Neuroanatomical Substrates of Arabic Number Processing, Numerical Comparison, and Simple Addition: A PET Study

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Abstract

■ Positron emission tomography was used to localize the cerebral networks specifically involved in three basic numerical processes: arabic numeral processing, numerical magnitude comparison, and retrieval of simple addition facts. Relative cerebral blood flow changes were measured while normal volunteers were resting with eyes closed, making physical judgment on nonnumerical characters or arabic digits, comparing, or adding the same digits. Processing arabic digits bilaterally produced a large nonspecific activation of occipito-parietal areas, as well as a specific activation of the right anterior insula. Comparison and simple addition fact retrieval revealed a fronto-parietal network involving mainly the left intraparietal sulcus, the superior parietal lobule and the precentral gyrus. Comparison also activated, but to a lesser extent, the right superior parietal lobe, whereas addition also activated the orbito-frontal areas and the anterior insula in the right hemisphere. Implications for current anatomo-functional models of numerical cognition are drawn. ■

INTRODUCTION

The development of functional imaging techniques in recent years has made it possible to identify the neuroanatomical correlates of cognitive functions in healthy subjects. With regard to arithmetical cognition (i.e., how numbers are mentally processed and represented), various theoretical proposals have been made for the cognitive components of number processing and simple calculation, but little is known as to the precise neural bases of these components. According to the Triple-code model, the most recent anatomo-functional model of arithmetical cognition (Dehaene, 1992; Dehaene & Cohen, 1995), processing arabic numerals would involve bilaterally occipito-temporal areas and processing magnitude information would take place in the parietal lobes. By contrast, the retrieval of simple arithmetical facts would involve language areas as well as subcortical structures, only in the left hemisphere. In the present study, these proposals were tested using positron emission tomography (PET) in an attempt to localize which cerebral areas are specifically involved in three basic numerical processes: arabic numeral processing, numerical magnitude comparison, and retrieval of simple addition facts. In this introduction, we will briefly summarize the classical findings concerning the lesion sites related to acalculic disorders, and we will review the data gathered using neuroimaging techniques. We will also present the Triple-code model and focus on those of its assumptions underlying the present study.

Neuropsychological Data for Arithmetic

The hypothesis of a unique "calculation center" was abandoned with Henschen's (1919) pioneer observations of calculation deficits resulting from lesions in various brain areas. Since then, group studies and case reports of patients with calculation deficits have revealed the dramatic effects of left posterior brain lesions (Jackson & Warrington, 1986; Dahmen, Hartje, Büssing, & Sturm, 1982; Grafman, Passafiume, Faglioni, & Boller, 1982; Ferro & Botelho, 1980; Collignon, Leclercq, & Mahy, 1977; Benson & Weir, 1972; Hécaen, Angelergues, & Houllier, 1961; Gerstmann, 1930; Henschen, 1919). They have also revealed the moderate effects of right posterior lesions (Dahmen et al., 1982; Grafman et al., 1982; Hécaen et al., 1961; Henschen, 1919) as well as the implication of frontal areas (Dahmen et al., 1982; Luria, 1966; Goldstein, 1948; Henschen, 1919) and subcortical structures (Corbett, McCuster, & Davidson, 1986; Whitaker, Habinger, & Ivers, 1985; Ojemann, 1974) in these deficits. These findings highlighted the large distribution of numerical processes in the brain but the precise functional role(s) of each area in number processing and calculation remained debatable due to methodological shortcomings and the lack of theoretical background of these studies.

In the late eighties and the early nineties, cognitive neuropsychologists overcame most of the methodological flaws of earlier studies and carried out theoretically well-grounded experiments. Unfortunately, most of the time, they were only concerned with the functional aspects of the deficits and paid little attention to the anatomical localization of the underlying lesions. Therefore, although it globally confirmed the past picture of predominantly left (Cipollotti & de Lacy-Costello, 1995; McNeil & Warrington, 1994; Cohen & Dehaene, 1991; Sokol, McCloskey, Cohen, & Aliminosa, 1991; McCloskey, Sokol, & Goodman, 1986; Warrington, 1982), sometimes right (Weddel & Davidoff, 1991), frontal (Fasotti, Eling, & Bremer, 1992) or even subcortical (Hittmair-Delazer, Semenza & Denes, 1994) involvement of brain areas, evidence gathered during this period did not substantially further our understanding of the neuroanatomical substrate of arithmetical cognition. Among the recent attempts to link anatomical and functional aspects of calculation deficits, the study of three patients with a diagnosis of isolated acalculia (i.e., deficits strictly restricted to calculation components, with no numeral comprehension nor production disorders, no impairments in arithmetical fact retrieval, spatial processing, borrowing and carrying mechanisms, and no aphasic nor memory deficits) showed that the overlapping lesions were located along the left intraparietal sulcus (Takayama, Sugishita, Akigushi, & Kimura, 1994).

Functional Brain Imaging Data for Arithmetic

Only a few neuroimaging studies have focused on the neural basis of arithmetical cognition. The first investigation of the cerebral physiological modifications related to mental calculation was carried out by Sokoloff, Mangold, Wechsler, Kennedy, and Kety (1955) with the Kety-Schmidt nitrous oxide technique. They found no difference in global oxygen consumption and cerebral blood flow between calculation and resting conditions. However, regional blood flow changes (rCBF) were subsequently found with the intracarotide ^{133}Xenon injection technique. Risberg and Ingvar (1973) observed, during a backward digit-span test, an increased flow restricted to the gray matter in the dominant hemisphere, with an anterior frontal implication. Roland and Friberg (1985) compared a repeated subtraction task (repeated subtraction of 3 from a given number) with a resting condition. They found increased rCBF bilaterally, with a right hemisphere predominance, in posterior areas (identified as the angular gyri) and in pre frontal, premotor, and motor areas.

Subtraction, automatic counting, and rest were studied with functional magnetic resonance imaging (fMRI). Significant activations were found in the middle frontal gyrus during subtraction but not during counting, with a strong left lateralization in right-handed subjects and a bilateral pattern in the left-handed (Burbaud et al., 1995). In this work, activity was recorded only in the frontal lobes for technical and theoretical reasons. Another study, covering most of the cerebral cortex, compared repeated subtraction and counting. All the subjects showed bilateral motor and premotor as well as left prefrontal cortex activation, and, most of them, right prefrontal and bilateral posterior-parietal cortex activations (Rueckert et al., 1996). Both studies revealed individual differences, with the left and right insula and the left temporal cortex activated only in some subjects. Compared to approximate calculation, verification of simple additions activated the inferior frontal lobe, the cingulate gyrus and the precuneus in the left hemisphere, the parieto-occipital sulcus and the middle temporal gyrus in the right hemisphere, and the angular gyri bilaterally (Dehaene, Spelke, Pinel, Stanescu, & Tsivkin, 1999). When subjects had to decide whether a number was smaller or larger than 5, activation related to numerical comparison was observed in the left and right inferior parietal lobules, with a left-sided predominance (Pinel et al., 1999).

Using PET, the repeated subtraction task was found to activate, relative to rest, the parietal cortex, the pre frontal cortex and the cerebellum bilaterally, as well as the left premotor and anterior cingulate cortices, and the Supplementary Motor Area (SMA) (Ghatan, Hsieh Peterson, Stone-Elander, & Ingvar, 1998). In the left parietal focus, the cerebral activity further increased when task-irrelevant speech was presented during calculation, which was interpreted by the authors as demonstrating the specific role of this area in arithmetical processing. Addition processes were also investigated as follows. Subjects listened to a series of digits and were instructed either to repeat them aloud or to add the last number heard to the penultimate one and to give the answer aloud (de Jong, Van Zomeren, Willemsen, & Paans, 1996). In this task, activations were observed in the inferior parietal lobules bilaterally and in the left premotor cortex and supplementary motor area, without significant involvement of the pre frontal cortex. In another study, mixed sets of oral additions and subtractions between 2- and 1-digit numbers were compared to two control conditions, spot fixation, and covert reading of the same numerals (Sakurai, Momose, Iwata, Sasaki, & Kanazawa, 1996). A region of interest-based analysis showed that the left prefrontal cortex was activated in calculation relative to reading, that the posterior superior temporal gyrus (including part of Wernike's area) was activated in calculation relative to fixation, and that the basal ganglia were activated and the right angular gyrus deactivated in calculation relative to both fixation and reading. With more basic numerical tasks, Dehaene et al. (1996) examined the organization of brain activations in number comparison and simple multiplication, contrasted with a passive resting condition. Subjects were presented visually with pairs of single digits and were required either to compare or to multiply them mentally. In both conditions, responses (the larger or the product of the pair) were given covertly. A region of interest-based analysis showed bilateral activations of the lateral occipital cortices, the precentral gyri and the supplementary motor area in both conditions, whereas the left and right inferior parietal lobules were activated only in multiplication.

