Acalculia

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Introduction

Neurologists' knowledge of number processing impairments is often limited to the notion that acalculia is part of Gerstmann's syndrome (Benton, 1992; Gerstmann, 1940). It may extend to the classical typology proposed by Hécaen, who distinguished aphasic, spatial, and anarithmetic acalculia (Hécaen et al., 1961). Actually, modern research on acalculia (a term coined by Henschen, (1920) has made considerable progress from this point, starting in the 1980s within the expanding framework of cognitive neuropsychology, and soon yielding refined cognitive models (Dehaene, 1992; Deloche and Seron, 1982; McCloskey et al., 1986). Presently, it is an important component of the cognitive neuroscience of numerical abilities, having close links to the methodology used in and theories arising from numerical cognition studies performed in animals, human infants, or normal adults. These methodologies include behavioural measures, functional and anatomical imaging, and electrophysiological techniques (for reviews see Butterworth, 1999; Dehaene and Cohen, 1995; Dehaene et al., 2004).

Beyond its fundamental interest, acalculia constitutes a frequent and incapacitating disorder following acquired, mostly left-hemisperic, brain lesions (Jackson and Warrington, 1986; Rosselli and Ardila, 1989). It interferes with many everyday life activities such as shopping, assessing the balance of a bank account, etc.

In this chapter we will: (1) summarize the basic facets of the normal number processing abilities, (2) sketch a simple model of their anatomical implementation, (3) describe an illustrative variety of calculation disorders, (4) briefly discuss the relationships of acalculia, Gerstmann's syndrome, and the parietal lobes, and (5) propose some guidelines for the assessment and rehabilitation of acalculia in stroke patients.

Basic number processing abilities

We will first summarize the main mental operations that we commonly perform when dealing with numbers, and consider their gross cognitive organization. The following inventory also provides the framework for a systematic bedside examination of calculation abilities.

The triple code. Knowledge of a number (e.g. the number 45), comprises three distinct formats under which this number is represented in our brain (Dehaene and Cohen, 1995): A sequence of words ("forty-five"), a string of arabic numerals (45), and as the representation of an abstract quantity independent from conventional symbols. The verbal and arabic formats are of course specific to adult humans educated within a given language and a given culturally-defined numerical system. These symbolic systems in principle allow a perfectly accurate encoding of any number. In contrast, the abstract quantity representation may be shared with preverbal infants (Feigenson et al., 2004), with adults using a language with a minimal number vocabulary (Pica et al., 2004), and with a wide range of animals (Hauser et al., 2003). There is evidence that this quantity representation is approximate, with a precision that decreases as number size increases (Dehaene, 2003). It has been modeled as an oriented mental "number line" on which numerosities are represented as zones of activation (Dehaene and Changeux, 1993). Larger numerosities are represented with an increasing spread of activation, and hence an increased overlap with nearby numerosities. Note that in addition to their main function of refering to quantities, some numerals also have a "nominal" function of refering to pieces of encyclopaedic knowledge, such as 52 refering to a bus line, or 1789 to the French Revolution.

Input/output. These three cerebral codes are linked to external objects by appropriate input/output processes. Thus, we can identify verbal numerals (like any other words) upon hearing or reading them, and conversely we can produce them orally or by spelling them out. Similarly, Arabic numerals, which exist only in a visual form, can be identified visually and written down. As for the representation of quantities, this can be activated, for instance, by extracting the numerosity of a set of visual objects (Mandler and Shebo, 1982) or by interpreting finger patterns (Thompson et al., in press). It may also drive hand gestures expressing quantities in a non-verbal form.

Transcoding. The three number codes can also be translated into one another by dedicated processes. For instance, reading aloud the Arabic numeral 45 requires that each digit be identified, together with its position in the string, in order eventually to retrieve from the lexicon the fourth word among those expressing tens ("forty"), and the fifth word expressing units (“five”) (Cohen and Dehaene, 1991; McCloskey et al., 1986). Other transcoding processes are involved in writing arabic or verbal numerals to dictation, in naming the numerosity of sets of dots, in accessing the quantity associated with verbal or Arabic numerals, etc.

Calculation. Finally, the three codes are variously involved, often in combination, in the heterogeneous variety of calculation procedures. For instance, familiar multiplication facts have been overlearned at school as rote word associations. Hence, a problem such as 5x9 is first translated into a *verbal representation* (“five times nine”) which allows for the retrieval of the result in verbal form (“five times nine is forty-five”). More complex calculations, such as 987x345, take advantage of the *arabic representation* of numbers, which is essential for applying the usual multidigit calculation algorithms. As a final example, number comparison (i.e. deciding which of two numbers is larger) relies on the abstract *quantity representation*. Thus, normal adults are faster and more accurate at comparing distant numbers (e.g. 1 vs 9) than close numbers (e.g. 5 vs 6), even when targets are presented as verbal or Arabic symbols (Moyer and Landauer, 1967), in agreement with the analogical quantity coding mentioned before. Naturally, coordinating those elementary abilities to solve more complex problems requires effective executive functioning, attentional resources, and working memory.

