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Approximate quantities and exact number words: dissociable systems

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Abstract

Numerical abilities are thought to rest on the integration of two distinct systems, a verbal system of number words and a non-symbolic representation of approximate quantities. This view has lead to the classification of acalculias into two broad categories depending on whether the deficit affects the verbal or the quantity system. Here, we test the association of deficits predicted by this theory, and particularly the presence or absence of impairments in non-symbolic quantity processing. We describe two acalculic patients, one with a focal lesion of the left parietal lobe and Gerstmann's syndrome and another with semantic dementia with predominantly left temporal hypometabolism. As predicted by a quantity deficit, the first patient was more impaired in subtraction than in multiplication, showed a severe slowness in approximation, and exhibited associated impairments in subitizing and numerical comparison tasks, both with Arabic digits and with arrays of dots. As predicted by a verbal deficit, the second patient was more impaired in multiplication than in subtraction, had intact approximation abilities, and showed preserved processing of non-symbolic numerosities.

Keywords: Acalculia; Aphasia; Gerstmann's syndrome; Semantic dementia

1. Introduction

In recent years, several studies have confirmed that an evolutionary precursor of human arithmetic abilities exists in animals. Behavioral studies have revealed that monkeys can performed simple operations such as ordering of two sets based on their numerosity (Brannon & Terrace, 1998), that this ability is cross-modal (Hauser, Dehaene, Dehaene-Lambertz, & Patalano, 2002), and that it is found even in untrained animals (Hauser, Carey, & Hauser, 2000). Three arguments suggest a genuine homology between such animal abilities and the human number sense. First, the neural bases of these abilities have begun to be explored at the single-cell level, revealing neurons tuned to number in frontal and parietal areas that are plausible homologs of the corresponding areas observed by functional neuroimaging during arithmetic tasks in humans (Dehaene, 2002; Nieder, Freedman, & Miller, 2002; Nieder & Miller, 2003; Sawamura, Shima, & Tanji, 2002; Simon, Mangin, Cohen, Le Bihan, & Dehaene, 2002). Second, human infants exhibit similar approximate number discrimination and comparison abilities in the first year of life, before the acquisition of number words (Brannon, 2002; Brannon, Wusthoff, Gallistel, & Gibbon, 2001; Wynn, Bloom, & Chiang, 2002; Xu & Spelke, 2000).

Third, adults who have learned number words and Arabic symbols, show approximation and non-symbolic distance effects parallel to those observed in animals and infants (Dehaene & Cohen, 1997; Dehaene, Spelke, Pinel, Stanescu, & Tsivkin, 1999). Of course, language competence enables humans to go beyond other species in arithmetic, and to develop symbol systems that support exact calculation and higher mathematics. These observations have led to the view that human arithmetic rests on the integration of two distinct systems, a verbal system of number words and a non-symbolic representation of approximate quantities.

In the present paper, we explore the consequences of this view for neuropsychology, by exhibiting two new cases with multiple double dissociations and within-subject associations of deficits. The verbal versus quantity distinction has already been used to account for several puzzling features of acalculia, including the dissociations between multiplication and subtraction, and between exact and approximate abilities. We now show that this distinction predicts whether a patient will show impairments in the processing of numbers

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presented non-symbolically as sets of dots, in basic tasks that are more similar to those used in young children and in animals.

The first dissociation that we examine is between different arithmetic operations with Arabic numerals. According to the triple-code model (Dehaene & Cohen, 1995), distinct arithmetic operations put a differential burden on verbal and quantity representations. Multiplication problems are thought to be solved by accessing a table of memorized facts (Ashcraft, 1992) stored in the form of verbal associations without reference to quantity. In contrast, subtraction facts are not learned by rote at school, and may be resolved through the mental manipulation of quantities. This view can explain the frequent observation of a double dissociation between those two operations (Cohen & Dehaene, 2000; Dagenbach & McCloskey, 1992; Dehaene & Cohen, 1997; Delazer & Benke, 1997; Lampl Eshel, Gilad, & Sarova-Pinhas, 1994; Lee, 2000; McNeil & Warrington, 1994; Pesenti, Seron, & Van der Linden, 1994; van Harskamp & Cipolotti, 2001; van Harskamp, Rudge, & Cipolotti, 2002). It also accounts for the frequent association of multiplication impairments with aphasia, and of subtraction impairments with a dysfunction of parietal lobe systems thought to be engaged in quantity processing (Dehaene & Cohen, 1997). Finally, it meshes well with the differences in brain activation observed during those two operations in normal subjects (Chochon, Cohen, Van de Moortele, & Dehaene, 1999; Lee, 2000) for recent discussion, see (Dehaene, Piazza, Pinel, & Cohen, 2003).

A second dissociation is predicted between exact and approximate calculation. In infants and animals, the preverbal quantity representation is approximate and supports only rough calculations such as approximate addition and subtraction. Only literate humans can discriminate precise large quantities and compute exact operations with large numbers. The distinction between exact and approximate calculation, and its link to symbolic versus quantity formats of number representation, receives support from behavioral and brain-imaging studies in normal adult (Dehaene, 1998; Spelke & Tsivkin, 2001). Furthermore, there is some neuropsychological evidence for a single dissociation between impaired exact calculation and preserved approximation. Patients with severe acalculia may exhibit a preserved ability to approximate the result of an operation (Dehaene & Cohen, 1991; Warrington, 1982). Note that our view further predicts an association of deficits: approximation should be preserved in those patients with impaired multiplication and spared subtraction, and approximation should be impaired in patients with the reverse deficit. Some support for these prediction can be found in our earlier study of patients MAR and BOO (Dehaene & Cohen, 1997), although approximation abilities were not studied in depth. We re-examine this issue in greater detail with the present patients BRI and LEC.

A third dissociation concerns the processing of numerical quantities that are presented non-symbolically, for instance as sets of objects. When an array of dots is briefly flashed, subjects can identify its numerosity without counting, and come up with an exact number name in the case of very small numbers ("subitizing") (Dehaene & Cohen, 1994; Mandler & Shebo, 1982) and with an approximate label subject to Weber's law in the case of larger numbers ("estimation") (Cordes, Gelman, Gallistel, & Whalen, 2001; Whalen, Gallistel, & Gelman, 1999). Subjects can even perform elementary operations such as comparison, addition or subtraction, again with variability (Barth, Kanwisher, & Spelke, 2003). The non-verbal quantity representation is thought to be crucial to such achievement. Verbal abilities, in contrast, play a role in the slower process of exact serial counting, which is largely specific to humans. Again, the verbal versus quantity distinction predicts that counting should dissociate from subitizing and estimation and that symbolic and non-symbolic deficits should be associated non-randomly. Aphasic patients with multiplication impairments linked to their reduced abilities to process verbal numerals should exhibit counting impairments, but their subitizing, estimation, and comparison should be preserved. Conversely, parietal lobe patients who show subtraction and approximation impairments when tested in symbolic formats such as Arabic notation should also show subitizing, estimation, comparison, and computation deficits with non-symbolic stimuli.

A few aspects of these predicted clusters of deficits have been tested in previous patients (e.g. Cappelleti, Butterworth, & Kopelman, 2001; Dehaene & Cohen, 1997; Delazer & Benke, 1997; Grafman, Kampen, Rosenberg, Salazar, & Boller, 1989; Pesenti et al., 1994; Polk, Reed, Keenan, Hogarth, & Anderson, 2001), though not with a systematic set of tasks. Here we attempt to systematize those observations by examining the same tasks in two new acalculic patients with opposite patterns of deficits, as well as in a large group of control subjects. Patient BRI showed aphasia and aspects of semantic dementia associated with predominantly left fronto-temporal atrophy. Patient LEC experienced difficulties in calculation and visuo-spatial processing with Gerstmann syndrome associated with a left parietal ischemic lesion. In both cases, we successively study the dissociations between multiplication and subtraction operations, between exact and approximate calculation, and between symbolic and non-symbolic tasks as well as the associations across pairs of tasks.

2. Clinical description of BRI

Patient BRI was a 45-year-old right-handed former secretary. In July 2000, she presented some behavioral changes (tears, apathy, and loss of weight . . .), and a diagnosis of depression was proposed. Some months later, memory problems and mild word-finding difficulties appeared. A neurological and cognitive assessment was performed in March 2001 (see Table 1).

The patient was impaired in both language production and comprehension. Conversational speech was fluent but not

Table 1
Results of neuropsychological background tests

Function and test	BRI's scores	LEC's scores
General intelligence		
PM 47	31	16*
MMSE	22/30*	19/30*
Language		
Picture-naming		
DENO 100	27/50*	
DO 80		70/80*
BORB item-matching	32/32	
BORB association	26/30	
Palm Tree Test (pictures)	12/20*	
Palm Tree Test (words)	15/20*	
Verbal fluency (semantic/phonemic)	3*/2*	13/9*
Memory		
Hebb	7/2*	5/2*
Corsi	5/6	5/4
Logical memory		
Immediate recognition	Impossible*	13/24*
Delayed recognition	Impossible*	2/24*
BEM 144		
Immediate recognition	22/24	
Delayed recognition	22/24	
Executive functions		
Rey picture	Type IV (35/36)	Type IV (9/36)*
Wisconsin	2 criteria*	
TMT A	51 s	275 s*
TMT B	131 s	400 s* (incomplete)
(B-A)	80 s*	125 s*

Note: PM: progressive matrices; MMSE: Mini Mental State Examination; DENO 100 and DO 80: Oral Denomination Tests; BEM 144: Batterie d'Efficience Mnésique; TMT: Trail Making Test.