Together, these results suggest that the left frontal cortex and the left and right parietal lobes play some substantial role in simple arithmetic. Unfortunately, a major problem when trying to articulate these results is, as for neuropsychological data, the lack of a theoretical background. Most of the tasks used did not focus on clearly defined numerical processes, often involved a heavy working memory load, and almost all studies required the subjects to verbalize their answer either aloud or covertly. For all these reasons, it is not easy to disentangle which activations were specifically linked to number processing and calculation, and which were related to more general processes, including, among others, attention, working memory, and language.

The Triple-Code Model: A Possible Anatomo-Functional Model

The Triple-code model postulates different types of numerical representation processed by different areas of the adult brain (Dehaene, 1992; Dehaene & Cohen, 1995). The hypotheses about these representations, their functional role and their anatomical substrates are summarized below and in Table 1.

At the functional level, the Triple-code model assumes three different representations directly interfaced by notation-specific comprehension and production mechanisms and connected by translation paths. Each representation would specifically be used for a given set of numerical tasks. A visual representation (i.e., strings of arabic digits manipulated on a spatially extended representational medium) would be used to process arabic numerals, in multi-digit operations and in parity judgments. A verbal representation (i.e., syntactically organized sequences of number words) would be involved when hearing or reading number words, when counting, and when solving simple additions and multiplications (e.g., $3 + 2 = 5$ or $3 \times 2 = 6$). These arithmetical facts would be stored and retrieved as declarative knowledge[1] through verbal associations. Finally, an analog representation (i.e., a mental continuum oriented left to right, from small to large numbers, and compressed near the large numbers, representing numerical quantities as distributions of activation) would give rise to approximate calculation and would be used in number comparison.

At the anatomical level, the possible implementation of these representations and their translation paths is as follows. On the one hand, the visual and the analog representations would be processed in both hemispheres; respectively, in the occipito-temporal areas (close to the ventral visual pathway) and in the inferior parietal lobes. On the other hand, the verbal representation would be processed only in the left hemisphere within classic perisylvian language areas. Within each hemisphere, there would be connections between the various representations; moreover, the left and right visual and analog representations would be interconnected via the corpus callosum.

These propositions of implementation mainly stem from a retrospective review of published acalculia cases as well as from recent single-case studies (Dehaene & Cohen, 1997; Cohen, Dehaene, & Verstichel, 1994; Cohen & Dehaene, 1996). However, divergent results were observed in Dehaene et al.'s neuroimaging studies which revealed the involvement of the parietal lobes in multiplication (fMRI, PET) but less in comparison (PET),

Table 1. Triple-Code Hypotheses About Numerical Representations, Their Functional Role and Their Anatomical Substrates (Dehaene and Cohen, 1995)

Representations	*Numerical tasks*	*Localizations*
Verbal	processing number names	L inferior frontal areas
	counting	
	simple addition facts	
	simple multiplication facts	
Visual	processing arabic digits	L and R occipito-temporal areas
	parity judgment	
	mental multi-digit operations	
Analog	processing analog quantities	L and R inferior parietal areas
	numerical comparison	
	approximate calculation	

and no involvement of the left inferior frontal areas in multiplication (PET). Several arguments have been offered to explain the discrepancies between the expectations of the model and these results. Firstly, the parietal activation in multiplication was tentatively interpreted as reflecting the need for semantic elaboration in some problems for which the answer was not directly retrieved from memory. Indeed, performance greatly varies across problems and individuals, and a direct memory retrieval accounts in fact for only 80% of the reported strategies. Subjects also use strategies such as application of rules, decomposition of difficult problems, or backup strategies (LeFevre, Bisanz, et al., 1996a; LeFevre, Sadesky & Bisanz, 1996b) which may require some processing of the magnitude information in the parietal areas. Secondly, from a methodological point of view, using a resting state as the control task in the PET study did not make it possible to distinguish the areas involved in number processing from those related to more general nonnumerical processes; moreover, the direct contrast between comparison and multiplication masked any common activations.

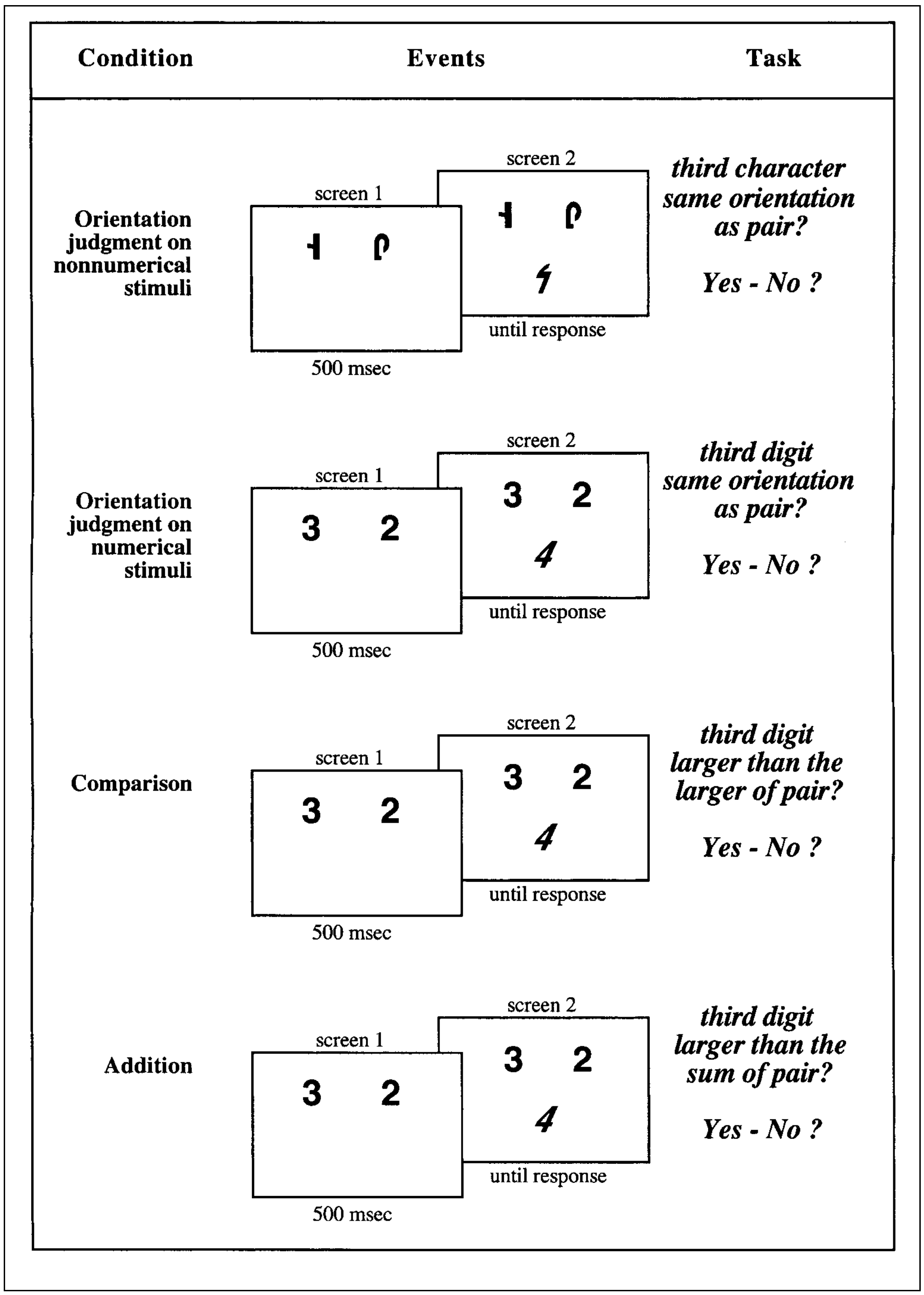


Figure 1. A typical sequence of events for each condition. Examples of nonnumerical characters are shown in Figure 5.

Furthermore, with regard to the absence of activation in language areas during multiplication in the PET study, the requirement to covertly name the answer introduced verbal processes in both experimental tasks that may have obscured specific verbal components of arithmetic facts retrieval. Such putative verbal components were, however, still not evidenced when the experimental tasks were compared to rest, which was interpreted by the authors as reflecting some possible internal speech in the latter condition. Even if this were to be true, the structure of the items should have nevertheless enhanced any verbalization in multiplication relative to comparison. Indeed, the pairs of digits were matched at presentation in both experimental tasks, but not the answers they led to. The answers were numbers between 1 and 9 in comparison but between 2 and 72 in multiplication, thus implying strong differences with regard to the numerical size of the answers as well as to the lexical and syntactical aspects of the covert verbal production. Besides this, there was no way to control whether the subjects actually did the tasks since no explicit answer was required.