Anatomical implementation

In order to understand which numerical deficits one might expect in brain-lesioned patients, we will delineate the core brain structures that are thought to subserve the above processes (Figure 1). Those hypotheses are based upon both lesion studies in brain-damaged patients and activation studies in normal subjects.

Insert Figure 1 about here

Verbal numerals and the language areas. Number words may be viewed as a subset of the general mental lexicon, and their specific combination principles as analogous to morphosyntactic word combination rules. It is therefore plausible that numbers in a verbal form should be processed within the classical set of left-hemispheric language areas, in the territory of the left middle cerebral artery. Indeed, impairments of input, output or transcoding of verbal numerals generally result from the same lesions as aphasia, with which they are generally associated. Within this verbal network, the left angular gyrus seems to be crucial for the retrieval of arithmetic facts stored in a verbal form, first and foremost the familiar multiplication facts ("five times nine is forty-five"), and more generally for the exact calculations afforded by verbal symbols (Cohen et al., 2000a; Delazer et al., 2003; Lampl et al., 1994). The retrieval of rote memories for arithmetical facts may also involve cortico-subcortical loops associated with the language cortex (Dehaene and Cohen, 1997; Delazer et al., 2004).

Arabic numerals and the occipitotemporal cortex. The identification of Arabic numerals, like the categorization of visual objects or printed words, depends on the left ventral occipitotemporal cortex, particularly the fusiform gyrus (Cohen et al., 2000b). There are indications that digits may have a more bilateral representation than letters (Cohen and Dehaene, 1995; Pinel et al., 2001).

Quantities and the HIPS. There is converging evidence that the horizontal segment of the intraparietal sulcus (HIPS) subserves the non-verbal representation of quantities, and is therefore crucial to all semantic manipulations of numbers. This view is supported by functional imaging data, which show activation of the HIPS in most numerical tasks. Importantly, activations increase in experimental conditions with a stronger quantity-related component: approximate vs exact addition; subtraction vs overlearned multiplication problems; novel vs trained arithmetic facts; calculations with large vs small numbers; comparison of close vs distant numbers (for a review see Dehaene et al., 2003). This localization is also compatible with the few studies of patients with acquired semantic deficits in the number domain (see below) (Dehaene and Cohen, 1997; Delazer and Benke, 1997; Lemer et al., 2003), and with data from developmental dyscalculia (Isaacs et al., 2001; Molko et al., 2003).

Connectivity. The cerebral modules implementing the triple-code model are thought to be connected both within and across hemispheres. Language-related mechanisms, which are strongly left-lateralized, are connected to the quantity system in the left intraparietal region and to the digit recognition system in the left fusiform gyrus. Furthermore, we propose that the left and right digit recognition system communicate via the splenium of the corpus callosum, and operate as a single functional unit. Similarly, the left and right quantity systems communicate via a more anterior segment of the corpus callosum. This pattern of connection explains for instance why, in patients with a selective lesion of the callosal splenium, the interhemispheric transfer of exact visual digit identity is impaired, while the transfer of approximate quantities is still possible through the anterior callosum (Cohen and Dehaene, 1996).

Finally, cerebral networks involved in general functions of attention, working and long-term memory, executive control, or visuo-spatial processing, contribute to various degrees in essentially all arithmetic tasks.

Varieties of acalculia

We will first consider patients whose lesions shed light on the overall pattern of lateralization of numerical abilities. We will then turn to a more analytic description of (1) impairments of number transcoding, which engages mostly verbal/symbolic processes, (2) impairments of non-symbolic quantity manipulation, and (3) impairments of mental arithmetic, which is sensitive to both verbal and quantitative aspects of number processing (Figure 2). Finally we will illustrate some meaningful dissociations between acalculia and general language impairments.

Hemispheric specialization

As reviewed above, the left hemisphere is thought to contain a complete number processing system. Accordingly, right-sided lesions generally do not induce acalculia. However this general view requires some qualifications. First, numerical functions may show atypical patterns of lateralization in individual subjects, particulary in left-handers, yielding severe acalculia following right-sided lesions (e.g. Dehaene and Cohen, 1997). Second, the so-called spatial acalculia, a side-effect of more diffuse spatial processing impairments, generally results from posterior right-hemispheric lesions (see below). Third, group studies suggest that some numerical tasks are impaired on average in right-lesioned patients, such as number comparison (Rosselli and Ardila, 1989) or infering the principles that underlie numerical series (Langdon and Warrington, 1997).

Moreover, the fact that right lesions generally do not notably affect number use does not imply that the right-hemisphere is not endowed with number processing abilities. Indeed, neuropsychological evidence supports the idea that some processes are represented both in the left and in the right hemispheres.