* Indicates a significant impairment (performance falling two standard deviations below the level of controls).

informative. BRI repeated words, pseudo-words and short sentences perfectly. Long sentences were repeated with some word substitutions. On a picture-naming test (DO 80), BRI showed word-finding difficulties. Semantic and phonemic verbal fluency were severely reduced. When the examiner asked her to tell a short story on the basis of a picture sequence, BRI was not able to construct a coherent story and her word-finding difficulties and lack of elaboration leading to an extremely poor narration. Oral comprehension was also mildly impaired. BRI was correct in a word-picture matching task but she made errors on sentence comprehension tests tapping syntactic structures and prepositions. Semantic processing was tested with two subtests of the BORB (Riddoch & Humphreys, 1993). On the item-matching test (e.g. matching two different pictures of houses), BRI was perfect, but she was impaired on the association-matching test (e.g. matching a hammer with a nail). The Pyramids and Palm Tree Test was impaired with both pictures and written words. BRI read words, pseudo-words and sentences perfectly. She made frequent spelling errors, and occasionally mixed uppercase and lowercase letters.

Besides language, BRI suffered from a severe impairment of verbal memory. She was no longer able to retrieve recent memories and failed to repeat three familiar words after less than 10 min. Formal testing of verbal long-term memory was impossible. In contrast, her visual memory was nearly normal. The patient seemed to identify pictures of celebrities, although her severe word-finding difficulties made the recognition difficult to ascertain. Moreover, she presented right–left disorientation, particularly when tested on a drawing or on the examiner's body. Naming or pointing to body parts and fingers were impaired, possibly due to general word processing difficulties. She was also impaired in the Wisconsin Card Sorting Test.

A brain MRI performed at the time of the present study (March 2001) showed frontal and temporal atrophy, predominantly affecting the left hemisphere. An important atrophy of the left hippocampus was also noted. A cerebral SPECT showed a diffuse left-hemispheric hypoperfusion with temporal and frontal predominance (Fig. 1).

2.1. Initial evaluation of number processing

During the initial testing, BRI was asked to read aloud a set of 33 Arabic numerals ranging from one to five digits. She responded without hesitation and did not make a single error. She was asked to write to dictation a list of 33 Arabic numerals matched to those used in the reading task. Again, she responded flawlessly, except for two spontaneous self-corrections. Finally, BRI was asked to write 17 spelled-out verbal numerals to dictation. She made only one phonologically plausible spelling error (700 → "setcent" instead of "septcents").

On simple arithmetic tasks, the patient solved 17/20 problems correctly, making errors only on multiplication problems. She was unable to solve written multi-digit multiplication problems, apparently due to difficulties with the retrieval of elementary facts and with access to general calculation procedures.

In brief, patient BRI showed preserved number transcoding abilities, contrasting with an apparently severe arithmetic impairment. There is a suggestion that this arithmetic deficit affected multiplication more severely than the other operations.

3. Clinical description of LEC

The second patient, LEC, was a 76-year-old right-handed retired midwife. In April 2001, LEC was presented an acute confusional state with word-finding difficulties, Gerstmann's syndrome including acalculia, apraxia, and right lower quadrantanopia. Brain MRI showed a hemorrhage in the left intraparietal region (Fig. 1). A subsequent MRI, performed in December 2001, revealed a small recent asymptomatic right occipital hemorrhage. A general neuropsychological assessment was performed in March 2002 (Table 1).

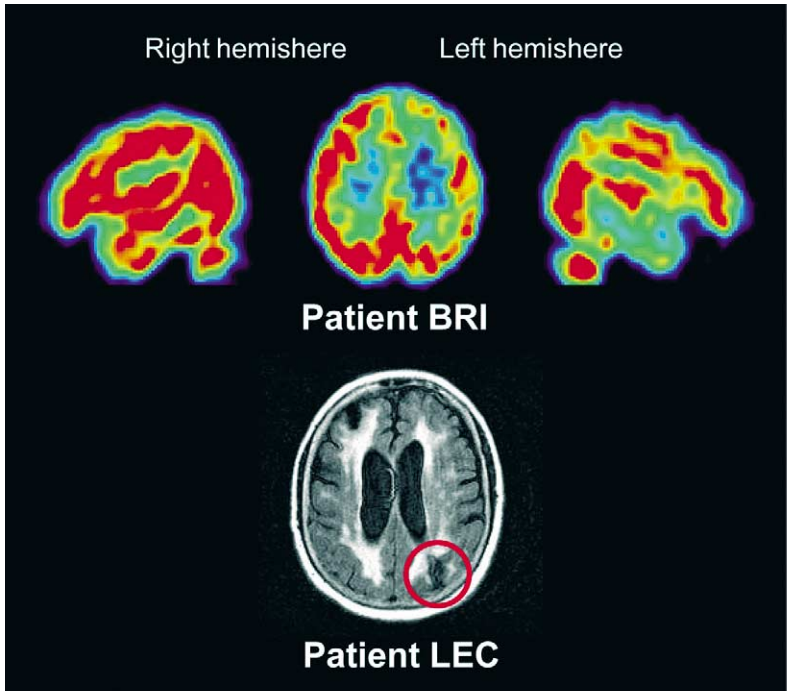

Fig. 1. Brain impairments in patients BRI and LEC. Top: sagital and axial cuts from patient BRI's SPECT, showing a marked left-hemispheric hypometabolism with temporal and frontal predominance. Bottom: axial MRI cut in patient LEC (FLAIR acquisition) showing the sequelae of a hemorrhage affecting the left intraparietal cortex. There are also more diffuse white matter hyperintensities.

LEC was impaired on tests of general efficiency. Her spontaneous speech was normal. Her picture-naming and verbal fluency revealed slight difficulties, though the scores remained in the normal range for her age. LEC was impaired on tests of verbal short-term memory, but she was in the normal range on visual tests. Her verbal long-term memory tests were impaired as well. Visual long-term memory was not tested because of a very poor copy of the Rey-Osterrieth Complex Figure. Additional tests of visual gnosis and praxis revealed visual difficulties. On the bell cancellation test, she made 14 omissions uniformly distributed on the whole sheet. There were no signs of neglect on line bisection tests. On the Navon letters task, LEC failed to recognize the large stimuli made up of smaller symbols. In a task of complex drawing (the flowers of Halligan), LEC reproduced details of the picture, but without respecting its global structure. Finally, the verbal description of a complex picture (Cookie Theft Picture) was limited to a correct report of isolated and unconnected elements of the scene. LEC's performance on these tasks suggests a variety of simultagnosia. Finally, neuropsychological testing also revealed moderate apraxia and agraphia, finger agnosia and right/left disorientation, amounting to a complete Gerstmann's syndrome.

4. Experimental investigation

The tests that were presented to the two patients are part of a battery set up in the INSERM 562 unit and supported by the European "Neuromath" network. Each patient was first compared to five normal women approximately matched in education level and in age (range 40–55 for BRI and 55–66 for LEC). The patients were then compared to a wider control group of 31 normal subjects, which included the matched controls. These two types of comparisons yielding similar results, we will present only analyses involving the larger group of 31 controls.

4.1. *Elementary arithmetic problems*

We first tested the patients' ability to solve simple arithmetic problems such as 3×6, $9 - 2$ or $5 + 1$. Our prediction was that patient BRI, who was aphasic, would be particularly impaired in rote verbal arithmetical fact retrieval and would therefore be more impaired in multiplication than in subtraction. Conversely patient LEC, who suffered from a parietal lesion and Gerstmann's syndrome, was predicted to suffer from an impairment of the parietal quantity representation that would particularly affect subtraction, while sparing multiplication.

4.1.1. *Method*

Patients were presented visually with multiplication, subtraction, addition and division problems. The problems were displayed on a computer screen and the subjects were instructed to produce the result orally. Stimuli remained visible until the subject responded. Latencies were measured using a voice-activated switch, and all testing sessions were recorded for subsequent scoring of errors.

We used simple multiplication, subtraction and addition problems with two single-digit operands. For each operation, the set of 54 problems corresponded to the 55 possible pairs of two digits 0–9, minus the 0–0 pair. For addition and subtraction problems, the larger operand was presented on the left. For multiplication problems, the smaller operand was presented on the left, respecting the more familiar order. Additional tests, including subtraction problems closely matched to multiplication problems and complex multi-digit addition problems, will be described below.