Rationale of the Present Study

In the present study, we tested the anatomical assumptions of each representation postulated in the Triple-code model while trying to overcome the above-mentioned problems. Three tasks were used to localize where arabic digits are mentally processed (i.e., test of the visual representation postulated in bilateral occipito-temporal areas), where they are mentally compared (i.e., test of the analog representation postulated in bilateral parietal areas) and where they are added (i.e., test of the verbal representation postulated in left inferior frontal areas). Five conditions were investigated in a stepwise design: (1) resting state with eyes closed, (2) judgment of orientation performed on nonnumerical stimuli (a triplet of nonmeaningful characters in an upright or italic orientation is presented; the task is to decide whether the third character has the same orientation as the other two), (3) judgment of orientation on numerical stimuli (same task with arabic digits as stimuli), (4) numerical comparison (same stimuli, Is the third digit larger than the larger of the other two?), and (5) simple addition (same stimuli, Is the third digit larger than the sum of the other two?). In all active conditions, the visual input (visually displayed triplets of characters or digits) and the response (yes–no decision on answer keys) were kept equivalent. Typical sequences of events in each condition are shown in Figure 1 and the putative cognitive processes involved are presented in Table 2. Processing of a visual input and giving a manual two-choice answer were similarly involved in all the tasks but rest. Following the subtractive method rationale, contrasting the physical judgment on nonnumerical stimuli with rest should reveal the areas involved in processing a visual stimulus, making the orientation judgment and answering. Next, contrasting the physical judgment on numerical stimuli with the judgment on nonnumerical stimuli should reveal the areas, if any, specifically involved in processing arabic digits after perceptual processing. Then, contrasting the magnitude and the physical judgments on arabic digits should reveal the areas specifically involved in coding and processing the semantic magnitude information. Finally, contrasting the addition and the magnitude comparison conditions should reveal the areas specifically involved in retrieving only the stored additive fact, since the comparison step and all other processes are involved in both conditions.

RESULTS

Behavioral Data

Error rates and response latencies for each task are given in Table 3. Separate analyses were carried out for the two orientation tasks, and for the comparison and addition tasks.

Orientation Tasks

For the orientation tasks, error rates did not differ significantly (paired *t* test: $t(6) = -.15$, *ns*). An analysis

Table 2. Putative Cognitive Processes Involved in Each Condition

		Orientation Judgment On			
	Rest	*Characters*	*Digits*	*Comparison*	*Addition*
Input processing	–	X	X	X	X
Arabic digit processing	–	–	X	X	X
Numerical comparison	–	–	–	X	X
Addition	–	–	–	–	X
Orientation judgment	–	X	X	–	–
Response	–	X	X	X	X

Table 3. Mean Percentage of Errors (± *SD*) and Response Latency in msec (± *SD*) as a Function of Condition. Medians are Averaged by Subject Across the Two Repetitions (Scans)

	Orientation Judgment On			
	Characters	*Digits*	*Comparison*	*Addition*
Error	2.1 (± 2.5)	2.2 (± 3.9)	1.1 (± 1.3)	3 (± 2.9)
Latency	620 (± 89)	610 (± 90)	598 (± 147)	711 (± 212)

of variance (ANOVA) was performed on the response latencies of correct answers with order of tasks (judgment on characters-then-digits vs. digits-then-characters), position of response keys (yes–no vs. no–yes) as between-subject, and response (yes vs. no), task (orientation on characters vs. digits) and repetition (first vs. second scan) as within-subject variables. Significant main effects were found for repetition (mean latencies for first scans: 631 msec, second scans: 599 msec; $F(1, 4) = 17.0$, $MSE = 1003.4$, $p < .02$) and response (yes: 597 msec, no: 633 msec; $F(1, 4) = 9.6$, $MSE = 2147.9$, $p < .04$). The task had no main effect and only entered in a nonrelevant interaction with keys ($F(1, 4) = 9.8$, $MSE = 7494.8$, $p < .04$). No other main effect or interaction was found.

The orientation judgment concerns the physical aspect of the stimuli. Yet it has been found that even when only a surface judgment is required on numerals, response times can be modulated by their magnitude, suggesting that semantic access may proceed automatically and unintentionally (Fias, Brysbaert, Geypens, & d'Ydewalle, 1996; Dehaene & Akhavein, 1995; Tzelgov, Meyer, & Henik, 1992; Henik & Tzelgov, 1982). Thus, although the magnitude of the presented digits was irrelevant for the orientation judgment required by the task, we looked at its potential effect, if any, which would have suggested that the participants were processing the stimuli semantically anyway. Latencies did not correlate with the magnitude of each digit in the triplet (first: $r = .08$; second: $r = -.02$; third: $r = .03$; *ns* in all cases), nor with their combined magnitude ($r = .03$, *ns*).

Comparison and Addition Tasks

For the comparison and addition tasks, error rates were slightly but not significantly different (paired t test: $t(6) = -2.3$, $p < .06$). Almost none of these errors could be attributed to subjects doing the wrong task (i.e., persevering in comparing the third digit with the larger instead of the sum, or vice versa). An ANOVA was performed on the latencies of correct answers with the same variables as above, to which the split between the third and the larger or the sum of the pair (split 1 vs. 2 vs. 3, 4, and 5) was added.[2] The main effect of repetition (first scans: 681 msec, second scans: 627 msec; $F(1, 4) = 50.5$, $MSE = 2740.4$, $p < .003$) and a marginal effect of response (yes: 636 msec, no: 672 msec; $F(1, 4) = 5.1$, $MSE = 11{,}856.9$, $p < .09$) were again found. There was only a marginal tendency for latencies to differ across tasks ($F(1, 4) = 7.5$, $MSE = 80732.8$, $p < .06$). The split had a significant main effect (split 1: 658 msec, splits 3–5: 625 msec, $F(2, 8) = 5.3$, $MSE = 9032.3$, $p < .04$) and interacted with task ($F(2, 8) = 5.6$, $MSE = 5701.1$, $p < .03$) revealing a constant decrease from small to large splits for comparison, whereas, though presenting the expected decreasing pattern, splits 1 and 2 only differed marginally in the addition condition.

The retrieval of additive facts was not required in the judgment of orientation on arabic digits and in the comparison conditions. However, chronometric studies showed that, under some conditions, there may be an automatic access to the answer of stored additive facts upon mere presentation of two digits (LeFevre, Bisanz, & Mrkonjic, 1988). In the present experiment, such an automatic access to a stored answer may be evaluated through the potential effect of the distance between the sum of the pair and the third digit. However, this effect was not found: Latencies did not correlate with this distance in the digit-orientation judgment ($r = -.05$; *ns*), nor in the comparison condition ($r = .02$, *ns*).[3]

Summary of Behavioral Data

Together, these results showed that the tasks were globally of similar complexity since performance was equally accurate and fast for all. The addition condition appeared to be slightly slower and more error prone, which is understandable since, contrary to the other conditions, it required performing two different tasks. However, this difference was not statistically significant,[4] which ensures that any critical difference in the neuroimaging data could not be attributed to different loads of the experimental conditions. Most importantly, the absence of any magnitude effect in the judgment of orientation on arabic digits suggests that the stimuli in this condition were not processed up to the semantic level, and the presence of the split effect in the comparison and addition conditions indicates that the participants were actually performing the right task. Since the items do not necessarily belong to the same split category depending on whether the task is to compare the third digit with the larger or with the sum of the pair, finding the adequate split effect is an indirect indicator of the actual task performed.

Neuroimaging Data

Tables 4 and 5 list, for each contrast of interest, the locations and peak Z scores of areas that exceeded the uncorrected $p < .001$ threshold.