Although rare, isolated callosal lesions are extremely informative on issues of hemispheric specialization. Thus, in a patient with a posterior callosal infarct, Arabic numerals presented selectively to the left hemisphere could successfully be used for any numerical tasks, including comparison, reading aloud, or arithmetic (Cohen and Dehaene, 1996). In contrast, digits presented to the right hemisphere yielded high error rates in reading aloud and in exact arithmetic tasks. However, numbers presented to either hemisphere could be successfully compared to a given standard. This pattern extends observations in callosotomy patients (Gazzaniga and Hillyard, 1971; Gazzaniga and Smylie, 1984; Seymour et al., 1994), and illustrates the ability of the right hemisphere not only to identify Arabic numerals, but also to access and manipulate their quantitative meaning, while verbal output and exact arithmetic is restricted to the left hemisphere. Similar observations were made in patients with Pure Alexia. Their intact right-hemispheric system allows them to compare numbers (Cohen and Dehaene, 1995), and even to perform some quantity-dependent arithmetic computations (Cohen and Dehaene, 2000), on the basis of Arabic stimuli that they cannot read aloud.

In support of the same ideas, patients with extensive left-hemispheric lesions generally show preserved Arabic number comparison abilities, while they may be severly aphasic and acalculic, and unable to read aloud numbers or solve even elementary calculations (Cohen et al., 1994; Dehaene and Cohen, 1991; Grafman et al., 1989; Warrington, 1982). Beyond number comparison, some patients with large left-sided lesions may show more substantial abilities of approximate number manipulation, possibly involving the intact right hemisphere. As an example, patient NAU proposed that there were 350 days in a year, or about 10 eggs in a dozen. He could even reject grossly erroneous addition problems (e.g. 1+2=9), while he was unable to discriminate exact from slightly false problems (Dehaene and Cohen, 1991).

Insert Figure 2 about here

Number transcoding deficits

If we consider the three symbolic representations of numbers (Arabic, oral verbal, written verbal), there are six distinct types of transcoding, most of which have been analyzed in detailed cognitive neuropsychological studies (Macaruso et al., 1993; Noël, 2001). Many studies have concentrated on the process of reading aloud Arabic numerals, and we will take this case as an illustrative instance of transcoding deficits.

Reading aloud Arabic numerals entails three successive stages: first, identification of the string of digits, second, translation of the string of digits into a sequence of words according to the appropriate rules, and finally the overt production of this word sequence. These three stages normally take place within the left hemisphere.

Impairments at the initial stage of digit identification correspond to Pure Alexia, and follow left ventral occipitotemporal lesions. As mentioned before, the corresponding right-hemispheric region has roughly equivalent abilities for the identification of Arabic numerals, explaining the fact that patients can paradoxically compare numbers that they cannot read aloud (Cohen and Dehaene, 1995). Impairments at the final stage of spoken or written word output probably depend on general word processing, although dissociations may be observed (see below).

As for the middle stage of translation into a word sequence, this has been analysed in a number of case studies, including the pioneering study by McCloskey *et al.* (1986) of patients HY and JG. HY produced so-called "lexical" reading errors, i.e. he substituted expected words with other words from the same category (e.g. 54 → "sixty four", or 612 → "six hundred and thirteen"). The patient prepared an adequate word frame (e.g. "a tens name followed by a unit name"), but made errors when selecting specific words to fill that frame. In contrast, patient JG mostly made "syntactic" errors (e.g. 54 → "five hundred and four"). He created erroneous syntactic frames, but selected the appropriate number words, i.e. corresponding to the stimulus digits, in order to fill that erroneous frame. This kind of data allows us to distinguish syntactic from lexical processes within number transcoding, and to clarify the organization of the lexicon of number words, which seems to be in parallel and ordered "stacks" for units ("one", "two", etc), teens ("eleven", "twelve", etc), and tens ("ten", "twenty", etc) (Deloche and Seron, 1984).

It is important to remember that patients with even major transcoding deficits, such as a complete inability to read aloud numbers, may still have a good comprehension of the same numbers. As mentioned before, they may access the quantitative meaning of numbers, and in addition, they may access their encyclopaedic meaning. Thus acalculic patients with Deep Dyslexia, altough unable to read them aloud, could readily access and report the historical meaning of the numerals 1789 or 1914 (Cohen et al., 2000a; Cohen et al., 1994).

Finally, patients who are unable to map Arabic numerals onto words normally often resort to verbal counting strategies. Thus they may say "one, two, three, four!" when presented with digit 4, or "ten, twenty, thirty!" for the number 30. This strategy requires preserved visual number identification, and preserved automatic counting series. Those two representations can then be matched in order to bypass the impaired direct route to number words: The patient knows that the proposed digit (4) corresponds to the fourth item in the counting series, allowing him to monitor this series and to stop when appropriate. As a further compensation for an impaired verbal output, patients may answer by displaying the appropriate number of fingers. Naturally, alternative output strategies such as counting, using one's fingers, or writing down the answer instead of saying it, are not restricted to transcoding tasks, but can be used in any numeric task requiring a verbal output. For instance, when patient ATH was asked to say how many eggs there are in a dozen, she wrote 12 while saying "sixteen". When presented with 7+5, she said "a dozen… eleven perhaps" while readily showing 12 (10 and 2) fingers (Cohen et al., 2000a).

Quantity processing deficits

Deficits primarily involving the manipulation of abstract quantities have received much less attention than the more easily diagnosed language-related impairments. Moreover, it is likely that the bilateral representation of quantity-related processes makes them more resistant to focal brain damage.