We also presented 18 division problems consisting of a number between 4 and 20 divided by a single digit, with a result ranging from 2 to 10 (largest problem: 20:4; smallest problem: 4:2).

Note that multiplication, subtraction and addition tasks problems included a small subset that could be solved by rule-governed strategies ($0 \times n = 0$; $1 \times n = n$; $n + 0 = n$; $n - 0 = n$). Such problems are presumably processed through the application of logical rules, the coding of which is not known (the operands and the rule itself could be encoded verbally, quantitatively, or through yet another system of symbols specific to algebra). In the following, we report the subjects' global performance averaged across all problems, but the same statistical analyses were also applied to non-rule problems only, with identical results.

Three types of statistical tests were used: χ^2-tests were used to compare error rates across two different tasks within a given patient, and ANOVAs to compare response times. In both cases, the source of variance was the individual trials, which were assumed to be independent of one another. To then compare the patient's values with those of controls, we used a z-score approach. We first calculated the value to be tested, for instance the difference between RT in multiplication and in subtraction, separately for the patient and for each of the controls. We then computed a z-score by taking the difference between the mean of the controls and the value of the patient, and dividing it by the standard deviation of the controls. Finally, the two-tailed probability of this z-score was used to decide if the patient was an outlier relative to the population of control subjects. Note that the use of a z-score instead of a t-score is justified by the relatively large population of control subjects ($n = 31$). When data were missing in a few control subjects, the corresponding n is indicated.

4.1.2. Controls

Controls were very efficient in the resolution of simple operations (see Fig. 2). They made less than 5% errors for each operation (mean error rate for multiplication: 4.3%; for subtraction: 2.2%; for addition: 1.9% and for division: 2.8%). There was nevertheless a significant difference between the four operations ($\chi^2(3) = 20.79$; $P < 0.0001$). Multiplication was significantly more difficult than addition ($\chi^2 = 15.87$; $P < 0.0001$) and subtraction ($\chi^2 = 11.61$; $P < 0.001$) and somewhat more difficult than division ($\chi^2 = 5.45$; $P = 0.02$). The differences between the latter operations were not significant.

Mean correct reaction times averaged about 1 s and increased in the order addition < subtraction < multiplication < division (Fig. 3). All comparisons between operations were significant (all $P < 0.0001$) except for the difference between multiplication and division ($F(1, 27) = 1.6$; NS).

4.1.3. Patient BRI

BRI and LEC's performance on simple arithmetic tasks are summarized in Fig. 2 for correct responses and in Fig. 3 for latencies. In the text below, their performances are compared with the normal group.

4.1.3.1. Multiplication. BRI made 42/54 (77.8%) errors ($z = 16.4$; $P < 0.0001$; $n = 29$) (Fig. 2). A majority of her erroneous responses (60%) consisted of the correct answer to the corresponding addition problem (e.g. $4 \times 5 \rightarrow$ '*nine*'). Note that this kind of error affected all problems of the type $0 \times n$ (e.g. $0 \times 4 \rightarrow$ '*four*') and $n \times 1$ (e.g. $4 \times 1 \rightarrow$ '*five*'). Small problems were relatively spared, as

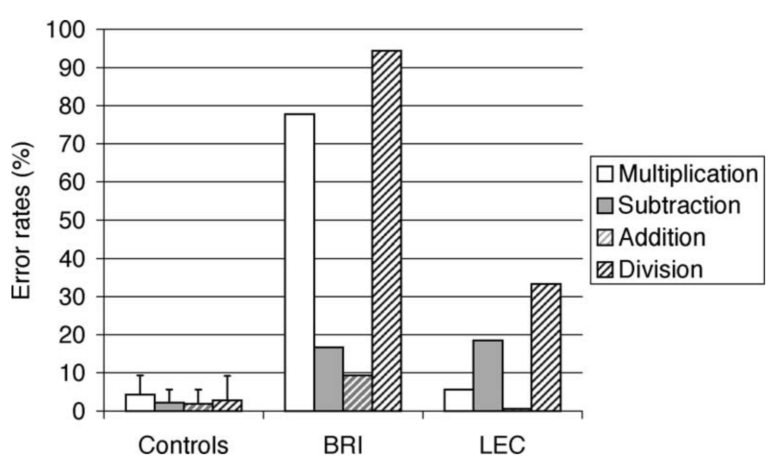

Fig. 2. Error rates in symbolic arithmetic. Percentage of errors for each arithmetical operation (for normal subjects, bars indicate one standard deviation).

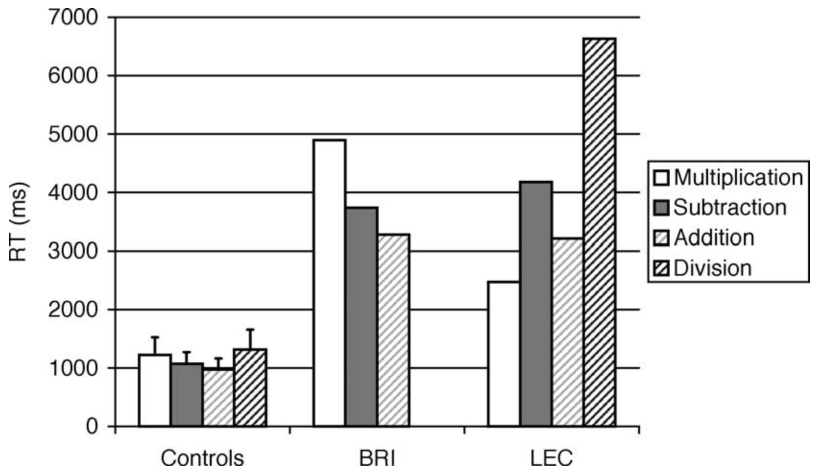

Fig. 3. Median correct response times in symbolic arithmetic tasks.

all 12 correct responses corresponded to problems with at least one operand smaller than 5.

4.1.3.2. Subtraction. BRI made only 9/54 (16.7%) errors ($z = 4.3$; $P < 0.001$; $n = 29$). Large problems were the most impaired, as 7/9 errors corresponded to a problem with at least one operand larger than 5. Rule-based problems were relatively spared, as BRI correctly solved 14/16 such problems. The two errors on rule problems suggested an incorrect rule application ($9 - 0 \rightarrow$ '*zero*', and $4 - 4 \rightarrow$ '*four*').

The apparent dissociation between multiplication and subtraction might result from the fact that the results of multiplication problems are larger than the results of the subtraction problems with the same operands. In order to control for this possible artifact, we presented BRI with 54 subtraction problems matched one-to-one with multiplication problems in terms of result. The first operand was always a decade, and the second operand a single digit (e.g. 80−8), each problem thus involving only two significant digits like the multiplication problems. Patient BRI made 4/54 errors (7.5%), thus still performing considerably better than in multiplication (77.8% errors).

4.1.3.3. Addition. BRI made 5/54 (9.3%) errors ($z = 2$; $P < 0.05$; $n = 29$). The five errors differed from the correct response by one unit. We presented BRI with a further set of 18 complex addition problems. She solved flawlessly nine problems consisting of a two-digit number plus a single digit (e.g. $61 + 2$). With problems involving 2 two-digit operands, she made 2/9 errors (22.2%) consisting of an omission of the carry.

4.1.3.4. Division. BRI responded correctly to only one item out of 18 (94.4% error rate) ($z = 5.5$; $P < 0.0001$; $n = 28$). On 16 items, the response of BRI was larger than the largest operand, suggesting that BRI was unaware of the meaning of the division operation.

4.1.3.5. Dissociations between operations. As indicated in Fig. 2, BRI's error rates differed across operations ($\chi^2(3) = 76.9$; $P < 0.0001$). Subtraction and addition were relatively spared, while multiplication and division were severely impaired. The error rate was significantly higher for multiplication and division than for the two other operations (multiplication versus subtraction: $\chi^2(1) = 40.5$; $P < 0.0001$; multiplication versus addition: $\chi^2(1) = 51.6$; $P < 0.0001$; division versus addition: $\chi^2(1) = 46.2$; $P < 0.0001$; division versus subtraction: $\chi^2(1) = 35.4$; $P < 0.0001$). There was no significant difference between addition and subtraction and between multiplication and division.

Reaction times for division were not included in the analysis of BRI's mean correct response latencies, because of BRI's very poor performance. The analysis of latencies on the other tasks revealed a pattern parallel to that of the analysis of errors with significant differences between operations ($F(2, 92) = 3.44$; $P = 0.02$). Multiplication (4896 ms) was slower than both subtraction (3735 ms; $F(1, 51) = 5.8$; $P < 0.05$) and addition (3275 ms; $F(1, 52) = 9.08$; $P < 0.005$), which did not differ ($F(1, 81) < 1$). Analyses excluding rule-based problems yielded the same pattern of dissociation for both errors and RT.