Table 4. Significant Activation Foci for the Active Tasks Contrasted with Rest

Orientation Judgment On																
Characters				*Digits*				*Comparison*				*Addition*				
s.c.				*s.c.*				*s.c.*				*s.c.*				
x	*y*	*z*	*Z score*	*x*	*y*	*z*	*Z score*	*x*	*y*	*z*	*Z score*	*x*	*y*	*z*	*Z score*	*Anatomical structure (BA)*
−6	−84	−8	7.4	−6	−86	−8	7.2	−8	−86	−6	7.7	−6	−88	−8	7.7	L lingual gyrus (BA 17)
−14	−80	−10	7.4	−26	−82	−10	7.2									L lingual/fusiform gyri (BA 18)
−36	−74	−6	7.6	−36	−74	−8	7.6	−36	−72	−6	7.5	−38	−76	−6	6.9	L lingual (BA 18)/mid occipital gyri (BA 19)
				−2	−76	−8	7.2									L lingual gyrus (BA 19)
−42	−28	54	7.2	−42	−28	54	7.2	−42	−28	54	7.4	−42	−28	54	7.2	L postcentral gyrus (BA 2)
−38	−36	36	5.5	−38	−36	36	5.3	−38	−38	36	6.6	−38	−42	38	5.9	L inf parietal lobule (BA 40)
												−30	−50	44	5.5	L inf parietal lobule (BA 40)
−32	−56	56	4.5	−32	−56	56	5.2	−30	−60	54	6.3	−32	−58	54	5.8	L sup parietal lobule (BA 7)
				−26	−10	50	3.9	−28	−8	50	6.2	−26	−12	52	5.6	L precentral gyrus (BA 4)
												−34	−18	62	5.8	L precentral gyrus (BA 4)
												−40	−4	30	4.5	L precentral gyrus (BA 4)
				−8	0	54	4.3	−8	2	52	4.9	−12	0	54	5	L cingulate gyrus (BA 24)
−20	−44	−40	5.6	−16	−44	−38	4.8	−18	−44	−42	4.6	−18	−42	−40	3.9	L cerebellum
−36	−48	−22	6.2	−22	−50	−14	5.6					−24	−50	−18	4.5	L cerebellum
−20	−22	12	4	−22	−20	6	3.5	−18	−20	6	3.9	−18	−20	10	4.1	L thalamus
				−16	−10	6	3.2	−4	−10	20	3.7					L thalamus
22	−86	−8	7.5	16	−84	−10	7.3	20	−86	−10	7.6	20	−88	−10	7.6	R lingual/fusiform gyri (BA 18)
16	−92	10	7.2	12	−92	6	6.8	10	−90	8	7.2					R lingual gyrus (BA 18)
34	−86	0	7.7	36	−84	−2	7.5	32	−84	20	6.6	34	−88	2	7.3	R inf/mif occipital gyrus (BA 18)
30	−60	46	4.6	28	−60	56	5.7	24	−62	52	6.3	30	−60	52	5.2	R inf/sup parietal lobule (BA 40/7)
								34	−40	46	4.5					R sup parietal lobule (BA 7)
				34	0	20	3.8									R anterior insula
4	−70	−18	7.8	6	−70	−18	7.4	4	−70	−18	7.7	4	−70	−18	7.6	R cerebellum
38	−64	−18	7.7	40	−62	−18	7.7	36	−66	−18	7.5	34	−66	−18	7.2	R cerebellum
20	−50	−24	7.5	20	−50	−22	7	18	−52	−22	6.8	18	−52	−22	7	R cerebellum
20	−58	−50	5.8	22	−58	−50	5.2	22	−58	−50	5.2	16	−58	−50	4.8	R cerebellum
												22	−28	4	3.4	R thalamus
0	−28	−8	6.3	0	−26	−10	4.7	2	−28	−10	4.4	2	−24	−8	4.9	cerebellar peduncle

Negative values correspond to voxels to the left (*x*), or below (*z*) the intercommissural line, or behind the intersection of the intercommisural and vertical anterior commissural lines (*y*). s.c. = stereotaxic coordinates; BA = Brodmann's area; L = left, R = right; inf = inferior, mid = middle, sup = superior.

Active Tasks Minus Rest

The four contrasts between each active task and rest presented highly similar patterns of rCBF changes revealing largely posterior activations. Each task bilaterally activated the primary and secondary visual areas (BA 17, 18, 19), the inferior and superior parietal lobules (BA 40, 7), the upper part of the cerebellum

Table 5. Significant Activation Foci for the Contrasts of Interest

Contrast	s.c.			Z score	Anatomical Structure (BA)
	x	*y*	*z*		
Numbers vs. Characters	34	14	2	4.38	R anterior insula
	48	−68	44	3.56	R angular gyrus (BA 39)
	50	−54	42	3.34	R angular/supramarginal gyri (BA 39/40)
	30	−62	60	3.21	R postcentral sulcus/sup parietal lobule (BA 7)
Comparison vs. Numbers	−24	−68	50	4.45	L intraparietal sulcus/sup parietal lobule (BA 7)
	−20	−98	−8	3.92	L lingual gyrus (BA 17)
	−12	−86	−8	3.58	L lingual gyrus (BA 18)
	−48	20	30	3.38	L inf frontal sulcus/middle frontal gyrus (BA 9)
	−32	−6	50	3.28	L mid frontal gyrus/precentral sulcus (BA 6)
	−58	−6	42	3.23	L precentral sulcus/precentral gyrus (BA 6)
	30	−94	−14	3.47	R lingual gyrus (BA 18)
Comparison vs. Characters (masked with Comparison vs. Rest)	−34	−2	48	4.43	L mid frontal gyrus/precentral sulcus (BA 6)
	−24	−66	50	4.16	L intraparietal sulcus/sup parietal lobule (BA 7)
	−40	−56	44	3.59	L inf parietal lobule (BA 40)
	20	−68	48	3.72	R sup parietal lobule (BA 7)
Addition vs. Comparison	28	32	−16	3.57	R orbitofrontal gyrus (BA 11)
	32	20	−4	3.43	R anterior insula
Addition vs. Characters (masked with Addition vs. Rest)	−18	2	58	4.61	L sup frontal gyrus/sup frontal sulcus (BA 6)
	−46	−2	38	4.07	L precentral sulcus (BA 4/6)
	−26	2	44	3.37	L middle frontal gyrus (BA 6)
	−40	−54	42	3.92	L inf parietal lobule (BA 40)
	−28	−70	50	3.91	L intraparietal sulcus/sup parietal lobule (BA 7)
Numbers vs. Comparison	−44	2	−10	3.50	L insula
	−32	2	−6	3.14	L insula/sup temporal gyrus
	32	16	0	3.90	R anterior insula
	52	−68	0	3.66	R middle occipital gyrus (BA 19)
	30	−30	−18	3.61	R parahippocampal/fusiform gyri (BA 36)
	64	−26	32	3.41	R inf parietal lobule (BA 40)
	56	−34	36	3.28	R inf parietal lobule (BA 40)

See note in Table 4 for further details.

and the cerebellar peduncle; foci were also found in the postcentral gyrus and in the thalamus only in the left hemisphere. In the three numerical conditions, however, the parietal foci were more extended than in the nonnumerical condition, and foci were found in the left precentral (BA 4) and in the cingulate (BA 24) gyri. Finally, the judgment of orientation on digits activated the anterior insula, and in addition, the thalamus only in the right hemisphere. The four reverse contrasts (rest minus each active task) led to highly similar patterns of rCBF changes, this time largely anterior, with a massive bilateral involvement of the whole frontal and temporal cortices. For each contrast, the main foci were found bilaterally in the superior temporal gyrus (BA 22, 38), in the middle frontal gyrus (BA 9, 10), at the junction between the cingulate gyrus and the precuneus (BA 23, 30, 31), and in or very close to Broca's area (BA 44, 45, 47) in the left and the homologous areas in the right hemisphere. Finally, bilateral activations were found in the lower part of the cerebellum.

Orientation Judgment on Digits Minus Orientation Judgment on Characters

The specific activations produced by processing arabic digits relative to nonnumerical characters were located in the right anterior insula, in a small area of the superior parietal lobule (BA 7) and at the junction between the right angular and supramarginal gyri (BA 39/40). However, these parietal foci appeared more activated in the numerical condition simply because of a deactivation in the nonnumerical one. The activity profiles indeed showed that this latter condition was much less activated than the other four, among which the judgment of orientation on arabic digits and the resting conditions were equally slightly higher.

Comparison Minus Orientation Judgment on Digits

When the activation of the orientation judgment on arabic digits was subtracted from the comparison condition, foci linked to numerical comparison were found in the intraparietal sulcus extending into the superior parietal lobule (BA 7), the inferior frontal sulcus extending into the middle frontal gyrus (BA 9), the precentral sulcus and gyrus (BA 6) and the lingual gyrus (BA 17, 18), all in the left hemisphere. A homologous but less extended area in the lingual gyrus was the only activated area found in the right hemisphere.

Comparison Minus Orientation Judgment on Characters

Although semantic processing of the stimuli in the judgment of orientation on arabic digit condition was not evidenced in the behavioral data (no magnitude effect), one cannot completely exclude some automatic access to the representation of magnitude which might then mask areas of interest in the previous contrast. In order to verify this, we subtracted the orientation judgment on characters from the comparison condition; to ensure that only true activations (i.e., relative to rest) were found, this contrast was masked with the comparison minus rest contrast. This confirmed the left intraparietal and superior parietal as well as the precentral activations already found in the previous contrast; moreover, it revealed a focus of activation in the inferior parietal lobule (BA 40). In the right hemisphere, only the superior parietal lobule (BA 7) was found activated. Finally, there was no occipital activation.[5]

Addition Minus Comparison

When the comparison condition was subtracted from the addition condition, the retrieval of simple addition facts activated the orbito-frontal gyrus (BA 11) and the anterior insula in the right hemisphere. A close inspection of the activity profiles of these foci showed that the differences arose from a relative deactivation in the comparison condition (Figure 2). In the left hemisphere, only a limited area in the superior part of the dorsolateral prefrontal cortex (BA 9/10) fell short of significance (uncorrected $p < .003$). No specific activity was found in the language areas (and none in Broca's area in particular; the activity profiles even showed that it was less activated during addition, and that it was deactivated in all experimental tasks relative to rest,[6] see Figure 2).