Core semantic deficits. Only a few patients have been reported who suffered from a core deficit in manipulating abstract quantities, in conjunction with spared language abilities (Dehaene and Cohen, 1997; Delazer and Benke, 1997; Lemer et al., 2003). Such patients are able to read aloud and otherwise transcode all numerical symbols, and to recite automated sequences of number words, such as serial counting or multiplication tables. However, their impairment affects all tasks which require the manipulation of quantities. Thus, patient MAR was mildly impaired at deciding which of two arabic numbers was larger, and utterly unable to perform a numerical bissection task, i.e. to decide which number fell in the middle of two others. In the arithmetic domain, he was unable to solve even the simplest subtraction problems, which are typically not stored in rote verbal memory (Dehaene and Cohen, 1997). In the same vein, evaluating the approximate result of additions without going through the exact calculation algorithm is particularly difficult for such patients (Lemer et al., 2003). Importantly, semantic deficits emerge irrespective of the format of input or output. Thus, patient LEC was impaired at deciding which of two 2-digit Arabic numerals was larger, but even more impaired when comparing the numerosity of two sets of dots (Lemer et al., 2003). Both patients MAR and LEC had lesions of their dominant intraparietal region, supporting a crucial role of this area in quantity processing.

Neglect and the "number line". Beyond core semantic deficits, there is recent evidence that spatial hemineglect may also affect the numerical domain. Thus, in the number bissection task mentioned before, neglect patients systematically selected a number larger than the actual midpoint (e.g. Which number falls in between 11 and 19? →17) (Zorzi et al., 2002). It is thought that neglect induces an attentional bias in accessing the quasi-spatial "number line" of quantity representation, therefore biasing the selection of responses to simple numerical questions.

Attention to space and the perception of numerosity. Perceiving the numerosity of visual displays may be impaired following visuospatial disorders, without implying an impairment of core numerical representations. A classical symptom of Bálint's sydrome, following superior parietal lesions, is an inability to perceive more than one object at a time. When such patients are asked to count a set of random dots, some dots are omitted while others may be counted several times (Luria, 1959). However, Bálint patients are generally quite accurate when estimating the numerosity of sets of 1, 2 or 3 items (Dehaene and Cohen, 1994). It is thought that perceiving the numerosity of such very small sets, a process known as "subitizing", reflects parallel visual processing and does not require the serial attentional scanning of each object, a process that is compromised in Balint's syndrome (Rizzo and Robin, 1990). A related phenomenon has been demonstrated in neglect patients, who can estimate the numerosity of sets up to 4 objects, even when some items fall in the extinguished hemifield and cannot be individually attended to (Vuilleumier and Rafal, 1999).

Impairments of mental calculation

The arithmetic abilities of educated adults (at a basic level the ability to solve addition, subtraction, multiplication, division problems, or combinations thereof), result from a complex interplay of heterogeneous cognitive components. Particularly, as mentioned before, both verbal and quantity-related deficits may interfere with calculation abilities, although in different ways. Stroke may affect those mechanisms in different ways, resulting in a wide variety of arithmetic disorders, all covered under such simplifying terms as anarithmetia or pure acalculia (Hécaen et al., 1961). We will analyze in turn the main cognitive components that may be affected, and the corresponding varieties of acalculia.

Symbolic input and output processes. Deficits affecting the identification of problem operands or the eventual production of responses may induce calculation errors without affecting the core of arithmetic processes. Thus, on the input side, patients with Pure Alexia make errors in identifying digits visually. Hence they translate digits into erroneous number words, eventually retrieving the wrong multiplication facts from verbal memory (e.g. 2x5 → "three times four is twelve") (Cohen and Dehaene, 2000; McNeil and Warrington, 1994). On the output side, patients with impaired oral production may produce erroneous solutions to arithmetic problems orally, but still solve them correctly in writing (e.g. 7+7 → spoken answer "twelve" but written answer 14) (Whalen et al., 2002). Also, errors in the identification of *operation symbols* (+, -, x, /) may be a cause of calculation errors, as has been reported in brain-damaged patients (Ferro and Botelho, 1980).

Spatial layout of arithmetic problems. Reading, writing down or solving multidigit operations on a sheet of paper requires that the component digits and symbols be correctly arrayed in lines and columns. Patients with space processing disorders such as Balint's syndrome, constructional apraxia, or neglect may be unable to solve such problems as a consequence of their inability to organize calculations properly in space. Spatial acalculia mostly results from posterior right-hemispheric lesions (Hécaen et al., 1961; Rosselli and Ardila, 1989).

Executive control and sequencing. All calculations except the simplest ones require some degree of executive processing, and deficits in this broad field may induce numerical impairments.

1) Mentally solving problems that involve several steps and the temporary storage of partial results may be disrupted by working memory impairments (Butterworth et al., 1996).
2) Performing multidigit calculations (e.g. 67 x 26) involves the scheduling and control of a strictly ordered sequence of elementary steps (e.g. compute 6 x 7; write down the digit 2; carry 4; compute 6 x 6; add the carry; etc). Those overall procedures may be disrupted while elementary calculations are fully preserved (Caramazza and McCloskey, 1987).
3) Patients may read aloud correctly simple problems, including the operation signs, but still select the wrong operation when retrieving the result (e.g. 3+3=9) (van Harskamp and Cipolotti, 2001).
4) At still a higher level of executive control, patients with prefrontal lesions may be impaired at working out adequate strategies for the resolution of concrete problems involving numbers, in the absence of acalculia strictly speaking (Fasotti et al., 1992b; Luria, 1966).

