		
L cingulate gyrus	–8	20	52	6.72	104	5
R cingulate gyrus	8	28	36	3.22		4
R inferior frontal gyrus	32	28	4	6.08	62	5
R dorsolateral prefrontal cortex	44	40	32	5.8	56	5
	36	52	20	3.92		
L inferior frontal gyrus	–44	20	4	5.33	62	3
	–36	32	0	5.19		1
R intraparietal sulcus	28	–56	52	4.91	53	4
	36	–48	48	4.37		4
	44	–44	48	4.36		4

R = right; L = left.

5.97) and the right inferior frontal gyrus (36, 28, 0; Z = 5.55). These regions were therefore expected to show a size effect during approximate calculation as well. However, the effect was not strong enough to reach a corrected level of significance in any area. The left cingulate gyrus and the right intraparietal sulcus did show a significant effect at $P < 0.001$, uncorrected (Z = 3.61, 10 voxels, and Z = 4.55, 16 voxels, respectively).

Inverse effects of problem size
For the sake of completeness, we also examined which areas showed a greater activation for small rather than for large numbers, although we had no theoretical predictions about such inverse problem size effects. In exact calculation, the areas were the left angular gyrus (–52, –68, 32; Z = 7.03), posterior cingulate/precuneus (0, –40, 32; Z = 6.86), right angular gyrus (48, –60, 32; Z = 6.62), mesial anterior frontal cortex (–8, 68, 8; Z = 5.80), right inferior precentral gyrus (64, 4, 8; Z = 5.54), right superior temporal gyrus (44, –8, –8; Z = 4.32), and left insula/supramarginal gyrus (–44, –12, 12; Z = 4.42 and –60, –28, 28; Z = 4.32). In approximate calculation, we found the left supramarginal gyrus (–64, –48, 28; Z = 5.65), right supramarginal gyrus (56, –32, 24; Z = 5.44), and right superior parietal lobule (36, –44, 68; Z = 4.56).

ERP results
Number versus letter processing
The first significant ERP difference between calculation and control was observed at 160 ms following operand onset (peak difference at 184 ms), characterized by more negative voltages during calculation over the right parietal region. On left and right parietal electrodes P3A and P4A, an interaction between hemisphere and the letter-calculation contrast [$F(1,11)$ = 7.85, P = 0.017] indicated a significant hemispheric asymmetry: the letter-calculation difference was highly significant over the right hemisphere [$F(1,11)$ = 19.3, P = 0.001] but not over the left ($F < 1$). No other effects were significant at this point. Examination of the waveforms showed that this early effect coincided in time and topography with the N170, a component of the visual ERP presumably arising from occipito-temporal cortices involved in object recognition. Indeed, a dipole model indicated that a single right infero-temporal dipole accounted for 73.8% of the variance in the number – letter difference. The suggested involvement of the right occipito-temporal pathway in number recognition more than in letter recognition is congruent with previous results (Dehaene *et al.*, 1996; Pinel *et al.*, 1999).

A second difference between calculation and letter processing, of greater magnitude, was observed starting at 320 ms (peak at 352 ms). Calculation yielded more negative voltages over parietal electrodes, particularly on the left, with a simultaneous central positivity (Fig. 6). An ANOVA on central electrode FzP confirmed a large calculation versus letters difference [$F(1,11)$ = 36.4, $P < 0.0001$]. Left and right temporo-parietal electrodes T5A and T6A showed a main effect of calculation versus letters [$F(1,11)$ = 10.3, P = 0.0084] which was significant on the left [$F(1,11)$ = 14.9, P = 0.0026; 0.90 µV difference] but not on the right [$F(1,11)$ = 2.69, P = 0.13; 0.41 µV], though the interaction fell short of significance [$F(1,11)$ = 3.52, P = 0.087]. The topography of this effect could be modelled by two symmetrical parietal dipoles placed at locations similar to those identified in the equivalent fMRI contrast. This model accounted for 87.1% of variance, and adding another left inferior frontal dipole had a negligible effect.