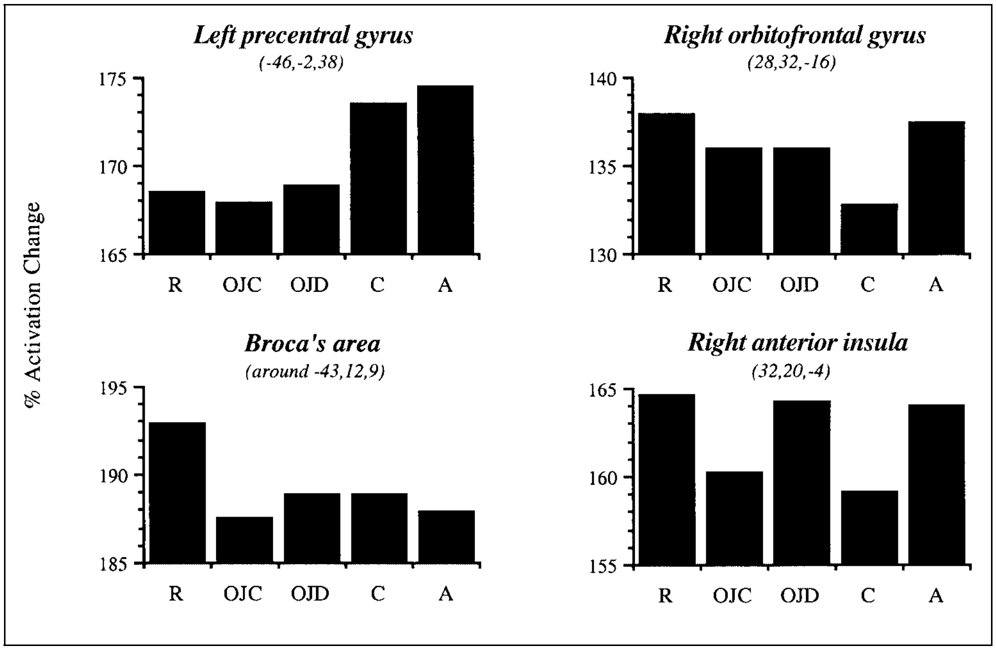
Addition Minus Orientation Judgment on Characters

Although the retrieval of addition facts was not required in the judgment of orientation on arabic digits and in the comparison conditions, one cannot completely exclude some automatic access to the stored answer of the addition for the pairs of digits. Had this happened, then some areas of interest might have disappeared in the previous contrast. We therefore subtracted the orientation judgment on characters from the addition condition; to ensure that only true activations (i.e., relative to rest) were found, this contrast was masked with the addition minus rest contrast. The results showed, as for the contrast between comparison and orientation judgment on characters, left inferior and superior parietal foci (BA 40, 7), along with middle frontal gyrus and precentral-sulcus foci (BA 4/6). However, this time, no activation was found in the right hemisphere, and a specific focus appeared in the superior frontal sulcus and gyrus (BA 6).[7] Again, no specific activity was found in language areas in this contrast.

Reverse Contrasts

Finally, a strong assumption of stepwise designs is that all the processes involved in a condition are also involved in the next one. This can be verified by looking at the reverse contrasts (i.e., subtracting the condition with more processes from the one with less processes): When the stepwise rationale is met, no residual activation is left. If one refers to the rationale of the present experiment outlined in Table 2, the only reverse contrast liable to reveal activations is the one between orientation judgment on arabic digits and

Figure 2. Percent of adjusted rCBF changes for the various foci of interest during addition as a function of condition. R = rest; OJC = orientation judgment on nonnumerical characters; OJD = orientation judgment on arabic digits; C = comparison; A = addition.



comparison. Indeed, although the digits were presented with the same orientation characteristics, the judgment of orientation was not involved in the comparison condition. As expected, none of the reverse contrasts revealed any activation left, except this one which showed activations involving mainly the right hemisphere, thus replicating previous findings (Dupont et al., 1993). Foci were located in the insula, at the occipito-temporal junction (BA 19), the fusiform gyrus and in the inferior parietal lobule (BA 40); in the left hemisphere, only the superior temporal gyrus and the insula were activated.

DISCUSSION

The aim of the present study was to localize the cerebral areas specifically involved in three basic numerical abilities—arabic numeral processing, magnitude comparison, and retrieval of simple addition facts—and, with this, to test the anatomo-functional proposals of the Triple-code model (Dehaene & Cohen, 1995). We will first summarize the major findings of this study, and we will then see how they improve our understanding of the cerebral bases of numerical processing in the light of the Triple-code model expectations.

Main Anatomical Results

To sum up the results of the various contrasts, processing visual inputs and making the orientation judgments produced a large bilateral activation of primary and secondary visual areas, slightly more pronounced in the right hemisphere, as well as bilateral activation of parietal areas; furthermore, giving the manual answers activated only the motor areas in the left hemisphere since all subjects answered with the right hand. Processing arabic digits and comparing numerical magnitudes activated, respectively, right- and left-sided frontal and parietal areas. The right areas were active when the surface judgment was required, and the left areas when the processing of magnitude was needed. Relative to comparison, addition only produced extra activation in the right frontal areas. Finally, the left precentral gyrus was found activated in comparison and addition, and a small area in the right superior lobule was found activated in comparison when these conditions were contrasted with the orientation judgment on nonnumerical characters.

In line with previous findings, the most interesting foci of activation were found in the parietal areas. As concerns the inferior parietal lobule, two foci were found only in the left hemisphere. The first one (around x, y, z: −38, −36, 36) appeared in all contrasts between active task and rest, and thus seemed not specific to number processing. On the contrary, the second focus (around x, y, z: −40, −56, 44), which was posterior to and above the previous one, reached significance only when digits were presented, and mostly when they were to be processed semantically in the comparison and addition conditions. When only the orientation judgment was required, this focus was less activated, though still more than during rest. The homologous areas in the right hemisphere never appeared significantly activated and were even sometimes deactivated when compared to rest. As concerns the superior parietal lobule, two different foci of activation were also revealed. Again, the first one appeared in all contrasts between active task and rest but, this time,

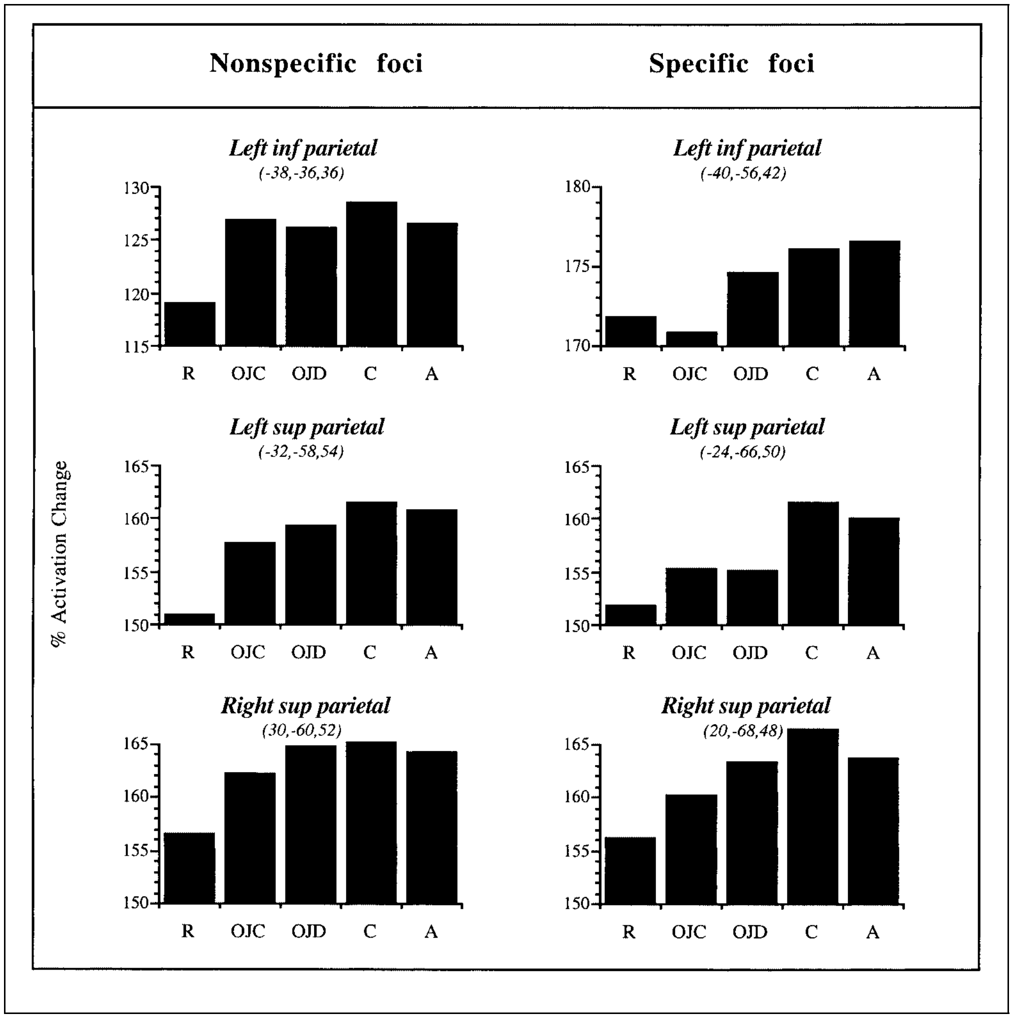


Figure 3. Percent of adjusted rCBF changes for the various foci of interest in the parietal lobes as a function of condition. The left and right plots show the activity profiles, respectively, in foci nonspecific and specific to numerical processing. (See Figure 2 for further details.)