Elementary calculation deficits. Patients may master perfectly the sequences of elementary operations involved in multidigit calculations, but fail to recover the elementary arithmetic facts that are required to actually carry out such sequences (Cohen and Dehaene, 1994). Moreover, elementary arithmetic facts themselves are not homogeneous and depend on distinct cognitive abilities, explaining the observation in some patients of clear-cut dissociations between operations. Some facts are learned by rote as automatic verbal associations, and do not require access to the quantitative meaning of numbers. This concerns particularly the most familiar multiplication facts (“five times nine is forty-five”). Other facts must be computed anew using counting and semantic number manipulations such as comparison and estimation. This is typically the case for even simple subtraction problems (e.g. 12-7). Finally, a special set of problems are solved by applying simple algebraic rules (e.g. nx0=0; nx1=n; etc), and may be impaired or preserved independently from other arithmetic facts (McCloskey et al., 1991). This main distinction between a verbal system supporting multiplication and other rote memory-based operations, and a quantity system supporting subtraction and other quantity manipulations, accounts nicely for most cases of dissociations between operations reported in the literature (for a review see e.g. Cohen and Dehaene, 2000). In general, patients with a predominantly verbal deficit are impaired in multiplication more than in subtraction, and frequently have associated language and number transcoding impairments (e.g. Cohen et al., 2000a; Dagenbach and McCloskey, 1992; Pesenti et al., 1994). Conversely, the rarer patients with a predominantly quantitative deficit show the opposite pattern, and may have associated quantity processing deficits, as mentioned above (Dehaene and Cohen, 1997; Delazer and Benke, 1997; Lemer et al., 2003). The strategies used for addition are highly variable across subjects and across tasks in their reliance on verbal and quantitative processes. As a consequence, patients’ performance with addition problems may be closer to their performance either in multiplication or in subtraction (Cohen and Dehaene, 2000; Cohen et al., 2000a; Dagenbach and McCloskey, 1992; Dehaene et al., 2003; van Harskamp and Cipolotti, 2001). This view predicts that no patient should show impaired multiplication and subtraction (reflecting impaired verbal and quantity systems), but preserved addition. The opposite pattern, i.e. preserved multiplication and subtraction (reflecting preserved verbal and quantity systems) with impaired addition, should also be impossible. This proposal, however, is still open to empirical controversies (van Harskamp and Cipolotti, 2001).

Approximate vs. exact calculation. Quantity manipulation abilities allow to evaluate the approximate result of simple problems, particularly of addition problems. Patients severely impaired at finding an exact solution to even the simplest problems may still be able to reject grossly erroneous calculations (Warrington, 1982). For instance, patient NAU judged 2+2=3 and 2+2=4 as equally plausible, but could readily reject 2+2=9 (Dehaene and Cohen, 1991). Conversely, patients with preserved exact calculation but impaired quantitative processing may find it difficult to discriminate slightly vs grossly erroneous results. Thus, when presented with problems such as 2+3, patient LEC was unable to choose the more plausible response among two proposed results (4 and 8), without first explicitly computing the exact solution (Lemer et al., 2003).

Algebra and conceptual arithmetic principles. Solving many numerical problems requires the mastery of principles such as axb=bxa, n+0=n, ax(b+c)=axb + axc, etc. Conceptual processing is thought to involve networks of frontal and parietal areas (Anderson et al., 2004). It is closely related to, and difficult to disentangle from, other previously discussed components of the number processing system, particularly executive control and abstract quantity processing (Delazer et al., 2004; Houde and Tzourio-Mazoyer, 2003). However, it has been shown repeatedly that patients who have forgotten memorized arithmetic facts may show a preserved mastery of algebraic rules (Cohen and Dehaene, 1994; Hittmair-Delazer et al., 1995; Hittmair-Delazer et al., 1994). For instance, when presented with 5x5, a patient spontaneously sketched 5 rows of 5 dots and counted them by successive additions (Cohen and Dehaene, 1994). More impressively, one patient could readily reach the forgotten result of 6x8 by successively computing 6x8=(5x8)+8; 5x8=(10x8)/2; 10x8=80; 80/2=40; 6x8=40+8=48 (Hittmair-Delazer et al., 1994). Conversely, although she retained memorized arithmetical facts, a patient with a semantic numerical impairment was unable to apply the simple principle commutativity of multiplication, or to perceive the equivalence between multiplication problems and the corresponding addition series (Delazer and Benke, 1997).

Dissociating numbers and language

The main features of the number processing model could apply to words in general. Thus, the representation of ordinary words, like numbers, associates non-verbal semantic representations with purely verbal information such as oral and written word forms and grammatical features. Nevertheless, many neuropsychological dissociations are observed between numbers and words.