Exact versus approximate calculation
The first difference between exact and approximate tasks was observed starting at 216 ms (peak at 232 ms). Exact

calculation yielded more negative voltages over left inferior frontal electrodes, with a simultaneous positivity over right occipito-parietal electrodes. Left and right frontal electrodes C3A and C4A showed a significant hemispheric asymmetry [hemisphere $\times$ task interaction, $F(1,11) = 11.2, P = 0.0065$]. On the left, the voltage was significantly more negative for exact than for approximate calculations [$F(1,11) = 7.37, P = 0.02; 0.33 \mu$V difference], while a marginal effect of reversed polarity was observed on the right [$F(1,11) = 4.19, P = 0.065; 0.19 \mu$V difference]. On posterior electrodes O1 and O2, a similar ANOVA revealed only a main effect of task [$F(1,11) = 11.3, P = 0.0064; 0.47 \mu$V], with no hemispheric asymmetry. No satisfactory dipole model of this complex topography could be found. The best fit, capturing 60% of variance, was obtained with three active dipoles; one left frontal and two symmetrical parietal ones. The reconstructed source waveforms suggested that at this time, most of the activation was imputable to simultaneous left inferior frontal and left parietal activity.

A second difference starting at 272 ms (peak at 280 ms) was due to more negative voltages in the approximation task over bilateral parietal electrodes, with a simultaneous difference of opposite sign on fronto-central sites (Fig. 6). On both sites, ANOVAs revealed only a main effect of task [$F(1,11) = 7.35, P = 0.020, 0.64 \mu$V difference and $F(1,11) = 7.74, P = 0.018, 0.40 \mu$V difference, respectively]. This topography was adequately modelled by two symmetrical parietal dipoles of approximately equal strength (87.5% of variance). No further gain was obtained by adding the left inferior frontal dipole.

Problem size effect in exact and approximate calculation

Problem size affected ERPs to exact calculation as early as 168 ms (peak difference around 200 ms). There was a left anterior inferior frontal negativity for large numbers relative to small numbers, accompanied by a broad difference of opposite sign elsewhere (Fig. 6). An ANOVA on inferior frontal electrodes F7A and F8A revealed a hemispheric asymmetry [hemisphere $\times$ size interaction in exact calculation, $F(1,11) = 5.59, P = 0.038$]. Follow-up tests revealed that the effect of number size was specific to the left frontal region in the exact calculation task [$F(1,11) = 14.2, P = 0.0031, 0.83 \mu$V difference], and was not significant on the right in the exact task, or bilaterally in the approximation task. This resulted in a task $\times$ size interaction on the left frontal electrode [$F(1,11) = 10.4, P = 0.0082$] and in a triple interaction of hemisphere, task and size that approached significance [$F(1,11) = 3.59, P = 0.085$]. A three-dipole model accounted for 86.6% of variance, with most of the topography being attributed to an intense activation of the left inferior frontal dipole. However, a good fit was obtained only when this dipole was placed posteriorily in the inferior frontal region (Fig. 6). This meshed well with

the equivalent fMRI contrast, which revealed an activation close to Broca's area.

A second effect of number size on exact calculation was observed starting at 248 ms. It first appeared over left temporo-parietal leads, with a maximum at 264 ms, then peaked over the right temporo-parietal leads at 288 ms. The topography was similar to the previous size effect, with a greater negativity for large numbers lateralized to the left frontal region, and a simultaneous opposite difference over posterior sites (Fig. 6). On left inferior frontal electrodes F7P and F8P, the ANOVA again showed a size by task interaction over the left [$F(1,11) = 13.3, P = 0.0039$] and a size effect only in exact calculation [$F(1,11) = 9.59, P = 0.010, 0.68 \mu$V difference], but not in approximate calculation. The same dipole model as above accounted for 76.9% of variance, and again most of the effect could be attributed to a left inferior frontal activation.

The impact of number size on approximate calculation was also examined. A first effect, starting at 224 ms and peaking at 240 ms, although too short-lived to achieve our criterion of five consecutive significant samples, was examined because it was intense and seen on many electrodes. The topography indicated more negative voltages for large numbers over posterior sites, with a smaller converse difference over centro-frontal sites. An ANOVA on electrodes P3P and P4P indicated a significant effect only during approximation over the left [$F(1,11) = 6.73, P = 0.025, 0.80 \mu$V difference], but not the right ($P = 0.28$), although there was no interaction with hemisphere, task, or both. A similar ANOVA on electrodes F3P and F4P show a main size effect [$F(1,11) = 8.44, P = 0.014, 0.32 \mu$V difference] which was significant only during approximation [$F(1,11) = 5.28, P = 0.042, 0.50 \mu$V difference] but not during exact calculation ($F < 1$), although the interaction again failed to reach significance. 75.0% of the variance could be accounted for by the co-activation of two parietal dipoles (Fig. 6). Adding a third dipole in the left inferior frontal region resulted only in a modest improvement of the fit, up to 78.7%. A slightly better model, however, was obtained by adding a third right inferior frontal dipole (81.5% of variance accounted for).