bilaterally (around x, y, z: −32, −58, 54, and 30, −60, 52). The second one was found in each contrast between the two numerical and the two orientation tasks in the left hemisphere only. Although close to the previous one, this peak lying in the intraparietal sulcus and extending, for its major part, into the superior parietal lobule (around x, y, z: −24, −68, 50) exhibited a different pattern of activation and thus appeared as a distinct focus. The homologous area in the right hemisphere appeared significantly activated only when comparison was contrasted with orientation judgment on nonnumerical characters. The activity profiles for these foci are shown in Figure 3.

A Network for Numerical Processing

The neuropsychological as well as the functional neuroimaging literature regularly ascribed to the parietal cortices, especially the left one, a critical though not clearly defined role in number processing and calculation. The present study thus confirmed the involvement of left and right parietal areas in numerical contexts and clarified their roles. These areas contribute to numerical processing at two different levels, one specific and one not specific to numbers.

Arabic Digits Processing

The processing of arabic digits shared with nonnumerical characters bilateral visual processing-related activations in the occipital areas. Lingual activity was observed in all conditions relative to rest, it was stronger during comparison and addition relative to orientation on digits, but not to orientation on nonnumerical characters. Thus, it might reflect either the digit identity processing or simply a higher visual processing demand of the tasks. Besides this perceptual stage, other nonspecific processes took place in the left inferior and left and right superior parietal areas, which were activated in all tasks compared to rest. The left inferior focus is part of what has been identified as the object working memory network (Smith et al., 1995), and is similar to areas observed in studies on visuo-spatial attention and eye movement control (Corbetta et al., 1998). All nonspecific foci are within or very close to what has been described as the visuo-spatial dorsal pathway involving occipito-parietal areas and devoted to processing information about where objects are in the environment (Haxby et al., 1994). Thus, the nonspecific foci are likely to correspond to the visuo-spatial and attentional processes required by processing digits and by the various tasks' demands. Despite their small amplitude due to the foveal presentation of the stimuli, eye movements could also have contributed to these activations.

With the required orientation judgment, the processing of arabic digits did not produce activation in the classical language areas, which suggests that digits were not automatically verbalized. The only activation specifically related to digit processing was found in the right anterior insula. Another focus in the left inferior parietal lobule fell short of significance (uncorrected $p < .003$) when compared to nonnumerical characters, suggesting a process going beyond the surface processing of the digits (see below).

Besides the expected visual activation in the occipital areas, the Triple-code model assumption of a digit processing extending into the temporal lobes was not confirmed here. Rather, the result of the perceptual stage in the occipital areas might have been sent into some sort of visuo-spatial representational medium in the parietal lobes. Whether this is the normal processing of arabic digits or the result of the present experimental design remains to be clarified.

Numerical Magnitude Processing

The occipital foci observed bilaterally in comparison were most probably due to the necessity of a visual processing and discrimination of individual digits in the triplets, not necessary for orientation judgments since a global perceptual analysis was then sufficient. It is unlikely that these foci reflect strictly numerical processes and they will not be discussed any further.

Specific magnitude processing and/or comparative mechanisms involved mainly the left inferior parietal lobule, the left intraparietal sulcus and the left superior parietal lobule and, to a lesser extent, the right one. It is possible that the inferior and the superior foci play different roles since only the inferior one was also slightly activated in the orientation judgment on digits. This focus cannot be distinguished from visuo-spatial attention areas (Corbetta et al., 1998) and one can thus not exclude the possibility that it corresponds to a slightly higher attentional demand in the comparison and addition tasks. However, as far as the anatomical precision of the neuroimaging techniques can tell, the intraparietal and superior parietal foci belong neither to the visuo-spatial dorsal pathway, nor to the visuo-spatial attention areas, nor to the areas involved in visually guided saccadic eye movements (Sweeney et al., 1996; Anderson et al., 1994). Moreover, they do not correspond to the areas found in working memory studies using letters, unfamiliar geometric drawings, irregular polygons, and/or locations as stimuli (Salmon et al., 1996; Smith et al., 1995; Paulesu, Frith, & Frackowiak, 1993), or in nonnumerical magnitude estimation (e.g., estimation of duration, intensity, size, etc.; Lejeune et al., 1997; Maquet et al., 1996). Interestingly, they correspond or fall very close to some of those repeatedly found to be activated in working memory studies using arabic digits as stimuli (Ghatan et al., 1998; Petrides, Alivisatos, Meyer, & Evans, 1993), even when the location of the digits on the screen was the only dimension to be explicitly remembered (Coull & Frith, 1998; Coull, Frith, Frackowiak, & Grasby, 1996). Since the working memory load was kept as equivalent as possible in the present experiment, the implication of these areas seems to go beyond the working memory components required by the tasks and may thus reflect the automatic and/or voluntary semantic processing of the magnitude dimension.

Our results partly support the Triple-code model's assumption regarding the processing of numerical magnitude information in the parietal areas, but they give rise to a finer understanding of their specific roles. Besides their involvement in nonspecific visuo-attentional and working memory processes, the parietal cortices play a critical role in magnitude processing. A left-sided predominance was recently observed in numerical comparison, mainly with small splits (Pinel et al., 1999). Our experiment confirms a greater participation of the left areas in comparative judgments, whereas the Triple-code model expected a right predominance (Cohen & Dehaene, 1996; Dehaene & Cohen, 1995, 1997). It is worth noting that this left-sided pattern is not an artefact of the contrast between the comparison, which would be bilateral, and the orientation tasks which would be more right-sided, since most of the right parietal areas were found deactivated relative to rest in the orientation tasks. At the anatomical level, our results indicate that the critical parietal areas for magnitude processing correspond to the intraparietal sulcus extending upward (Figure 4), which perfectly fits with the localization found in the lesional study carried out by Takayama et al. (1994) but appears to be more posterior and superior to what was stated in the Triple-code model and observed in recent studies (Pinel et al., 1999; Sathian et al., 1999; Dehaene, Dehaene-Lambertz, & Cohen, 1998).

Finally, our experiment revealed the involvement of the left precentral gyrus and close areas in the frontal lobe. Although it was not expected by the Triple-code model, the left precentral gyrus has been found activated in multiplication, comparison, and approximate calculation (Pinel et al., 1999; Dehaene et al., 1996, 1999) as well as in several other studies involving numerical tasks (see Introduction). The potential role of these areas in numerical comparison is discussed below.

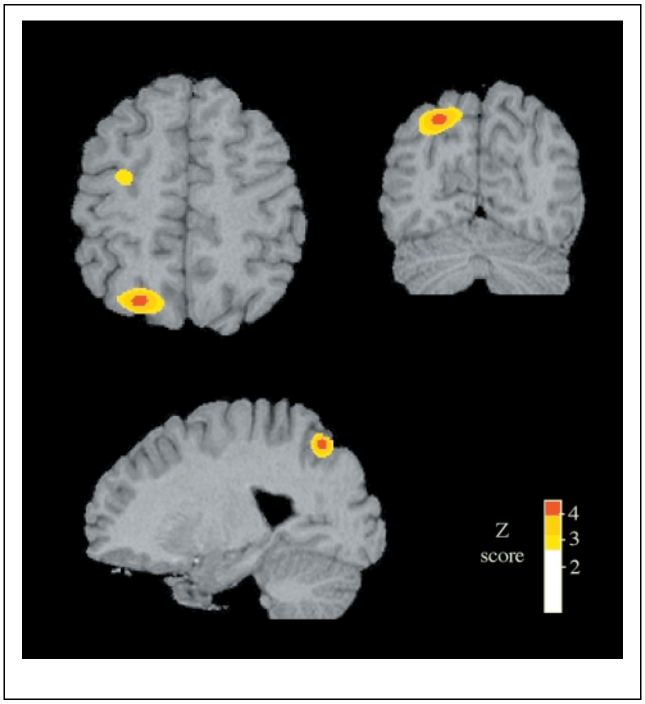


Figure 4. Left intraparietal/superior parietal focus (x, y, z: −24, −68, 50) related to numerical processing in the comparison minus orientation judgment on digits contrast. The anterior focus shows the top of the precentral activation (x, y, z: −32, −6, 50). Activation profiles are shown in Figures 2 and 3.