4.1.4. Patient LEC

4.1.4.1. Multiplication. LEC made 3/54 (5.6%) errors ($z = 0.25$; NS; $n = 29$). Two of the three errors concerned a large problem ($4 \times 7 = 42$ and $6 \times 9 = 36$) and the third a rule-based problem ($0 \times 7 = 7$).

4.1.4.2. Subtraction. LEC made 10/54 (18.5%) errors ($z = 4.9$; $P < 0.0001$; $n = 29$). Errors were distributed across all type of subtractions (for examples: $7 - 1 = 8$; $9 - 1 = 9$ or $6 - 5 = 0$).

4.1.4.3. Addition. LEC made no errors.

4.1.4.4. Division. LEC made 8/24 (33.3%) errors ($z = 1.68$; NS; $n = 28$): two non-responses, two out-of-range answers (e.g. 14 : 7 = 21), and four intra-table answers (12 : 4 = 6).

4.1.4.5. Dissociations between operations. LEC's error rates differed across operations ($\chi^2(3) = 23.1$; $P < 0.0001$). Addition and multiplication were relatively spared while subtraction and division were impaired. Error rates were significantly higher for subtraction and division than for the two other operations (multiplication versus subtraction: $\chi^2(1) = 4.3$; $P < 0.05$; division versus addition: $\chi^2(1) = 20.1$; $P < 0.001$; addition versus subtraction: $\chi^2(1) = 11$; $P < 0.0001$; multiplication versus division: $\chi^2(1) = 10.58$; $P < 0.005$). There was no significant difference between multiplication and addition ($\chi^2(1) = 3.1$; NS) or between division and subtraction ($\chi^2(1) = 2.1$; NS).

LEC's mean correct response latencies differed significantly across operations ($F(3, 149) = 17.35$; $P < 0.0001$). The mean latency was faster for multiplication (2473 ms) than for either subtraction (4178 ms; $F(1, 88) = 27.3$; $P < 0.0001$) or addition (3041 ms; $F(1, 97) = 6.2$; $P < 0.05$) or division (4187 ms; $F(1, 54) = 9.86$; $P < 0.005$). Subtraction problems were answered more slowly than addition problems ($F(1, 90) = 12.7$; $P < 0.001$). The mean latency for division did not differ from the latency for subtraction ($F(1, 48) < 1$; NS) but was marginally slower than for addition ($F(1, 56) = 4.6$; $P < 0.05$). Analyses excluding rule-based problems yielded the same pattern of dissociation for both errors and RT (e.g. 7.2% errors in multiplication versus 22.2% errors in subtraction, $\chi^2(1) = 4.9$; $P < 0.05$).

4.1.5. Discussion

Patients BRI and LEC exhibited a double dissociation between arithmetic operations. Patient BRI, who was aphasic, was more impaired on multiplication than on subtraction tasks. Conversely, patient LEC, who showed Gerstmann's syndrome, was more impaired on subtraction than on multiplication tasks. Note that LEC was globally less impaired than BRI. However, the evidence for a dissociation is not based on a direct comparison on error rates between patients for each operation, but on the demonstration of an opposite pattern of dissociation between the operations across the two patients. These observations replicate our earlier findings of a similar double dissociation in patients MAR and BOO (Dehaene & Cohen, 1997). In the literature, several single cases with a more severe impairment of subtraction than multiplication have been described (Dehaene & Cohen, 1997; Delazer & Benke, 1997; van Harskamp & Cipolotti, 2001; van Harskamp et al., 2002). Like patient LEC, all of them suffered from left parietal lesion or atrophy, and all but one were reported to present Gerstmann's syndrome. Conversely, several single cases of more severe impairment on multiplication than on subtraction have been reported (Cohen & Dehaene, 2000; Dagenbach & McCloskey, 1992; Dehaene & Cohen, 1997; Lampl et al., 1994; Lee, 2000; McNeil & Warrington, 1994; Pesenti et al., 1994; van Harskamp & Cipolotti, 2001). Most of them, like patient BRI, suffered from additional language impairments.

Addition performance was relatively preserved in both of our patients. This is compatible with the hypothesis that addition problems can be solved in multiple ways by normal subjects. Many subjects have learned addition tables at school, and can therefore retrieve addition facts from rote verbal memory. The preservation of verbal memory in patient LEC might thus explain her good addition performance (indeed, LEC reported having considerable training in arithmetic since childhood). If memory retrieval fails, however, normal subjects can resort to various strategies that are analogous to those used for subtraction. Patient BRI, who had much less training that LEC in arithmetic, could have used such strategies to achieve an equal performance in addition and in subtraction. Indeed, both were strikingly better preserved than multiplication, though performance was slow relative to control subjects.

Finally, we included a few simple division problems in our battery for exploratory purposes. Patient BRI was completely unable to perform division, while patient LEC was only marginally worse than the control population. Psychological research with normal subjects provides evidence that multiplication and division are intimately linked (Campbell, 1997, 1999; LeFevre & Morris, 1999). Thus, it should not be surprising that patient BRI, who experienced a devastating impairment of memory for multiplication facts, was so impaired in division. However, we tentatively suggest, as a hypothesis for future research, that division problems may also tax the quantity manipulation system. To find the answer to a simple division such as 12/3, one must search the multiplication table. The search is generally not random, but is guided by an initial estimate (subjects typically try out 3×3 but not 3×9), and is then narrowed down by step-by-step increases or decreases based on a comparison of the current tentative result with the desired one. Impairments to approximation and comparison processes therefore could explain patient LEC's poor performance with division problems.

4.2. Exact versus approximate calculation

Having observed a double dissociation between subtraction and multiplication, we now turn to the predicted associated deficits. The triple-code model postulates that the verbal representation plays a crucial role in exact calculation, while the quantity representation plays a crucial role in our ability to approximate simple calculations, for instance in deciding that $12 + 13$ cannot possibly be as large as 95. Patient BRI should therefore be more impaired in exact than in approximate addition, while the converse should be true for patient LEC. Alternatively, if dissociations between operations are due to random impairments to distinct memory stores (e.g. Dagenbach & McCloskey, 1992), then there should be no specific association between multiplication and subtraction on the one hand, and exact and approximate addition on the other hand.

4.2.1. Method

We used our previously described exact and approximate calculation tasks (Dehaene, 1998; Stanescu-Cosson et al., 2000), with unlimited presentation time. Subjects were presented with single-digit addition problems displayed horizontally on a computer screen with two proposed responses simultaneously displayed side by side below the problem until subjects answered. On each trial, they were asked to choose between the two responses, indicating their choice by pressing the key on the same side as the selected response. For the exact calculation block, instructions stressed that one of the proposed results was correct and that the other was false, and the task was to identify the correct result. For the approximation block, instructions explicitly stated that neither proposed responses was exactly correct, and that the subject should choose the response closer to the correct sum.

The complete list of problem can be found in Stanescu-Cosson et al. publication (Stanescu-Cosson et al., 2000). For small problems, operands ranged from 1 to 5, and for large problems they ranged from 5 to 9. 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 & 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.

4.2.2. Controls

Error rates and mean RTs are presented in Figs. 4 and 5. Normal subjects presented a non-significant task effect on error rates (3.9% for exact calculation and 3.2% for approximation, $F(1, 30) < 1$), indicating that the two tasks were matched for difficulty. The size effect was significant ($F(1, 30) = 4.76$; $P < 0.05$), with subjects showing more difficulty with large numbers than with small numbers. The interaction of task with size was also significant ($F(1, 30) = 8.08$; $P < 0.01$), the size effect being larger in the exact than in the approximation task. On response time, the two main effects (task and size effect) and interaction were all significant (all $P < 0.01$). Again, the size effect was larger in the exact than in the approximate condition. Those results replicate earlier ones (Dehaene, 1998; Stanescu-Cosson et al., 2000).

4.2.3. Patient BRI

Overall, BRI performed worse than normal controls ($z = 2.30$; $P < 0.05$). However, errors were essentially restricted to exact calculation with large items (32.5% errors, $z = 2.17$; $P < 0.05$), with a smaller impairment in approximate calculation with small items (15% errors, $z = 2.52$; $P < 0.01$), and normal performance in the other two conditions. A two-step analysis clarified these results. First, BRI showed the same general pattern as controls, namely a main effect of problem size ($\chi^2(1) = 4.4$; $P < 0.05$). Second, as indicated on Fig. 4, her difference with controls consisted of a widely exaggerated size effect in the exact task (interaction $z = 2.22$; $P < 0.05$). A further difference relative to controls was an apparent inversion of the size effect in the approximation task. However the size effect did not differ significantly between BRI and controls for this task ($z = 1.76$; NS). In sum, BRI's only clear-cut deficit was a severe impairment in solving exact large problems, contrasting with a relatively preserved ability to identify an approximate solution for the same problems.