A second effect was found starting at 384 ms and peaking at 408 ms. Voltages were more negative for large numbers over the left temporo-parietal region, with a simultaneous right frontal inversion. Fronto-central electrodes F3P and F4P showed a marginal main effect of number size [$F(1,11) = 4.73, P = 0.052$], significant during approximation [$F(1,11) = 6.48, P = 0.027; 0.38 \mu$V difference], but not during exact calculation ($F < 1$), although the interaction was not significant. Follow-up analyses showed a significant size effect only over right frontal electrodes during approximate calculation [$F(1,11) = 14.4, P = 0.003; 0.52 \mu$V difference]. Similar effects were observed on temporo-parietal electrodes T5 and T6 [main size effect: $F(1,11) = 4.44, P = 0.059$; size effect during approximation: $F(1,11) = 6.86, P = 0.024, 0.46 \mu$V difference; size effect during approximation on left

parietal region: $F(1,11) = 15.9$, $P = 0.0021$, 0.52 µV difference]. Eighty-one per cent of the variance was explained by two symmetrical parietal dipoles (Fig. 6). The fit was somewhat improved when a third inferior frontal dipole was included either in the left hemisphere (86.9%) or in the right (86.5%).

Discussion

The present experiment had three main goals: (i) replicating the inferior parietal activation during number processing while controlling for task difficulty; (ii) identifying cerebral regions showing differential activation during exact and approximate calculation, and (iii) evaluating the effects of number size on those regions. In this discussion, we consider those three points in turn, before turning to their relevance for dyscalculia cases.

Controlling for task difficulty in number processing

A methodological criticism which applies to all previous imaging studies of calculation is that task difficulty was not controlled for. The present study used as a reference condition a letter matching task which controlled for task difficulty and other non-numerical factors. Because subjects had to memorize two letters and their locations for the same duration of time as in the numerical tasks of interest, and they had to make similar spatial decisions and manual responses in both cases, working memory and visuo-spatial requirements were arguably as important in the control task as in the calculation tasks. Furthermore, performance, as assessed by response times and error rates recorded during imaging, was similar to or worse than in the control task in the calculation tasks with small numbers. The exact and approximate calculation tasks were also indistinguishable in performance levels. Finally, though eye movements were not recorded in the fMRI scanner, ERP recordings from eye-channel leads indicated that they were very rare, as would be expected given the short presentation time of the stimuli (200 ms).

Even with all these controls, our brain imaging results remained similar to those reported in the literature (Roland and Friberg, 1985; Burbaud *et al*., 1995; Dehaene *et al*., 1996; Rueckert *et al*., 1996; Chochon *et al*., 1999; Pesenti *et al*., 2000). Numerical tasks activated a reproducible network comprising the bilateral intraparietal sulci, dorsolateral and inferior frontal gyri, and the anterior cingulate. When tasks with small numbers were considered, activation was only significant in those regions in the right hemisphere. However, the left fronto-parietal network was again observed when exact and approximate tasks were separated. In approximation with small numbers versus letter matching, in particular, the full bilateral fronto-parietal network was again observed (Fig. 3, bottom left).

ERPs confirmed systematic differences between calculation and control, and permitted us to evaluate their timing. Analyses comparing ERPs during calculation tasks relative to control showed a peak difference around 350 ms following visual presentation, which could be attributed to a bilateral parietal activation. Even earlier estimates of activation times, between 200 and 300 ms, were obtained when considering separately the exact and approximate tasks.