Addition Facts Retrieval Mechanisms

In this experiment, one cannot easily separate the processes involved in addition facts retrieval from those involved in magnitude comparison since both processes were required in the addition condition, leading to highly similar patterns of activation. Only two additional foci were found in the right orbitofrontal lobe and the anterior insula. It is interesting to note that, although these foci appeared activated because of a deactivation in the comparison condition (Figure 2), they are nevertheless likely to reflect processes related to fact retrieval. Indeed, these foci were highly deactivated during comparison relative to rest; since comparison was also involved in the addition condition, these areas should have been equally deactivated in the latter. On the contrary, they did not appear different from rest, which must be seen as reflecting an averaged level between periods of deactivation (comparison stage) and periods of higher activation (addition stage). These areas may thus underlie some processes occurring during the memory-based retrieval of addition facts. A speculative but plausible explanation is the well-known role played by the anterior insula and the connected orbitofrontal cortex in the motivational-affectual aspects of learning and memory (for a review, see Flynn, Benson, & Ardila, 1999). In our experiment, the explicitly arithmetical context of the addition condition might have increased the mathematics-anxiety level (Ashcraft & Faust, 1994), hence activating these areas.

A critical point is that, contrary to the Triple-code model's expectation, none of the left language areas usually involved in verbal processes were found activated during fact retrieval. This was true when addition was contrasted with comparison, but also when it was contrasted with rest or with the orientation judgment on nonnumerical characters. This shows not only that verbal processes were not involved in facts retrieval, but also that digits were not spontaneously verbally processed or named. In the initial formulation of the Triple-code model, no distinction was made between operations concerning the arithmetical facts retrieval process involved. Consequently, additions and multiplications were both supposed to be performed by directly retrieving the answer from long-term declarative networks. However, it has been proposed in subsequent publications that simple additions and multiplications may basically differ in the way they are processed by adults: Multiplications would mainly be solved through verbal-retrieval processes whereas additions would more often lead to computation strategies which may then involve the magnitude representation.[8] Such a proposal would explain at the same time the absence of activation of the language areas and the close activation patterns observed for comparison and addition in the present experiment. Some caution is, however, needed before this view can be accepted. Firstly, although the study of brain-damaged patients often reveals dissociated performances between the two operations (Pesenti, Seron, & Van der Linden, 1994; McCloskey, Harley, & Sokol, 1991), classical chronometric studies showed a high correlation between response latencies for addition and multiplication of the same pair of digits. For any pair, the latency for each operation was the best predictor of the other one, and it was a better predictor than structural variables (such as the smaller, the larger, the sum, the product of the pair, etc.) or even the time to compare the same digits. This strongly supports the view that addition and multiplication involve similar cognitive processes, namely, the retrieval from networks of stored answers (Miller, Perlmutter, & Keating, 1984). Secondly, in the present experiment, we purposely selected very simple addition facts (with answers never larger than 9) for which the probability to retrieve directly the answer is much larger (about .90) than the probability of counting (less than .10) or transforming the problem (less than .05; LeFevre et al., 1996b). It is thus likely that, even if addition and multiplication strategies were to be globally different, the set of additive problems used here cancelled this difference.

Further chronometric as well as neuroimaging investigation is thus needed to decide whether one should consider simple additions and multiplications as relying on different processes. For example, it has been shown that cortical stimulation of a single site in the left anterior parietal lobule disrupted performance in multiplication but not addition fact retrieval (Whalen, McCloskey, Lesser, & Gordon, 1997). Yet, this does not imply different processes (e.g., retrieval vs. computation): multiplication and addition fact networks could simply be stored in different brain areas. What our experiment clearly shows is that when verbal processes are not induced either by the stimuli notation or by the response (overt or covert) production requirements, simple additions can be solved without verbal activation. A similar conclusion was recently drawn from studies exploiting some specificities of the French and Dutch verbal numeral systems. Indeed, in the French numeral system (as in English), both the verbal and the arabic notations agree with respect to the position of units and tens (e.g., 24 is said *vingt-quatre*, i.e., twenty-four), whereas this is not the case in Dutch (24 is said *vierentwintig*, i.e., four-and-twenty). Several experiments have shown that these linguistic specificities have little if any effect on the addition and multiplication retrieval processes, and that any difference further disappeared when the input and production notations were controlled and did not require verbal translation (Brysbaert, Fias, & Noël, 1998; Noël, Fias, & Brysbaert, 1997). Whether completely different resolution strategies are induced by the stimuli/response notations (as suggested in Campbell, 1994; Campbell, Kanz, & Xue, 1999) or whether verbal strategies only appear in addition to others is still to be clarified.

Because a comparison stage was involved in the addition condition, the actual implication of the left-parietal areas during the addition fact retrieval must be considered with caution. As a matter of fact, the intraparietal areas were not observed in Dehaene et al.'s (1999) addition retrieval condition when compared to approximate calculation. However, we do not think that this actually runs against our results. In fact, Dehaene et al.'s exact addition condition also involved a comparison stage. Subjects were first presented with an addition and then with two answers to choose from. Thus, once the fact has been retrieved from memory, it must be compared to the proposed results (Cohen et al., 1994). Then, if the parietal areas are involved in both comparison and fact retrieval, this was masked in that experiment since they were found active during approximate calculation. In our view, the possible role of the parietal cortex in addition must be seen as linked with the role of left precentral and -frontal areas.

Indeed, the left precentral gyrus was slightly more activated in the addition than in the comparison condition which means that it may play a role in addition beyond its involvement in the comparative processes. The role of this structure in numerical processes is still undefined and might be explained in two ways. On the one hand, it could reflect some verbal-motor components related to covert naming of number names or retrieval of arithmetical facts based on verbal routines. Although this possibility cannot be excluded, it seems unlikely given the absence of activation in any other verbal areas. On the other hand, similar precentral and left frontal activations were found when subjects were required to covertly name the use of tools which was interpreted as related to the motoric aspects of object semantics (Grafton, Fadiga, Arbib, & Rizzolatti, 1997). In the present case, the joint activation of these frontal areas with the parietal ones may reflect the involvement of the finger-movement network that may underlie finger counting (Butterworth, 1999; Simon, 1999), one of the basic numerical learning strategies spontaneously developed in children (Fuson, 1988). By extension, this network may become the substrate of numerical knowledge and processes. This interpretation is supported by a recent study showing that performance on finger-knowledge tests (e.g., digital gnosia, digital discrimination, etc.) was the best predictor of arithmetical achievement in 5- to 6-year-old children (Fayol, Barrouillet, & Marinthe, 1998). It is also in line with neuropsychological data showing a frequent association between finger agnosia and acalculia (Gerstmann's syndrome).

Conclusions

The present PET study was aimed at localizing the cerebral networks involved in numerical processing. More specifically, arabic digit processing, magnitude comparison, and addition were tested in experimental tasks in which the visual complexity of the stimuli, the response, and the working memory load were kept equivalent, as confirmed by the behavioral results. In agreement with the neuropsychological as well as the functional neuroimaging literature, the activation data revealed the major involvement of the parietal lobes and the precentral gyrus in the left hemisphere. The parietal lobes appeared involved at two different levels. Firstly, they were involved at a level not specific to numbers, most probably through general working memory, visuospatial and attentional processes. Secondly, they played a specific role in the processing of numerical magnitude information. This double role explains the importance of parietal lobes in numerical processing, the frequency as well as the great variety of numerical deficits after lesions to these areas. Some of these deficits thus directly stem from lesions to truly numerical areas and others from lesions to areas underlying important but not strictly numerical processes. At the anatomical level, we found the main foci in the posterior and superior parts of the parietal lobules, and a greater participation of the left hemisphere in these processes. The addition facts retrieval mechanisms rely on the same left intraparietal and superior parietal area as well as on the precentral gyrus; they also implicate the right orbitofrontal lobe and the anterior insula possibly through peripheral processes related to the motivational-affectual aspects of learning. The language areas remained inactivated, which suggests that the retrieval of simple arithmetical facts does not necessarily imply some sort of verbal process.

Functional neuroimaging studies devoted to the study of numerical processing remain very scarce. The present experiment replicates and confirms previous results regarding the parietal lobes, but it shows that most of the frontal activation found in previous studies was likely due to the working memory aspects of the tasks which were nonspecific to numerical contexts. We suggest that the numerical processing involves an occipito-parietal network dedicated to perceptual and representational processing of arabic digits and a parieto-frontal network dedicated to more semantic processing. As far as our experimental tasks indicate, magnitude comparison and addition seem to similarly involve this latter network, with a greater parietal implication in comparison and a greater precentral implication in addition. This network may originate from the early experience of counting and representing numerosity with fingers and thus be related to finger movement areas.