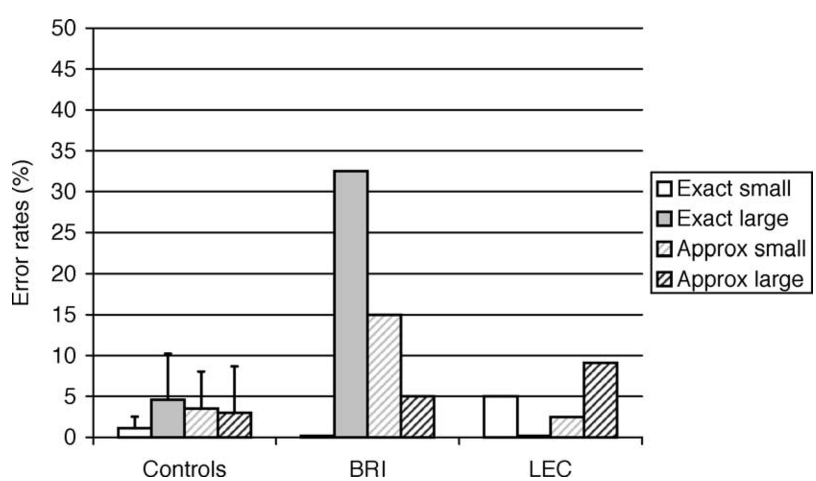

Fig. 4. Error rates in exact and approximation calculation tasks.

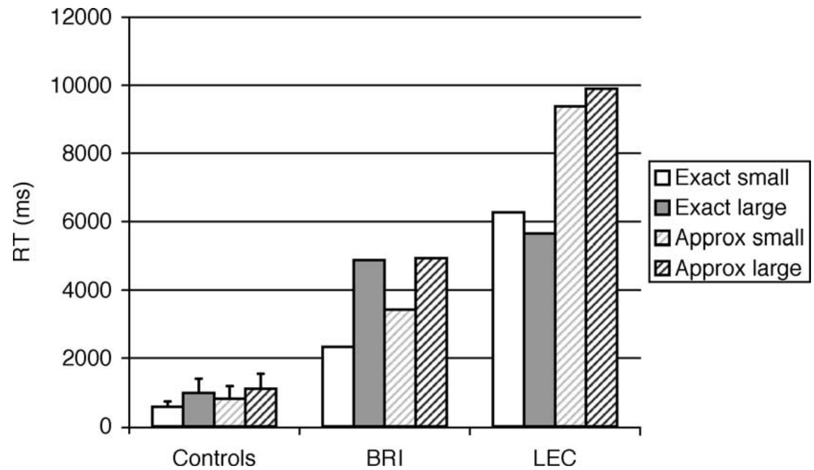

Fig. 5. Median correct response times in exact and approximation tasks.

The pattern of response times was parallel to that of error rates. BRI was significantly slower than controls overall ($z = 10.06$; $P < 0.0001$). Her slowness was particularly pronounced with large operands, resulting in a significantly larger size effect relative to controls ($z = 5.58$; $P < 0.0001$) (Fig. 5). The interaction of task by size was also significantly larger in BRI than in controls ($z = 3.02$; $P < 0.005$), indicating that the size effect in BRI was disproportionately larger in exact calculation than in approximation. It is noteworthy that patient BRI was equally slow in both exact and approximate calculation with large numbers, but that she eventually attained the correct response to most approximation problems (5% errors) while she often erred with exact problems (32.5%). Thus a speed-accuracy trade-off might have affected her performance in approximate calculation, but not in exact calculation where both RTs and error rates suggest a genuine deficit.

4.2.4. Patient LEC

As shown on Fig. 4, LEC's overall level of performance was normal with a mean of 4.4% errors ($z = 0.2$; NS). There was no significant size effect ($\chi^2(1) = 0.03$; $P > 0.5$), and no interaction of problem size with task ($\chi^2(1) = 2.7$; NS), perhaps because of the small sample size.

Despite an excellent performance level, however, LEC's behavior was abnormal in several respects. First, the patient initially refused to perform the approximation task, claiming that she was utterly unable to do this. When she eventually agreed to try to solve the approximate problems, she indicated that she mentally computed the exact result and compared the result to the proposed answers. According to her introspection, she never resorted to an approximation strategy.

Second, her response latencies were severely slowed down (mean latency = 2992 ms; $z = 23.04$; $P < 0.0001$). Furthermore, her latencies in the approximation task were as much as 1434 ms slower than in the exact task. This relative difficulty of the approximation task was much larger than in normal controls ($z = 23.58$; $P < 0.0001$). LEC's latencies were not significantly affected by problem size.

4.2.5. Discussion

In the exact and approximate addition tasks, patients BRI and LEC both differed from normal subjects but showed dissimilar patterns.

Patient BRI had a very high error rate for large exact problems and a lower error rate for the approximation task. These results suggest that, as predicted, her verbal impairment mostly interfered with exact calculation while sparing approximation abilities. What remains surprising is that, in approximation, she was essentially perfect with large problems (5% errors), but somewhat impaired on small problems (15% errors). In control subjects, an automatic activation of the retrieval of addition facts has been observed (Girelli & Delazer, 1996; Lefevre, Bisanz, & Mrkonjic, 1988; Lemaire, Barrett, Fayol, & Abdi, 1994). Thus, it is possible that, in spite of instructions to avoid calculating the exact result, subjects cannot help but access their exact memory store in the approximation condition with small problems. FMRI in normal subjects provides some support for this hypothesis by showing that the supramarginal region, which has been implicated in verbal memory, was more activated by small than by large approximation problems (Stanescu-Cosson et al., 2000). Assuming that patient BRI had the same bias, her few errors with small approximation problems could then be explained by an occasional automatic activation of her impaired store of arithmetic facts. Whatever the merits of this interpretation, BRI's superior performance in approximation than in exact calculation with large problems clearly indicates a dissociation in the predicted direction.

In contrast, patient LEC made few errors on both tasks, but she was very severely slowed, most strikingly in the approximation task. It should be noted that the approximation task could always be solved by performing the exact calculation in full and then selecting the closest result. Thus, in principle it is difficult to evidence a selective deficit of approximation in a patient with relatively preserved exact calculation abilities. In general, one should not expect such a deficit to show up in elevated error rates, but rather in a drastic slowing down of responses to grossly false problems that a normal subject would never resolve by tedious exact calculation. Patient LEC's behavior is compatible with these predictions. She spontaneously claimed that she was unable to approximate and that she had to calculate first, then compare her result with the proposed choices. Her abnormally slow performance in approximation supports this introspection and provides evidence that approximation can be severely impaired in Gerstmann's syndrome.

4.3. Subitizing and counting

We now turn to the assessment of non-symbolic number processing abilities. According to the triple-code model, the quantity representation plays an important role in our ability to evaluate the numerosity of arrays of dots. We first evaluate this prediction in the range of small numerosities 1–8, using an exact enumeration task in which subjects have to name the exact numerosity of an array of dots. Verbal counting is the default strategy for the precise enumeration of objects. However, numerosities in the range 1–3 can be "subitized" precisely without counting (Mandler & Shebo, 1982), presumably because over this range, the quantity representation is sufficiently precise to be associated with a unique number word (Dehaene & Cohen, 1994). Thus, the triple-code model predicts that patient BRI should show spared subitizing, but that her aphasia would interfere with counting. Conversely, patient LEC's quantity impairment should be reflected in a subitizing deficit.

4.3.1. Method

Patients and control subjects were asked to name as fast as possible the numerosity of arrays of 1–8 randomly arranged squares. The squares were white on a black background, and varied in size from trial to trial, in order to avoid any confound between numerosity and luminance. A stimulus remained on the screen until subjects responded. Ten trials were presented for each numerosity, for a total of 80 trials.

4.3.2. Controls

Normal subjects performed very well (2.1% errors). Errors affected primarily the largest numerosities (70% of the errors were on items 7 and 8). The mean correct reaction time was 1155 ms. As expected, distinct response profiles were observed over the subitizing range and the counting range (Fig. 6). From 1 to 3 dots, the response times curve was almost flat, with a mean slope of 24 ms per dot (S.D. = 49.6) suggesting the use of a fast numerosity apprehension procedure ("subitizing": Mandler & Shebo, 1982). For larger quantities, response times increased linearly with numerosity (mean slope 291 ms, S.D. = 85), suggesting the use of a counting strategy.

4.3.3. Patient BRI

BRI made 6/80 errors (7.5%), thus performing at a lower level of accuracy than controls ($z = 2.04$; $P < 0.05$). As in normal subjects, BRI's errors affected trials with a large number of squares (100% of her errors occurred on items 7 and 8). As usual, BRI was slower than controls (BRI's mean RT: 2518 ms; $z = 6.87$; $P < 0.0001$) but her subitizing seemed to be preserved, with a mean slope of 77 ms per dot for numerosities 1–3, which was non-significantly slower than normals ($z = 1.05$, NS). For larger numerosities, her slope was much steeper (1196 ms per dot; $R^2 = 0.56$; $z = 10.7$; $P < 0.0001$) and was significantly slower than normals ($z = 10.69$, $P < 0.0001$). The drop in RT for the largest numerosity (8) could be attributed to a "guessing end effect" (Mandler & Shebo, 1982). Thus, BRI's performance indicated a qualitatively normal pattern of subitizing, but a significant slowness and somewhat elevated error rate during counting.