While these results clearly indicate that the parietal activations during number processing cannot be attributed solely to artefacts of task difficulty, eye movements or other uncontrolled visuo-spatial components, they do not allow us to conclude that any of those areas are specifically dedicated to number processing. In fact, the extent of those activations suggests that this is unlikely. There seems to be a considerable overlap between the intraparietal activations reported here and those observed in non-numerical tasks such as visually guided hand and eye movements (Kawashima *et al*., 1996), mental rotation (Kawamichi *et al*., 1998), attention orienting (Corbetta *et al*., 1995; Nobre *et al*., 1997) and other visuo-spatial coordinate transformation paradigms (Andersen, 1997; Snyder *et al*., 1998). Furthermore, all the parietal regions that were found to be active during calculation also showed greater activation during letter matching, which involved visuo-spatial attention, memory and response, but no numerical processing.

Overall, the evidence suggests that the internal manipulation of numbers draws on visuo-spatial resources also recruited for other spatial tasks. This conclusion is consistent with psychological evidence for an automatic activation of spatial coordinates whenever numbers are processed (Dehaene *et al*., 1993) and with models that picture the internal representation of numbers as a spatially extended 'number line' (Restle, 1970; Dehaene, 1992; Gallistel and Gelman, 1992).

Dissociation between approximate and exact calculation

Exact and approximate calculation tasks yielded distinct activation patterns. In fMRI, parietal and frontal areas were significantly more active during approximation than during exact calculation. This difference was particularly clear in the intraparietal sulci. ERPs further confirmed this finding by revealing an important voltage difference between exact and approximate calculation by 280 ms post-stimulus, which was attributed by dipole modelling to a bilateral parietal activation. Conversely, a distributed set of areas, comprising notably a left anterior inferior frontal region and the bilateral angular gyri, showed greater activation during exact calculation in fMRI. Congruent with this, the exact versus approximate contrast in ERPs revealed a left-lateralized negativity over inferior frontal electrodes by ~220 ms. It is particularly noteworthy that ERP differences were observed during a time window in which only the addition problems, which were strictly identical in the exact and approximate

blocks, had been presented. The finding of ERP differences at such an early stage thus indicates that subjects adopted genuinely distinct calculation strategies for the two tasks (Dehaene *et al*., 1999).

The triple-code model predicted that approximation would show a greater reliance on the intraparietal network than would exact calculation. The results confirm this prediction, but also indicate that a critical distinction must be made between two nearby regions in the parietal lobe, which appear to contribute differentially to number processing. While the left and right intraparietal sulci contribute more to approximation, the angular gyri contribute more to exact calculation, particularly when very small numbers are involved (Fig. 4). In the left hemisphere, the angular gyrus participates in a vast perisylvian language processing network and is known to activate in various lexico-semantic word processing tasks (Démonet *et al*., 1992; Vandenberghe *et al*., 1996; Price, 1998). Its activation in our study is thus compatible with the triple-code hypothesis of a verbal coding of rote exact arithmetic facts.

The differential reliance of exact and approximate calculation on verbal and quantity codes for number is supported by Spelke and Tsivkin's recent behavioural studies of bilinguals (Dehaene *et al*., 1999). Bilingual subjects were first trained with a small set of exact or approximate arithmetic problems presented in one of their two languages. They were later tested for generalization to the other language and to new arithmetical problems involving similar quantities. The results indicated that language and problem switching had a strong impact on performance in the exact task, but no measurable impact on performance in the approximate task. This suggested that the trained approximate facts had been stored in a non-linguistic quantity-based format, while the exact facts were stored in a language-dependent code.

The left inferior frontal region may play a particularly important role in this language-dependent arithmetic memory, given its greater activation during exact than during approximate calculation in fMRI, its clear lateralization to the left hemisphere, and the finding of similar left frontal differences in ERPs. The coordinates of this region fall within 1.5 cm of those observed during the verb generation task (Petersen *et al*., 1988; Raichle *et al*., 1994), and clearly anterior to the activations that have been observed during phonological and/or syntactic processing in the vicinity of Broca's area (e.g. Démonet *et al*., 1992; Paulesu *et al*., 1993; Stromswold *et al*., 1996). They coincide, in the left hemisphere, with a bilateral anterior frontal activation associated with the performance of a complex verbal task (Koechlin *et al*., 1999). This region may thus be involved in the control of verbal retrieval processes implemented in more posterior cortico-subcortical verbal networks. The latter may involve not only the left angular gyrus, but also the left putamen which showed a small area of greater activation during exact calculation, compatible with previous reports of aphasia and verbal acalculia following left subcortical damage (Hittmair-Delazer *et al*., 1994; Dehaene and Cohen, 1997).