At the semantic level, patients with profound loss of semantics (generally due to frontotemporal dementia) may show a remarkable sparing of calculation as well as number production and comprehension abilities (Butterworth et al., 2001; Cappelletti et al., 2001; Thioux et al., 1998), supporting the idea that numerical semantics rely on parietal regions. Conversely, patients with quantity processing deficits show preserved general semantic abilities (Dehaene and Cohen, 1997; Delazer and Benke, 1997). For instance parient MAR, although unable to decide which number is the mid-point between 4 and 8, could easily determine that Wednesday falls in the middle of Monday and Friday.

At the input level, reports of a possible sparing of Arabic numerals in Pure Alexia date back to Dejerine, who noted that “the patient recognizes very well all digits”, although “he cannot recognize a single letter” (Cohen and Dehaene, 1995; Dejerine, 1892; Holender and Peereman, 1987). This may result from a better compensation by right occipitotemporal regions for the identification of Arabic numerals than of alphabetic stimuli (Pinel et al., 2001).

Dissociations have also been reported at the level of symbolic output. Thus Anderson *et al.* (1990) described a patient with severe agraphia who was unable to trace even single letters, but whose writing of multidigit Arabic numerals was entirely spared (see also Delazer et al., 2002). Similarly, some patients with a phonemic jargon affecting the oral production of ordinary words may produce number words without any phonological errors (Cohen et al., 1997; Geschwind, 1965).

Numbers, Gerstmann’s syndrome, and the parietal lobes

Over a series of publications from 1924 to 1957, Josef Gerstmann delineated a syndrome which still carries his name, consisting of acalculia, left-right disorientation, agraphia, and finger agnosia (Gerstmann, 1940). He considered that this association of deficits resulted specifically from lesions affecting the “transitional region of the angular and the middle occipital convolution”, and that its four components reflected a common underlying mechanism, namely some form of impairment of the body schema, affecting particularly the hands and fingers. Thus Gerstmann speculated that the link between numbers and body schema stemmed from the “important part (which) is played by the individual fingers and their right and left laterality in acquisition of the functions of writing and calculating”.

While the value of Gerstmann’s syndrome in localizing lesions to the dominant posterior inferior parietal lobule was largely validated, the hypothesis of a single core deficit was seriously challenged (for a review see Mayer et al., 1999). For instance, Benton (1961; 1992) showed not only that the four cardinal features of the syndrome could be dissociated from one another, but also that “the particular combination of behavioural deficits which form the syndrome show no stronger internal associative bonds than do a score of other combinations of behavioural deficits”.

According to this view, Gerstmann’s syndrome would reflect the accidental association of deficits affecting distinct systems which all happen to be located in the inferior parietal region. Indeed, functional imaging shows such a functional mosaic in the intraparietal cortex, with regions activated more strongly during calculation, manual tasks, spatial-attentional tasks, or a phonemic language task (Simon et al., 2002). However, some commonality between the components of Gerstmann's syndrome might still be found in the general spatial and sensorimotor functions implemented by the parietal lobes.

Insert Figure 3 about here

Importantly, as we would predict from the location of Gerstmann lesions and what we know about the role of the intraparietal sulcus in the representation of quantity, the acalculia observed in cases of "pure" Gerstmann's syndrome without aphasia fits with a semantic deficit of quantity processing. Still, the close proximity of the HIPS, the inferior parietal language area, and the superior parietal space-processing cortex, may account for different or more complex patterns of number processing impairments (Figure 3).

Assessment and rehabilitation of acalculia

The basic examination of numerical abilities in brain-damaged patients should include both verbal and non-verbal aspects of number processing. Guidelines for a bedside examination are proposed in Table 1. Naturally, the patient's behaviour should be interpreted on the background of a wider assessment of language, vision, attention, executive functioning.

Insert Table 1 about here

Relatively few controlled studies have been devoted to the rehabilitation of acquired acalculia (for recent reviews see Girelli and Seron, 2000; Lochy et al., in press). Most of them have targeted transcoding processes (Deloche et al., 1989), the retrieval of simple arithmetical facts through drill (Girelli et al., 1996) or through conceptual training (Domahs, 2003; Girelli et al., 2002), or the creation of strategies for solving concrete problems (Fasotti et al., 1992a).

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Table 1

Suggested tests for the clinical examination of numerical abilities

- Forward and backward digit span.
- Forward and backward counting.
- Symbolic transcoding (reading aloud and taking dictation of simple and multidigit numerals).
- Single-digit arithmetic. To reduce the contribution of input and output deficits to the patient's performance, problems may be simultaneously presented in written form and read aloud by the examiner. Familiar multiplication problems and simple subtractions should be tested in priority, as they reflect rote verbal and quantity-based processes, respectively.
- Multidigit written calculations.
- Concrete arithmetic problems requiring some planning.
- Evaluation of the numerosity of sets of dots, presented either briefly to test estimation abilities, or for an unlimited duration to allow for serial counting.
- Evaluation to check for other components of Gerstmann's syndrome.

Legends for figures

Figure 1: Schematic depiction of the triple-code model of number processing.