4.3.4. Patient LEC

LEC made 2/80 errors (2.5%), both with large numerosities (6 and 8), thus performing at the same level of accuracy

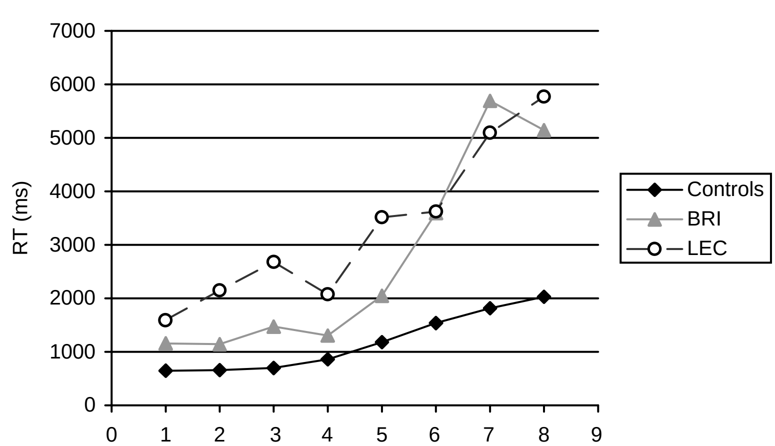

Fig. 6. Performance in subitizing and counting. Median correct reaction times for each correctly identified numerosity for patients and control subjects.

as controls ($z = 0.15$; NS). However, LEC was slower than controls (3115 ms; $z = 9.88$; $P < 0.0001$). Furthermore, she showed an increase in RTs for numerosities in the range 1–3 (540 ms per dot; $R^2 = 0.31$; $P < 0.005$) that was significantly larger than controls ($z = 10.3$; $P < 0.0001$). She also showed a steep progression of RT as numerosities increased from 4 to 8 (838 ms per dot; $R^2 = 0.52$; $P < 0.001$), which exceeded that of controls ($z = 6.5$; $P < 0.0001$). This pattern of response times suggests that LEC did not subitize small sets of dots, and also was slow in counting.

Butterworth (1999) described a similar case of impaired subitizing in the patient Charles. However, recent testing of this patient indicates that when targets were presented very briefly, he showed a pattern of subitizing similar to normals (Manuela Piazza, personal communication, September 2002). This suggests that the initial impairment might have resulted from a lack of self-confidence rather than a genuine deficit: the patient felt that he had count even for numbers that he could have subitized. In order to test whether this procedure would also normalize LEC's behavior, we presented 54 arrays of dots varying in numerosity between 1 and 6, each for a short duration (500 ms). LEC made more errors (24.1%) than in the standard task (2.5%). Crucially, errors were present even for small numerosities (25% errors for numerosity 1, where she responded "two"; 33% errors for numerosity 2, where she responded "three"). Furthermore, LEC did not present the traditional pattern of reaction times. Her RTs were now flat as a function of numerosity (slope −30 ms in the range 1–6; $R^2 = 0.08$; NS). Overall, these results suggest that flashing the dots prevented LEC from counting and that under those conditions; she made a large number of errors with small numerosities, confirming the presence of major subitizing impairment.

4.3.5. Discussion

BRI and LEC presented dissociated patterns of subitizing. BRI showed normal subitizing but disproportionately slow counting, consistent with the thesis that counting, but not subitizing, is bound to verbal processes. BRI's verbal impairment reduced her speed of reciting numerals, which probably explains her slower counting rate. The fact that the subitizing range was not affected by a similar slowness confirms that subitizing relies on a non-verbal estimation process (Dehaene & Cohen, 1994; Gallistel & Gelman, 1992; Mandler & Shebo, 1982; Whalen et al., 1999).

Conversely, LEC showed impaired subitizing, with an increase of 540 ms per item in the 1–3 range. The use of a control task with fast presentation revealed that this impairment did not result from a lack of self-confidence but from a genuine deficit in quantification of small numerosities. Such a deficit may also parsimoniously account for her slower counting. Normal subjects typically report counting by small groups of two or three items. Impaired subitizing would prevent this strategy and oblige patient LEC to count the items one by one, even if her counting procedure itself was perfectly intact. The fact that LEC's counting rate was two to three times slower than that of controls is consistent with this hypothesis.

In the literature, a few cases of dissociation between subitizing and counting have already been described. A pattern of impaired counting and intact subitizing was described in simultagnosic patients (Dehaene & Cohen, 1994): These patients with visual impairments associated with parietal lesions were impaired on counting but showed preserved subitizing. Conversely, impairments in subitizing have been described only twice. In the first case (Butterworth, 1999), as described above, the authors discovered a posteriori that the results normalized when a very fast presentation was used. The second case (Cipolotti, Butterworth, & Denes, 1991) is a patient with severe acalculia and a complete inability to process numbers above 4. Even below this limit, she did not succeed in saying how many dots were presented on a screen unless she could count verbally using finger pointing. It could thus be argued that both subitizing and counting were severely impaired. Patient LEC's results suffer from the same problem—and indeed, as argued above, it is likely that any impairment in subitizing would also impact on the speed of counting a larger number of items. Furthermore, LEC's results need to be interpreted cautiously given the presence of simultagnosia on clinical testing, which may also contribute to slower counting. Nevertheless, the presence of a subitizing deficit in patient LEC is supported by fine-grained response time data (a very elevated slope of 540 ms per item) as well as errors on even the simplest displays when the stimuli were flashed.

Overall, the finding that subitizing may or may not be impaired in two patients with superficially similar counting behavior confirms that these two quantification processes are distinct (Dehaene & Cohen, 1994; Gallistel & Gelman, 1992; Mandler & Shebo, 1982; Whalen et al., 1999), and refute models that view them as lying on a single continuum of difficulty (Balakrishnan & Ashby, 1992). The relation between counting and subitizing is likely to be more complex that a simple relation of continuity: counting is facilitated by the ability to subitize small groups of items, but also calls on specific processes of verbal recitation and attention orientation that are not required for subitizing (Piazza et al., 2003).

4.4. Comparison and addition of quantities

As a final evaluation of our hypothesis, we evaluated the patients' ability to process large approximate numbers in symbolic and non-symbolic form. We presented numbers between 11 and 99, either as two-digit Arabic numerals, or as a cloud of dots that could not be precisely enumerated. The patients either had to compare two such numbers, or to compute an approximate addition on two such numbers and compare its result to a third number. We predicted that LEC would be severely impaired on all such tasks, consistent with her hypothesized impairment in the quantity representation. BRI, on the other hand, was predicted to perform normally since her verbal impairment was not expected to impact on the evaluation and comparison of approximate quantities.

4.4.1. Method

The two patients and the control subjects were given two experimental tasks (simple comparison and addition + comparison), each with two formats of stimuli (Arabic numerals and arrays of dots), resulting in a total of four experiments.

In the simple comparison task, subjects were first presented with a number presented in yellow displayed for 400 ms, followed by a second number presented in light blue for 400 ms (e.g. 34 followed by 67). Subjects had to choose the larger of the two numbers. They were instructed to respond using a right-hand key if the blue number was larger and a left-hand key if the yellow number was larger. In 50% of trials the larger number was presented first. The two numbers were selected pseudo-randomly with the following constraints: (1) the first number was between 23 and 49 and the second between 11 and 99; (2) tens (20, 30, etc) were excluded from the stimulus set in order to discourage exact symbolic calculation; (3) on equal numbers of problems, the ratio of the two numbers was about 1.3, 1.5 or 2. Our goal with this manipulation was to measure the psychometric curve for discrimination and derive the Weber fraction for each subject, but since this test was taken only once, the data were not sufficient for this calculation.

The addition + comparison task was derived from the simple comparison task by dividing the first quantity into two successively presented numbers, both displayed in yellow color for 400 ms. The blue number was then presented as in the simple comparison task (e.g. 12, then 22, followed by 67). Subjects had to decide whether the sum of the yellow numbers was larger or smaller than the blue number, and they responded following the same method as in simple comparison.

In the non-symbolic version of the tasks (arrays of dots), precautions were taken to prevent confounds with non-numerical variables. The visual parameters that we took into account were dot size, density, total luminance and total occupied area (for examples, see Fig. 7). Each visual parameter was congruent with numerosity on half of the trials and incongruent with numerosity on the other trials. Thus, subjects could not consistently base their responses on any parameter other than numerosity.

4.4.2. Controls

The performance of controls and patients is summarized in Figs. 8 and 9. Tasks with dots produced higher error rates than tasks with Arabic digits ($F(1, 27) = 59.78$; $P < 0.0001$). Simple comparison and addition + comparison were similar in difficulty ($F(1, 27) = 0.1$; NS). The interaction between task and format also was non-significant ($F(1, 27) = 0.01$; NS).