We close this discussion by noting that two language-related areas, although not presented in the main exact versus approximate contrast, showed an effect of number size only in exact calculation. First, Broca's area proper was significantly more active for large than for small exact calculations. Secondly, a vast region encompassing the left insula and left supramarginal gyrus was significantly more active for small than for large exact calculations. The latter region, which has been associated with phonological processing (Paulesu *et al*., 1993; Price, 1998), may be involved in the fast retrieval of highly overlearned small addition facts, while the former may reflect processes requiring more effort associated with the lesser known facts involving large numbers.

Cerebral basis of the number size effect

Further confirmation of the partial dissociability of exact and approximate calculation came from the examination of the impact of number size on these operations. Behaviourally, number size had a greater impact on performance in exact calculation than in approximation. This replicated Ashcraft and Stazyk's results (Ashcraft and Stazyk, 1981). Their interpretation was that, in the approximation task, subjects can reject grossly false results without completing the exact calculation, and thus without being as sensitive to the number size factor. Supporting this interpretation, we observed no fMRI increases with number size during approximation. There were only some differences in the opposite direction (greater activation for small numbers) in the bilateral supramarginal gyri and the right superior parietal lobule. Although these were not predicted, tentative explanations may be proposed. The right superior parietal activation may indicate that the right-hemispheric parietal quantity system is biased towards small quantities (Cipolotti *et al*., 1991). The supramarginal activation, which overlaps with the one observed in the small exact blocks, may indicate an automatic activation of a verbal store for small addition facts, as reported by many subjects and demonstrated empirically by LeFevre *et al*. (1988).

As expected, number size had a much larger impact during exact calculation. A large bilateral network of areas showed greater activation for large than for small exact problems (Fig. 5). Three of them, all left-lateralized (left intraparietal, left precentral and left inferior frontal) showed a significant task by size interaction, thus constituting the cerebral bases of the behavioural problem size effect. Psychological research has indicated that increasing number size does not simply result in an increase in processing difficulty within the fact retrieval system, but also results in the use of distinct strategies such as counting or transforming the problem to a simpler one (e.g. $9 + 6 = 10 + 5 = 15$) (LeFevre *et al*., 1996). Our observed activations may be interpreted as reflecting both effects. The increased activity in Broca's area suggests more effort in processing within the verbal fact retrieval system, while the bilateral intraparietal recruitment

at regions identical to those active during approximation suggests the mobilization of the parietal quantity system for large exact problems. The latter result indicates that the networks for exact and approximate processing are not mutually exclusive, but are functionally integrated and are co-activated when solving difficult problems.

ERP results allowed us to localize the influence of problem size in time. During exact calculation, ERPs were more negative for large than for small numbers by 200 ms over the left inferior frontal region. A dipole model indicated that this effect was compatible with the activation of Broca's area, as seen in fMRI. During approximation, the effect of number size was also significant, but with a strikingly different topography (although the very same problems were involved). Large numbers yielded more negative voltages by 240 ms over the bilateral parietal lobe, which could be accounted for by the simultaneous activation of two bilateral dipoles. Examination of the ERP curves suggested that the effect could be due to a slightly delayed parietal activation for larger numbers, which might explain why the effect was not found with fMRI.

Relevance for understanding subtypes of dyscalculia

The hypothesis that two neighbouring regions for verbal and quantity representations of numbers co-exist within the parietal lobe may help make sense of single-case studies of dyscalculia. It is not infrequent for a patient to be much more impaired in, say, multiplication than in subtraction, while in another the opposite may be true (Dagenbach and McCloskey, 1992; Lampl *et al.*, 1994; Pesenti *et al.*, 1994; Dehaene and Cohen, 1997; Delazer and Benke, 1997; Cohen and Dehaene, 2000; Cohen *et al.*, 2000). In addition to such dissociations between operations, there are also dissociations within operations; for example, because problems with large numbers are often strikingly more impaired than problems with smaller numbers (McCloskey *et al.*, 1991). The present results suggest that such dissociations may be due to the subjects' differential reliance on verbal or quantity processing of numbers for different arithmetic problems. Even superficially analogous inferior parietal lesions should cause different patterns of acalculia depending on whether the lesion affects the intraparietal or the angular gyrus regions. Indeed, lesions of the intraparietal region, particularly in the dominant hemisphere, are frequently associated with acalculia in the context of Gerstmann's syndrome, often with associated finger anomia and spatial deficits (Takayama *et al.*, 1994). Single-case studies suggest that the calculation impairment in such cases concerns particularly the comprehension of numerical quantity and its manipulation in tasks such as subtraction, bisection or number comparison. Rote multiplication tables can be relatively spared, presumably because they can still be retrieved using the intact verbal memory system (Dehaene and Cohen, 1997; Delazer and Benke, 1997).