Figure 2: Diagram of information-processing pathways involved in processing Arabic digits during various arithmetic tasks. Although still insufficiently specified at both anatomical and functional levels, such diagrams may begin to explain the various neuropsychological dissociations that are observed in human adult lesion cases (functional lesion sites are indicated with stars). Lesion 1, associated with pure alexia, would create an inability to read numbers and to multiply, but not to compare or subtract (Cohen and Dehaene, 1995; Cohen and Dehaene, 2000). Lesion 2, associated with phonological dyslexia, would create an inability to read numbers, but not to multiply, subtract or compare (Garcia-Orza et al., 2003). Lesions 3 and 4 might explain the frequent double dissociation between multiplication and subtraction in patients who can still read numbers (van Harskamp and Cipolotti, 2001; van Harskamp et al., 2002; Whalen et al., 2002), and the presence or absence of associated deficits in comparison and non-symbolic numerosity processing (Lemer et al., 2003). Lesion 5 might explain residual calculation abilities in patients who fail to produce the solution of arithmetic problems orally, but can still solve them in writing (Whalen et al., 2002). Abbreviations: left AG, left angular gyrus; FuG, fusiform gyrus; HIPS, horizontal segment of intraparietal sulcus; IFG, inferior frontal gyrus. Adapted from (Dehaene et al., 2004).

Figure 3: Three parietal circuits for number processing. Intersection of activations clusters from a metanalysis of fMRI activation studies. Red: The horizontal segment of the intraparietal sulcus (HIPS) was activated bilaterally in a variety of contrasts sharing a component of numerical quantity manipulation. Green: The left angular gyrus was activated during arithmetic tasks with a strong verbal component. Blue: The posterior superior parietal lobule was activated bilaterally in a few numerical tasks, overlapping with tasks of non-numerical visual attention shift. Reproduced from (Dehaene et al., 2003).