The reaction times analysis presents a different pattern: a significant task effect ($F(1, 27) = 6.72$; $P < 0.05$), no significant format effect ($F(1, 27) = 3.36$; NS) and a highly significant interaction ($F(1, 27) = 25.28$; $P < 0.001$). In the Arabic format, the addition + comparison task was slower than the simple comparison task.

4.4.3. Patient BRI

BRI's error rates did not differ from controls in any of the four experimental conditions (all $P > 0.1$), and the effects of task, format, and their interaction also did not differ. BRI was significantly slower than controls overall ($z = 6.15$; $P < 0.0001$; $n = 28$). This betrayed only a global slowness however, since the effects of task, format, and their interaction did not differ between BRI and controls (all $P > 0.1$).

4.4.4. Patient LEC

LEC made many errors in all four tasks (Fig. 8). Her performance was significantly worse than controls ($z = 6.51$; $P < 0.0001$; $n = 28$), although the effects of task, format, and their interaction did not differ (all $P > 0.5$). Most strikingly, LEC was essentially at chance on the tasks with dots,

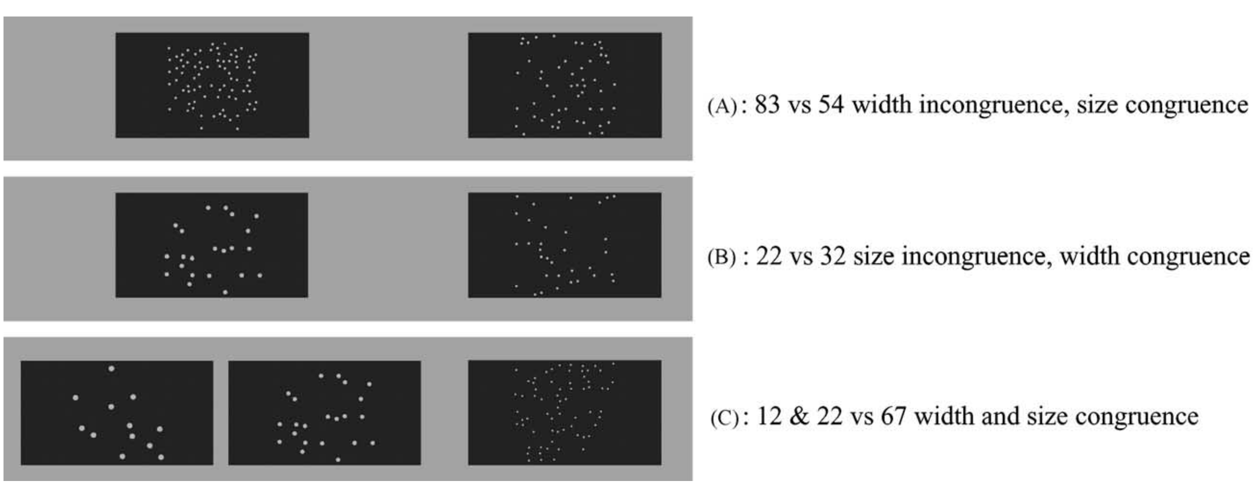

Fig. 7. Sample stimuli for the non-symbolic number tasks. Panels A and B show stimulus pairs for the comparison task, at a Weber ratio of 1.5 corresponding to the medium level of difficulty used in the test. Panel C shows a typical stimulus pair for the addition + comparison task.

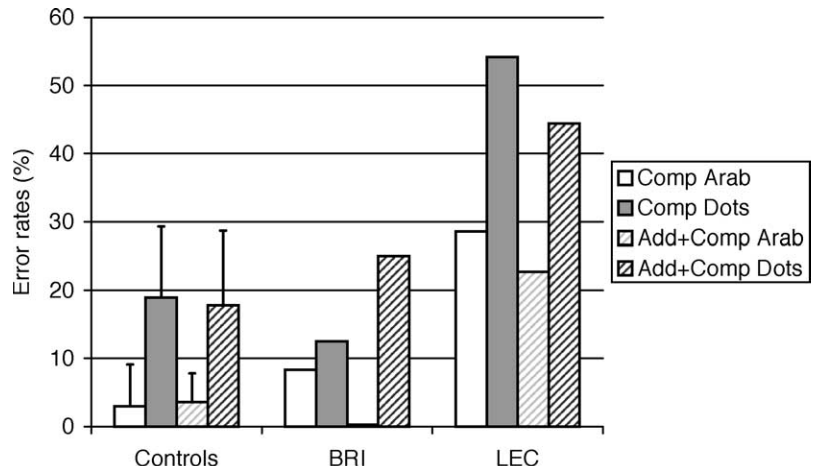

Fig. 8. Error rates in symbolic and non-symbolic numerical tasks.

and severely impaired with Arabic digits. In both cases, performance was approximately equally bad at all levels of the ratio between the targets numbers. LEC was also significantly slower than normal subjects ($z = 11.55$; $P < 0.0001$; $n = 28$). However, the slowing was not equivalent across the tasks (interaction $z = 6.37$; $P < 0.0001$; $n = 28$). LEC was slower in the addition + comparison task and this effect was larger than in controls ($z = 11.7$; $P < 0.0001$; $n = 28$). Moreover, as shown on Fig. 9, there was an exaggerated slowing of responses for Arabic stimuli in the patient relative to controls (interaction z=5.43; $P < 0.0001$; $n = 28$).

4.4.5. Discussion

As in the previous quantity processing tasks, patient BRI showed slow but otherwise normal performance. Patient LEC, in contrast, presented an abnormal pattern of performance with a high rate of errors and very slow RTs, particularly with Arabic digits. LEC performed at chance on comparing dot patterns, and her slow and error-prone performance with Arabic digits suggests that she lacked any intuition of numerical quantity relations and had to resort to complex strategies.

5. General discussion

5.1. Summary of BRI and LEC's results

In simple arithmetic, the aphasic patient BRI presented a severe deterioration of multiplication fact retrieval (78% errors) with a significantly better ability to subtract (17% errors). Tests of exact and approximate calculation revealed an impairment in exact addition with large problems (33% errors) but normal performance on large approximate addition. Finally, with arrays of dots, BRI showed normal performance both in subitizing small numbers and in comparing and calculating with large quantities, but severely showed performance in tasks requiring verbal counting. Conversely, patient LEC, who presented with Gerstmann's syndrome, showed a moderate impairment in subtraction (19% errors),

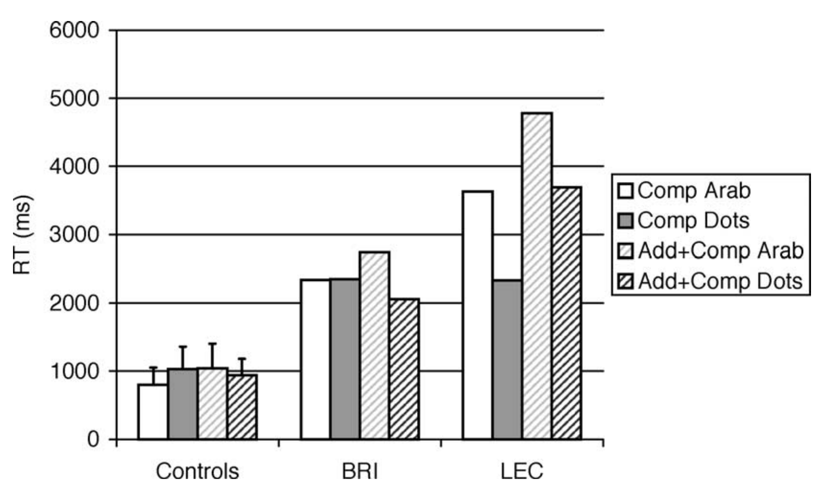

Fig. 9. Median correct response time in symbolic and non-symbolic numerical tasks.

with a significantly better ability for multiplication (6% errors). Although error rates in tests of exact and approximate calculations were low (<10%), LEC was drastically slower in approximation and claimed that she resorted to exact calculation followed by comparison to perform the approximation task. With dot arrays, she gave evidence of impaired subitizing: she enumerated small sets using a slow but accurate serial counting procedure. Finally, she exhibited high error rates in comparing and calculating with large quantities of dots.

5.2. Two distinct patterns of acalculia

The goal of our paper was to identify two distinct clusters of deficits (“associations of dissociations”) that could be predicted from the hypothesis of a basic distinction between verbal and quantity systems for number processing. Our results provide support for this approach.