Conversely, Cohen *et al.* reported a single case study of a patient with acalculia following a perisylvian lesion that affected the inferior parietal region and part of the angular gyrus, but mostly spared the intraparietal sulcus (Cohen *et al.*, 2000). This patient was unimpaired in the spatial domain, but was aphasic. In the number domain, he exhibited a deficit essentially opposite to Gerstmann's syndrome cases, with a greater impairment for rote multiplication tables than for quantity-based operations such as subtraction and bisection. Cohen *et al.* proposed that patients with a selective impairment of multiplication should generally show spared intraparietal cortex and preserved understanding of approximate quantities.

Because the parietal activation associated with approximation is bilateral, while the activations associated with exact calculation (and particularly with the problem size effect) are left-lateralized, the results suggest that in many cases of dyscalculia with left-hemispheric lesions, the intact right hemisphere may suffice to provide a non-verbal understanding of the approximate relations between numbers. Unfortunately, in the vast majority of studies of acalculia, only exact calculation has been assessed. Nevertheless, two case reports have described preserved approximation associated with severe dyscalculia: patient N.A.U. (Dehaene and Cohen, 1991), described in the introduction, and patient D.R.C. (Warrington, 1982). D.R.C. suffered from a small left intraparietal lesion and acalculia particularly affecting the retrieval of addition and subtraction facts such as $6 + 7$, yet could often provide a correct estimate of the result, and made errors that were systematically close to the correct result. Our interpretation, in the light of the present findings in normal subjects, is that the left intraparietal lesion affected a crucial element of the left-lateralized network associated with the problem size effect during exact calculation (Fig. 6), and therefore disrupted exact calculation with large operands (results >10); while the lesion spared the right-hemispheric intraparietal sulcus and other right-hemispheric areas active during addition approximation, that may suffice to approximate an addition or subtraction result.

Conclusion

The main contribution of the present study is to clarify the role of subregions of the parietal lobe in number processing. The results indicate that the bilateral intraparietal region is the main active area during simple arithmetic. It remains active even when the difficulty level and other non-specific parameters are factored out. It shows significantly greater activation during approximation than during exact calculation, and more activation for large numbers than for small numbers. Finally, it shows little or no activation for very simple addition facts that have been learned by rote, in which case a distinct region in the angular gyrus is involved. These observations help understand why brain-lesioned patients can show dissociated performance in exact and approximate calculation, and with small versus large numbers.

References

Andersen RA. Multimodal integration for the representation of space in the posterior parietal cortex. [Review]. Philos Trans R Soc Lond B Biol Sci 1997; 352: 1421–8.

Ashcraft MH. Cognitive arithmetic: review of data and theory. [Review]. Cognition 1992; 44: 75–106.

Ashcraft MH, Stazyk EH. Mental addition: test of three verification models. Mem Cognit 1981; 9: 185–96.

Burbaud P, Degreze P, Lafon P, Franconi J-M, Bouligand B, Bioulac B, et al. Lateralization of prefrontal activation during internal mental calculation: functional magnetic resonance imaging study. J Neurophysiol 1995; 74: 2194–200.

Chochon F, Cohen L, van de Moortele PF, Dehaene S. Differential contributions of the left and right inferior parietal lobules to number processing. J Cognit Neurosci 1999; 11: 617–30.

Cipolotti L, Butterworth B, Denes G. A specific deficit for numbers in a case of dense acalculia. Brain 1991; 114: 2619–37.

Cohen L, Dehaene S. Calculating without reading: unsuspected residual abilities in pure alexia. Cognit Neuropsychol. In press 2000.

Cohen L, Dehaene S, Chochon F, Lehéricy S, Naccache L. Language and calculation within the parietal lobe: a combined cognitive, anatomical and fMRI study. Neuropsychologia 2000; 38: 1426–40.