Figure 1

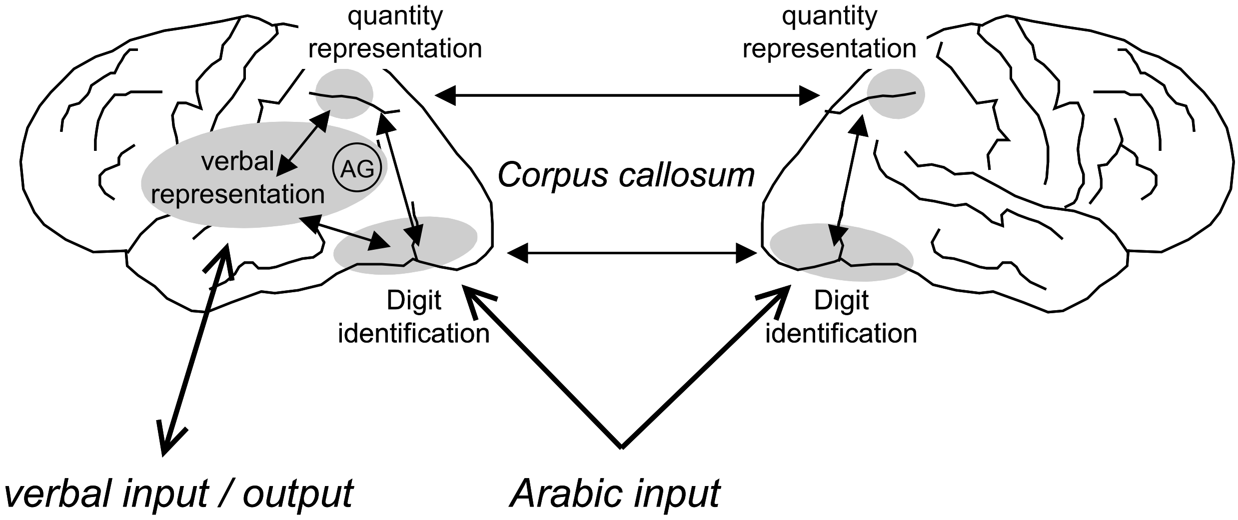
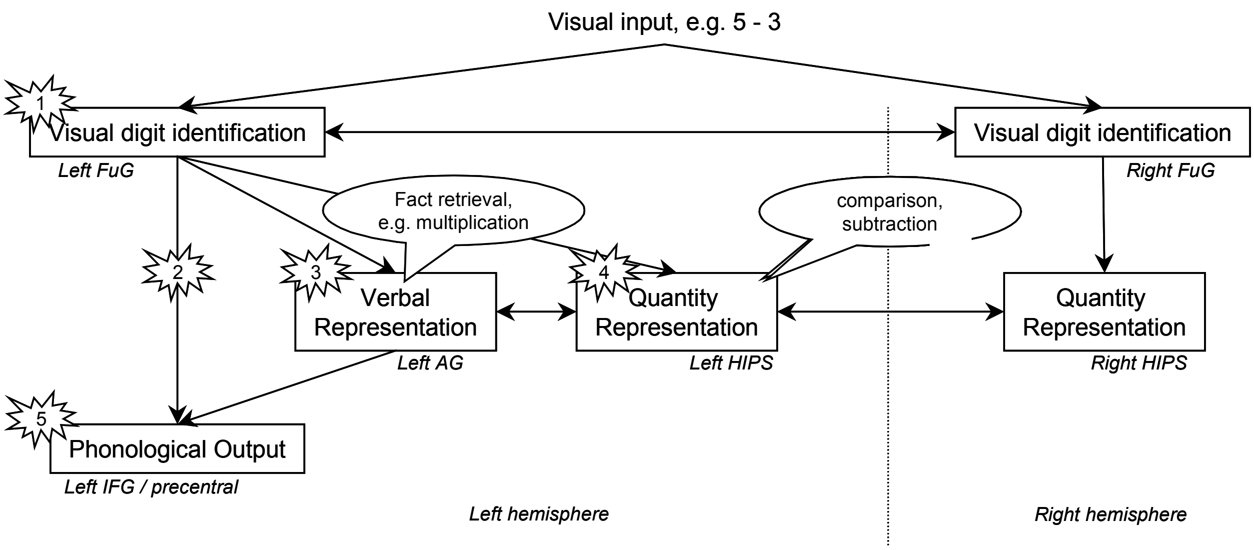
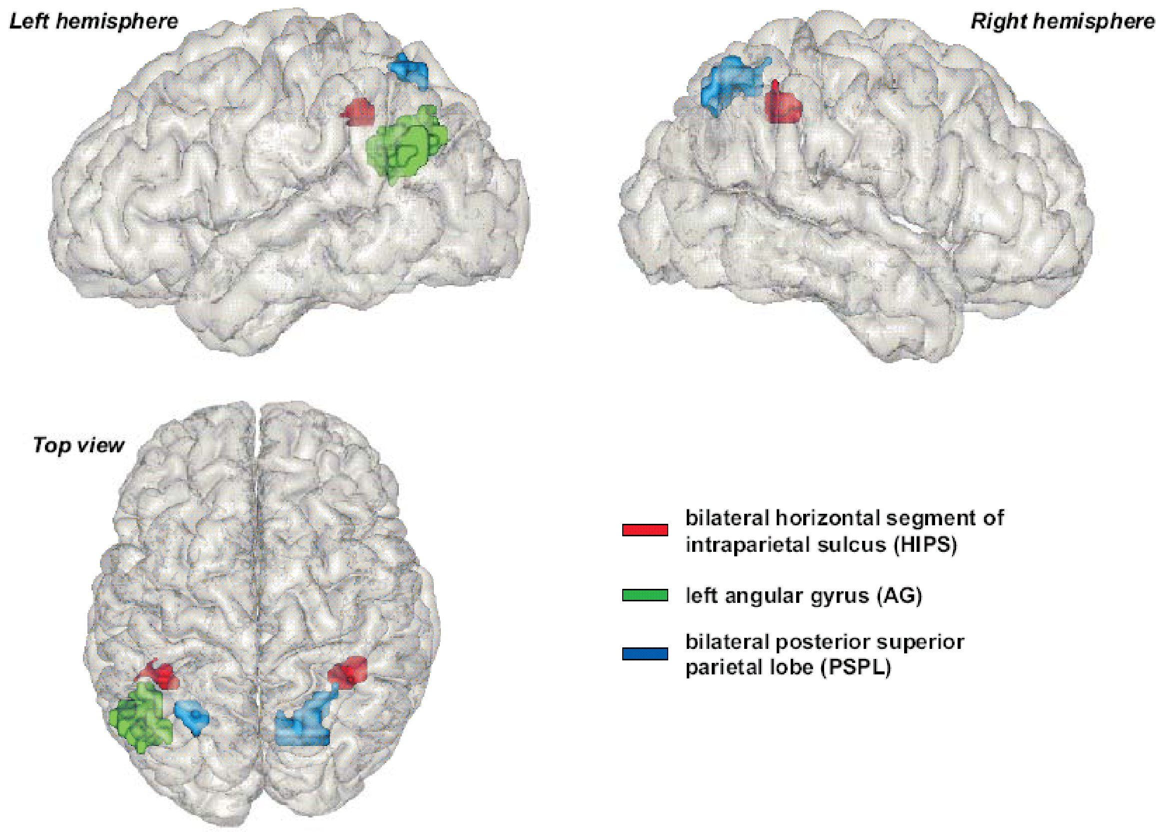

quantity
representation
quantity
representation
verbal
representation
AG
Corpus callosum
Digit
identification
Digit
identification
verbal input / output
Arabic input

Figure 2



Visual input, e.g. 5 - 3
1
Visual digit identification
Left FuG
Visual digit identification
Right FuG
Fact retrieval,
e.g. multiplication
comparison,
subtraction
2
3
Verbal
Representation
Left AG
4
Quantity
Representation
Left HIPS
Quantity
Representation
Right HIPS
5
Phonological Output
Left IFG / precentral
Left hemisphere
Right hemisphere

Figure 3


Left hemisphere
Right hemisphere
Top view
bilateral horizontal segment of intraparietal sulcus (HIPS)
left angular gyrus (AG)
bilateral posterior superior parietal lobe (PSPL)