A first cluster of deficits was observed in patient BRI. In a nutshell, we found impaired multiplication, associated with a relative preservation of subtraction and, more generally, of quantity knowledge in symbolic and non-symbolic tasks. Similar evidence for a relative sparing of elementary numerical abilities has been reported before in other patients with semantic dementia and aphasia (Cappelleti et al., 2001; Grafman et al., 1989; Pesenti et al., 1994). Patient BB (Pesenti et al., 1994) showed early-onset dementia with moderate deficits in language, memory and intellectual functions together with strong impairments in calculation. Like BRI, BB showed a relative preservation of quantity-based operations, with a dissociation between multiplication (57% errors), addition (33% errors), and subtraction (8% errors). Even more strikingly, patient IH (Cappelleti et al., 2001) showed a total preservation of number semantics in the context of a severe semantic dementia for other domains of words knowledge. Again, subtraction was much better than multiplication (5% versus 27% errors), and symbolic tasks (bisection of numbers, comparison of magnitude from Arabic numbers) as well as non-symbolic tasks (comparisons of sets of dots) were preserved.

The presence of dementia raises the question whether such patients might merely show greater deficits for the more difficult tasks. At least for patients BRI and GC (Grafman et al., 1989), this explanation can be rejected. Patient BRI was not systematically more impaired on tasks that were also more difficult for the controls. She showed difficulties even in tasks that were very easy for the controls, such as counting or exact calculation with small items, and she performed well on some tasks that were judged more difficult such as approximate calculation. The double dissociations observed between patients BRI and LEC on the same tasks confirm that task difficulty alone cannot explain BRI’s cluster of results.

We propose instead that BRI’s pattern of impairment can be understood in terms of the basic distinction between the specifically human verbal system of number representation and an evolutionarily older non-verbal quantity system. The present evidence supplements existing data in babies and animals by showing that a whole set of tasks (approximate addition, subtraction, and comparison of sets) are, to a large extent, independent of language and exact number knowledge. BRI’s case illustrates how one can be severely acalculic, to the point of not being to calculate 3×4, and yet remain as accurate as controls in judging whether one large set plus a second set is smaller or larger than a third set.

A different cluster of deficits was observed in patient LEC. This patient was unable to perform very easy numerical tasks such as subitizing 2 or 3 dots, or comparing the numerosities of two arrays of dots differing in a ratio of 2:1 (36 versus 72 dots). This dramatic loss of quantity processing was coincident with a moderate deterioration of subtraction, as predicted by the triple-code model, while multiplication was performed at the same level as control subjects. Patient LEC suggests that reading and writing numbers, counting, and retrieving arithmetic facts from memory can be preserved in the face of profound deficits in the basic manipulation of small and large quantities.

Patient LEC suffered from a parietal lesion and Gerstmann’s syndrome, but also showed clinical signs of associated visual impairments (simultagnosia). Thus, her results need to be interpreted cautiously, as there is a possibility that some of her impairments were due to visual rather than quantity-based deficits. We doubt, however, that visual factors alone can explain LEC’s cluster of deficits, because LEC was impaired even in tasks requiring no overt or covert spatial movement of gaze or attention, such as subitizing, which has been shown often to be preserved in simultagnosia (Dehaene & Cohen, 1994). Visual deficits might have contributed to LEC’s difficulties in comparing large sets of dots, but they cannot explain that she was also severely impaired when the same task was performed with Arabic digits, or that the approximate calculation task was more impaired than the exact version, even though the two tasks used nearly identical visual stimuli. These arguments suggest that visual difficulties played only a limited role in LEC’s impairment, although they may have contributed to her chance performance in the non-symbolic tasks with large displays of dot patterns. Further work should try to better disentangle visual and quantity-based factors by varying the stimulus displays, for instance using visual versus auditory stimuli (Barth et al., 2003), and by attempting to find formal parallels between deficits in symbolic and non-symbolic operations (for instance as a function of the Weber fraction), thus reducing the probability that their association could be due to two unrelated impairments.

Several single cases with a more severe impairment of subtraction than multiplication, have been described (Dehaene & Cohen, 1997; Delazer & Benke, 1997; van Harskamp & Cipolotti, 2001; van Harskamp et al., 2002). Like patient LEC, all of them suffered from left parietal lesion or atrophy, and all but one were reported to present Gerstmann’s syndrome. Particularly interesting is the case of JG, a patient of Delazer and Benke (1997) who could resolve simple multiplications with few errors (8% errors) but who seemed unable to understand the meaning of the numbers or operations involved. Similarly, Dehaene and Cohen (1997) described patient MAR who could still multiply but failed in tasks of number comparison, approximation, and bisection of numerical intervals. Compared to those earlier cases, the study of patient LEC adds an important new set of non-verbal tasks with arrays of dots similar to those used in infants and animals, and that reveal striking impairments. Such tasks provide simple indicators that can be used profitably in neuropsychological research.

5.3. Anatomical correlations

Concerning the anatomy of number processing, the present observations fit relatively well with the hypotheses of the triple-code model. Verbal acalculia (patient BRI) was associated with a left-hemispheric atrophy more marked around the left temporal language areas. Quantity impairments (patient LEC) were associated with a lesion centered on the intraparietal sulcus.

However, one complication concerns the lateralization of quantity representations. The triple-code model postulates a redundancy of quantity representations in the left and right parietal lobes. This is based on two observations: the bilateral parietal activations that are generally observed in neuroimaging of number processing tasks (Dehaene et al., 1999), and the fact that a single disconnected right hemispheric can perform elementary quantity-based tasks (Seymour, Reuter-Lorenz, & Gazzaniga, 1994). The model therefore predicts that only a bilateral or diffuse cerebral lesion should cause extended difficulties in quantity processing, whereas LEC presented only a left parietal lesion. Why was her putative right-hemisphere quantity representation not sufficient to perform the requested quantity tasks? A similar issue was raised for patients CG (Cipolotti et al., 1991) and MC (Polk et al., 2001), two cases with broad numerical impairments due to a unilateral left parietal lesion.

One should first note that, in the absence of direct functional neuroimaging evidence, we cannot exclude a dysfunction of the right parietal lobe. The deafferentation of the right parietal lobe following the degeneracy of callosal fibers from the lesioned controlateral parietal lobe may cause distant dysfunction, a "diaschisis" which might have been revealed by SPECT or PET examinations. Note that the patient's MRI showed relatively diffuse white matter hyperintensities that may have favored such deafferentation processes. Furthermore, patient LEC did suffer from a small occipital hemorrhage that occurred after the parietal lesion and the associated acalculia, but before the present experimental study, a lesion that may or may not play a functional role in the present observations.

Another interpretation relies on inter-subject variability. The capacities of the right hemisphere may differ across individuals, and some may be strictly left-lateralized for numerical processing. Such inter-individual variability is not apparent in most neuroimaging studies, which average across a group of subjects. Chochon et al.'s fMRI study (Chochon et al., 1999) was designed to study the implication of the left and right parietal lobes in tasks of digit naming, comparison, multiplication and subtraction. Some inter-individual differences were noted. Five subjects showed a clearly bilateral pattern of activation in the vicinity of the intraparietal sulcus, but three subjects showed significant activation only in the left intraparietal region. Perhaps patient LEC was more similar to the latter subjects premorbidly. Such a hypothesis might explain the differences between patients MAR (Dehaene & Cohen, 1997) and LEC. Although such a comparison is complicated by the fact that MAR was left-handed, suffered from a unilateral right parietal lesion, and thus seems to have been cross-lateralized, both MAR and LEC presented Gerstmann's syndrome and a greater impairment for subtraction than for multiplication. Patient MAR was impaired when the quantities were presented in verbal or in Arabic digits, while he performed much better when the input was non-symbolic. Patient LEC presented impairments in quantity manipulation regardless of the input format. One explanation could be the presence, in MAR but not in LEC, of a rich quantity representation in the non-dominant hemisphere.

A final element of note is that, even within the triple-code model, the left and right parietal lobe representations of quantity are *not* equivalent. Both are involved in manipulating quantity information, but only the left parietal region provides a direct interconnection of the quantity representation with the linguistic code (Dehaene & Cohen, 1995). This may explain the greater severity of acalculia following a left parietal lesion. In order to tap purely on quantity processing, we attempted to design tasks that were strictly non-verbal and were inspired from the infant and animal literature, such as the task of selecting the larger of two sets of dots, or of adding two such sets. Nevertheless, instructions for those tasks were given verbally, and we cannot exclude that a significant component of verbal working memory or some other verbal mediation contaminated our results. In that respect, the quantity processing capacities of the right hemisphere may be easier to evidence in cases of callosal disconnection (Seymour et al., 1994) or large left-hemispheric lesion (Cohen & Dehaene, 1991; Grafman et al., 1989), than in patients with focal left parietal damage. We have often seen that, in the latter cases, attempts at verbalizing the operation actually impede successful performance.

6. Conclusion

The main contribution of the present work is to begin the exploration of acalculia using non-symbolic quantity processing tasks of subitizing, approximation and comparison. We suggest that such tasks cluster in a theoretically coherent manner with other deficits such as multiplication or subtraction impairments. Of course, an association of deficits is more difficult to prove than a dissociation, and cannot firmly established on the basis of only two cases. Further studies should evaluate the proposed associations with a large series of cases, and also establish the range of inter-individual variability in number processing.

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