Corbetta M, Shulman GL, Miezin FM, Petersen SE. Superior parietal cortex activation during spatial attention shifts and visual feature conjunction. Science 1995; 270: 802–5.

Dagenbach D, McCloskey M. The organization of arithmetic facts in memory: evidence from a brain-damaged patient. Brain Cognit 1992; 20: 345–66.

Dehaene S. Varieties of numerical abilities. [Review]. Cognition 1992; 44: 1–42.

Dehaene S, Cohen L. Two mental calculation systems: case study of severe acalculia with preserved approximation. Neuropsychologia 1991; 29: 1045–54.

Dehaene S, Cohen L. Towards an anatomical and functional model of number processing. Math Cognit 1995; 1: 83–120.

Dehaene S, Cohen L. Cerebral pathways for calculation: double dissociation between rote verbal and quantitative knowledge of arithmetic. Cortex 1997; 33: 219–50.

Dehaene S, Bossini S, Giraux P. The mental representation of parity and number magnitude. J Exp Psychol Gen 1993; 122: 371–96.

Dehaene S, Tzourio N, Frak V, Raynaud L, Cohen L, Mehler J, et al. Cerebral activations during number multiplication and comparison: a PET study. Neuropsychologia 1996; 34: 1097–106.

Dehaene S, Spelke E, Pinel P, Stanescu R, Tsivkin S. Sources of mathematical thinking: behavioral and brain-imaging evidence. Science 1999; 284: 970–4.

Delazer M, Benke T. Arithmetic facts without meaning. Cortex 1997; 33: 697–710.

Démonet J-F, Chollet F, Ramsay S, Cardebat D, Nespoulous J-L, Wise R, et al. The anatomy of phonological and semantic processing in normal subjects. Brain 1992; 115: 1753–68.

Gallistel CR, Gelman R. Preverbal and verbal counting and computation. [Review]. Cognition 1992; 44: 43–74.

Gerstmann J. Syndrome of finger agnosia, disorientation for right and left agraphia and acalculia. Arch Neurol Psychiat 1940; 44: 398–408.

Henschen SE. Uber Sprach- Musik- und Rechenmechanismen und ihre Lokalisationen im Grosshirn. Zges Neurol Psychiat 1919; 52: 273–98.

Hittmair-Delazer M, Semenza C, Denes G. Concepts and facts in calculation. Brain 1994; 117: 715–28.

Kawamichi H, Kikuchi Y, Endo H, Takeda T, Yoshizawa S. Temporal structure of implicit motor imagery in visual hand-shape discrimination as revealed by MEG. Neuroreport 1998; 9: 1127–32.

Kawashima R, Naitoh E, Matsumura M, Itoh H, Ono S, Satoh K, et al. Topographic representation in human intraparietal sulcus of reaching and saccade. Neuroreport 1996; 7: 1253–6.

Kiefer M, Dehaene S. The time course of parietal activation in single-digit multiplication: evidence from event-related potentials. Math Cognit 1997; 3: 1–30.

Koechlin E, Basso G, Pietrini P, Panzer S, Grafman J. The role of the anterior prefrontal cortex in human cognition. [Letter]. Nature 1999; 399: 148–51.

Krueger LE, Hallford EW. Why $2+2 = 5$ looks so wrong: on the odd-even rule in sum verification. Mem Cognit 1984; 12: 171–80.

Lampl Y, Eshel Y, Gilad R, Sarova-Pinhas I. Selective acalculia with sparing of the subtraction process in a patient with left parietotemporal hemorrhage. Neurology 1994; 44: 1759–61.

LeFevre JA, Bisanz J, Mrkonjic L. Cognitive arithmetic: evidence for obligatory activation of arithmetic facts. Mem Cognit 1988; 16: 45–53.

LeFevre JA, Sadesky GS, Bisanz J. Selection of procedures in mental addition: reassessing the problem size effect in adults. J Exp Psychol Learn Mem Cogn 1996; 22: 216–30.

McCloskey M. Cognitive mechanisms in numerical processing: evidence from acquired dyscalculia. [Review]. Cognition 1992; 44: 107–57.

McCloskey M, Harley W, Sokol SM. Models of arithmetic fact retrieval: An evaluation in light of findings from normal and brain-damaged subjects. J Exp Psychol Learn Mem Cogn 1991; 17: 377–97.