Figure 5. Examples of nonmeaningful characters (upright and italic orientations).

METHODS

Participants

Eight healthy male volunteers gave their written informed consent to participate in this study. They were aged between 21 and 29, were all right-handed and had corrected-to-normal vision. The study was approved by the local Biomedical Ethics Committee.

Stimuli

Nine nonmeaningful characters were created so as to avoid any lexicalization (no alphanumeric characters, no symbols) and to match their visual complexity with the one of arabic digits (see examples in Figure 5). Triplets consisted of three characters or three digits from 1 to 9. In all conditions, half of the pairs were in an italic orientation and the remaining half in an upright orientation; the third stimulus in a triplet had the same orientation as the pair in half of the cases. In the three numerical conditions, the pairs were identical and the third digit was selected with the following constraints. Firstly, the split between the third digit and the larger or the sum of the pair ranged from −4 to 5 but was never equal to 0. The complexity of the critical comparison in the comparison and addition conditions was kept equivalent by equalizing as much as possible the splits. For example, for the triplet (2, 3, 4), the split is 1 in comparison (3 vs. 4) as well as in addition (5 vs. 4). Splits were not equalized item by item but across lists (for splits 1 to 5, respectively, comparison list: 30, 25, 16, 2, and 1 items, mean split: 1.9; addition list: 29, 21, 15, 2, and 1 items, mean split: 1.5). This resulted in two lists of 74 and 68 items for comparison and addition, respectively. Secondly, the sum of the pair was never larger than 9 in order to equalize magnitude and verbal complexity of the answer to be produced in response to the comparisons and to the sums. Thirdly, within conditions, the third digit was larger than the sum of the pair in half of the cases, and smaller in the other half. As a consequence of these constraints, for the *no* answers, the third digit was equal to the smaller of the pair in 3 and 5 items of the comparison and addition lists, respectively, and smaller than one of the pair digit in 15 items of the addition list.[9] Two other 74-item lists were constructed for the orientation conditions by picking out alternatively items from the comparison and multiplication lists. Each of the four lists was then divided into two blocks used in only one scan.

Experimental Procedure

In the resting condition, subjects were asked to rest silently with eyes closed and no other particular instructions were given except to relax. The judgment of orientation on nonnumerical stimuli consisted of the following sequence of events (Figure 1). A pair of 4.5 cm-high nonmeaningful characters was presented with an upright or italic orientation, on the upper part of a Macintosh 17 AV computer screen in black on a light grey background; after 500 msec, a third upright or italic character was presented above the pair which remained on the screen. The subject had to decide if its orientation was the same as the one of the pair by pressing with the major or the index of his right hand one of two keys identified as *yes* and *no* on a two-button response box connected to the computer. The key press made the triplet disappear and another trial started after a 500 msec-blank screen. In the judgment of orientation on numerical stimuli, the same sequence of events was presented with arabic digits instead of nonmeaningful characters. In the numerical comparison, the subject had to decide if the third digit was larger than the larger of the pair. In the addition condition, the subject had to decide if the third digit was larger than the sum of the pair. A delay between the presentation of the pair and the third element was decided to ensure that the subject actually made the addition and did not base his decision on approximate calculation. The triplet remained present on the screen until the response so as to keep the short-term memory load to a minimum. In the comparison and addition condition, subjects were instructed not to pay any attention to orientation.

To equilibrate attentional demands across the four active conditions, the rate of presentation of the items was self-paced by the answer, which resulted in a mean rate of one item every 2.2 sec for orientation and comparison conditions, and one item every 2.3 sec for the addition condition. Half of the subjects responded *yes* with the index and *no* with the major; the order of the keys was reversed for the other half. Before the first scan, the subjects went through a 15-min practice session to get familiarized with the correct response-key association, with the nonmeaningful characters and with the distinction between upright and italic characters and digits. Before each scan, they also practiced the task itself until they felt comfortable with it; the lists of practice items were different from the experimental lists.

Each condition was administered twice in fixed counterbalanced orders with the following constraints: (1) all the subjects were studied in the resting state as the first and last conditions, (2) the two judgment of orientation tasks were always administered before the two other tasks to avoid contamination of "deeper" numerical processing on the more "surface" ones, and (3) the two repetitions of each active condition were always administered in a row. There were thus four orders (half of the subjects starting the orientation tasks with the nonmeaningful characters and half with the digits, half starting the numerical tasks with the comparison and half with addition), with two subjects in each order.

Image Acquisition Procedure and Analysis

Relative cerebral blood flow (rCBF) changes related to activation conditions were assessed using an ECAT-EXACT HR tomograph (CTI-Siemens) which allows simultaneous imaging of 47 transaxial slices in 3-D (septa retracted) mode, with an effective resolution of 8 mm full width-at-half-maximum (Wienhard et al., 1994) and a slice thickness of 3.125 mm. The subject was positioned in the gantry by aligning two sets of low-power laser beams with the canthomeathal line and the sagittal line, respectively. Head-restraining adhesive bands were used. A 22-gauge catheter was then placed in the antecubital vein of the left arm for radiotracer injection (8 mCi/injection of $H_2{}^{15}O$), administered as a slow bolus injection of 20-sec duration. Since stress and novelty effects are commonly observed during the first scan in neuroimaging experiments, a "blank-first-scan procedure" was adopted in order to decrease as much as possible these potential effects on cerebral activations. A key-press practice condition was administered as the first scan: After a false bolus injection in which, without the subjects knowledge, the radiotracer was replaced by a saline solution, subjects had to press the correct key in response to the words *yes* and *no* randomly displayed on the screen. For each condition, scan acquisition and task both started 10 sec after the beginning of injection; they stopped, respectively, 80 and 100 sec later. The between-scan interval to allow for decay was 12 min during which subjects held the practice sessions for the next task.

For each subject, rCBF images were analyzed in correlation with the individually coregistered neuroanatomical data (3-D MRI obtained on a 1.5-Tesla Sigma unit, General Electric, using the Spoiled Grass (SPGR) technique). PET images were realigned to correct for interscan movements and coregistered with the subject's MRI using AIR 3.0 (Woods, Grafton, Holmes, Cherry, & Mazziotta, 1998). The resulting matching brain images were spatially normalized using SPM96 (Friston et al., 1995), in the Talairach and Turnoux (1988) coordinate system with a cubic (2 × 2 × 2 mm) voxel size. The data were smoothed with a 15-mm Gaussian filter to account for residual intersubject differences and were corrected for differences in global activity by proportional scaling. Differences between conditions were assessed by a voxel-by-voxel analysis with statistical parametric mapping (SPM96).

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Notes

1. Models of simple arithmetic assume that adults solve such simple problems by retrieving the answer from a network of

stored declarative associations without any actual computation (Ashcraft, 1992).

2. It is indeed a robust finding that the time required to compare two digits decreases as the numerical distance (split) between them increases (Moyer & Landauer, 1967). This effect can be used as evidence of automatic semantic access for it is observed even when pairs of digits are processed nonnumerically (Dehaene & Akhavein, 1995).

3. The effect was not found at the level of individual performance (r ranging from $-.13$ to $.17$ for the orientation judgment and from $-.05$ to $.19$ for the comparison condition; all p values are not significant).

4. This was, in fact, nonsignificant in preliminary chronometric studies with more participants.

5. Without the masking procedure, other foci were found in the inferior (BA 9/8), middle (BA 6) and medial (BA 6, pre-SMA) frontal gyri, and in the anterior-cingulate gyrus (BA 24/32) in the left hemisphere, as well as right homologous areas in the superior frontal sulcus and gyrus (BA 8), and at the junction between the medial frontal and the cingulate gyri (BA 6/32). These foci were thus more active during comparison than during the orientation judgment but no more than during rest.

6. Individual profiles showed that Broca's area was slightly more activated in the addition than in the comparison condition for three subjects, but never more than during rest.

7. Without the masking procedure, other foci were found bilaterally in frontal areas (BA 4, 6, 8, 9), and in the cingulate gyrus (BA 32) and the parieto-occipital sulcus (BA 7/19) in the right hemisphere. These foci were thus more active during addition than during the orientation judgment but no more than during rest.

8. But, even in these publications, the authors acknowledge that "the normal strategy is to retrieve addition facts from verbal memory" (Dehaene & Cohen, 1995, p. 108). They also recently used simple addition facts to test the hypothesis of verbal processes (Dehaene et al., 1999).

9. This might constitute a bias since decision could be made by comparison of the digits alone without using the additive fact. However, careful debriefing on that specific point after the experiment showed that only one subject realized after the second addition scan this peculiarity of the items structure, but he reported he never used it to take his decision; none of the other subjects reported using conscious short-cuts to perform the tasks. It is worth noting that small splits (splits 1 and 2) represented 70% of the items and large splits (4 and 5) only 4%, thus making a decision based on approximation not very efficient and implausible given the subjects' good performance.

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