Nobre AC, Sebestyen GN, Gitelman DR, Mesulam MM, Frackowiak RS, Frith CD. Functional localization of the system for visuospatial attention using positron emission tomography. Brain 1997; 120: 515–33.

Pallier C, Dupoux E, Jeannin X. EXPE: an expandable programming language for on-line psychological experiments. Behav Res Methods Instrum Comput 1997; 29: 322–7.

Paulesu E, Frith CD, Frackowiak RS. The neural correlates of the verbal component of working memory. Nature 1993; 362: 342–5.

Perrin F, Pernier J, Bertrand D, Echallier JF. Spherical splines for scalp potential and current density mapping. Electroencephalogr Clin Neurophysiol 1989; 72: 184–7.

Pesenti M, Seron X, van der Linden M. Selective impairment as evidence for mental organisation of arithmetical facts: BB, a case of preserved subtraction? Cortex 1994; 30: 661–71.

Pesenti M, Thioux M, Seron X, De Volder A. Neuroanatomical substrates of Arabic number processing, numerical comparison and simple addition: A PET study. J Cognit Neurosci 2000; 12: 461–79.

Petersen SE, Fox PT, Posner MI, Mintun M, Raichle ME. Positron emission tomographic studies of the cortical anatomy of single-word processing. Nature 1988; 331: 585–9.

Pinel P, Le Clec'H G, van de Moortele PF, Naccache L, Le Bihan D, Dehaene S. Event-related fMRI analysis of the cerebral circuit for number comparison. Neuroreport 1999; 10: 1473–9.

Price CJ. The functional anatomy of word comprehension and production. Trends Cogn Sci 1998; 2: 281–8.

Raichle ME, Fiez JA, Videen TO, MacLeod AK, Pardo JV, Fox PT. Practice-related changes in human brain functional anatomy during nonmotor learning. Cerebr Cortex 1994; 4: 8–26.

Restle F. Speed of adding and comparing numbers. J Exp Psychol 1970; 83: 274–8.

Roland PE, Friberg L. Localization of cortical areas activated by thinking. J Neurophysiol 1985; 53: 1219–43.

Rueckert L, Lange N, Partiot A, Appollonio I, Litvan I, Le Bihan D, et al. Visualizing cortical activation during mental calculation with functional MRI. Neuroimage 1996; 3: 97–103.

Scherg M, Berg P. BESA – Brain electric source analysis handbook. Munich: Max Planck Institute for Psychiatry; 1990.

Snyder LH, Grieve KL, Brotchie P, Andersen RA. Separate body- and world-referenced representations of visual space in parietal cortex. Nature 1998; 394: 887–91.

Stromswold K, Caplan D, Alpert N, Rauch S. Localization of syntactic comprehension by positron emission tomography. Brain Lang 1996; 52: 452–73.

Takayama Y, Sugishita M, Akiguchi I, Kimura J. Isolated acalculia due to left parietal lesion. Arch Neurol 1994; 51: 286–91.

Tucker DM. Spatial sampling of head electrical fields: the geodesic sensor net. Electroencephalogr Clin Neurophysiol 1993; 87: 154–63.

Vandenberghe R, Price C, Wise R, Josephs O, Frackowiak RS. Functional anatomy of a common semantic system for words and pictures. Nature 1996; 383: 254–6.

Warrington EK. The fractionation of arithmetical skills: a single case study. Q J Exp Psychol 1982; 34A: 31–51.

Appendix *List of arithmetic problems used*

	Small problems					Large problems			
	Exact choices		Approximation choices			Exact choices		Approximation choices	
1 + 2	3	4	4	8	5 + 6	11	13	10	18
1 + 3	4	2	3	8	5 + 7	12	14	11	19
1 + 4	5	3	6	2	5 + 8	13	11	12	17
1 + 5	6	4	7	9	5 + 9	14	16	15	11
2 + 3	5	7	4	8	6 + 7	13	11	12	18
2 + 4	6	8	5	9	6 + 8	14	12	13	19
2 + 5	7	9	8	3	6 + 9	15	17	14	10
3 + 4	7	5	8	2	7 + 8	15	13	16	10
3 + 5	8	6	7	2	7 + 9	16	15	15	11
4 + 5	9	7	8	3	8 + 9	17	15	18	11