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Counting or Chunking?:

Mathematical and heuristic abilities in patients with corticobasal syndrome and posterior cortical atrophy

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Abstract

A growing amount of empirical data is showing that the ability to manipulate quantities in a precise and efficient fashion is rooted in cognitive mechanisms devoted to specific aspects of numbers processing. The Analog number system (ANS) has a reasonable representation of quantities up to about 4, and represents larger quantities on the basis of a numerical ratio between quantities. In order to represent the precise cardinality of a number, the ANS may be supported by external algorithms such as language, leading to a “Precise Number System”. In the setting of limited language, other number-related systems can appear. For example the Parallel Individuation system (PIS) supports a “chunking mechanism” that clusters units of larger numerosities into smaller subsets. In the present study we investigated number processing in non-aphasic patients with Corticobasal Syndrome (CBS) and Posterior Cortical Atrophy (PCA), two neurodegenerative conditions that are associated with progressive parietal atrophy. The present study investigated these number systems in CBS and PCA by assessing the property of the ANS associated with smaller and larger numerosities, and the chunking property of the PIS. The results revealed that CBS/PCA patients are impaired in simple calculations (e.g., addition and subtraction) and that their performance strongly correlates with the size of the numbers involved in these calculations, revealing a clear magnitude effect. This magnitude effect correlated with gray matter atrophy in parietal regions. Moreover, a numeral-dots transcoding task showed that CBS/PCA patients are able to take advantage of clustering in the spatial distribution of the dots of the array. The relative advantage associated with chunking compared to a random spatial distribution correlated with both parietal and prefrontal regions. These results shed light on the properties of systems for representing number knowledge in non-aphasic patients with CBS and PCA.

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Keywords

Number knowledge; Corticobasal Syndrome; Posterior Cortical Atrophy; Chunking; parietal; prefrontal

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1. Introduction

Number knowledge is an essential facet of human cognition (e.g., Feigenson, Dehaene, & Spelke, 2004; Nieder & Dehaene, 2009; Piazza & Dehaene, 2004; Piazza, 2010; Piazza et al., 2010; Piazza, Mechelli, Price, & Butterworth, 2006; Pinel, Piazza, Bihan, & Dehaene, 2004). Several studies revealed that number knowledge is rooted in a core mechanism that represents quantities in an approximate fashion. While very small numbers are represented relatively precisely, quantities larger than about 4 are represented as a ratio, following Weber's Law (Fechner, 1860). The accuracy of numerosity estimation based on this system, called the "Analog number system" (ANS) (Dehaene, 1997; Hyde & Spelke, 2011; Izard, Sann, Spelke, & Streri, 2009), decreases with increasing numerical magnitude, according to the Weber fraction (Dehaene, 2003; Halberda & Feigenson, 2008; Piazza et al., 2010). The ANS thus provides an estimate of a quantity but it does not identify the exact cardinality of a number or a set of objects. In order to precisely manipulate numbers that are larger than about 4, the ANS is hypothesized to depend on the support of external algorithms involving the so-called "Precise number system" (Izard & Dehaene, 2008a). Algorithms derived from verbally-mediated counting, from this perspective, allow us to identify exact numbers and quantities of any magnitude.

It is still a matter of debate to what extent number knowledge is rooted in language-related abilities (Gordon, 2004; Izard & Dehaene, 2008b; Nieder & Dehaene, 2009b) or if numbers and words depend upon different cognitive infrastructures (Halpern et al., 2004; Halpern et al., 2004; Koss et al, 2010; Morgan et al, 2011). Evidence that number knowledge depends on verbally-mediated representations comes from observations of unilingual speakers of languages without an apparent number system (Pica et al, 2004; Gordon et al, 2004), pre-linguistic young children (Lipton & Spelke, 2005; K Wynn, 1992; Karen Wynn, 1990) and deaf signers in linguistically isolated communities (Coppola, Spaepen, & Goldin-Meadow, 2013; Spaepen, Coppola, Spelke, Carey, & Goldin-Meadow, 2011). This work suggests that individuals with restricted language have limited use of a precise number system. For example, Spaepen et al., (2011) found that illiterate home-signers living in a cultural environment in Nicaragua that uses numbers are able to employ gestures to represent numbers. However, they appear to have significant difficulties in accurately gesturing precise numbers bigger than about 3.

There is growing evidence, on the other hand, suggesting a double dissociation between number knowledge and language processing (Halpern, Clark, Moore, Cross, & Grossman, 2007; Varley, Klessinger, Romanowski, & Siegal, 2005; Halpern et al., 2004; Halpern, McMillan, Moore, Dennis, & Grossman, 2003). From this perspective, the ability to manipulate numbers and quantities appears to depend on the inferior parietal lobule (IPL), a brain area that is not part of the traditional, peri-Sylvian language system. Focal

neurodegenerative disease patients with corticobasal syndrome (CBS) and posterior cortical atrophy (PCA) have disease primarily localized to the IPL, and thus have relatively spared language abilities with profound deficits in precise number knowledge (Halpern et al., 2003, Halpern et al., 2007). This is reflected in their poor performance on measures assessing arithmetic calculations, matching or counting dots of an array, and other simple tasks which involve numbers and quantities (e.g., Koss et al, 2010; Morgan et al, 2011; Halpern, Clark, Moore, Cross, & Grossman, 2007; Halpern et al., 2004; Halpern et al., 2004; Halpern, McMillan, Moore, Dennis, & Grossman, 2003). These patients are not aphasic, so their deficit with numbers cannot be easily attributed to a disorder of language. Similar evidence comes from cases of isolated acalculia without aphasia after stroke (Cipolotti, Butterworth, & Denes, 1991; Martory et al., 2003; Takayama, Sugishita, Akiguchi, & Kimura, 1994). Imaging and autopsy studies relate number deficits in CBS and PCA to atrophy in IPL (Koss et al., 2010; McMillan, Clark, Moore, & Grossman, 2006; Morgan et al., 2011; Pantelyat et al, 2011). Given the overlapping anatomic locus of parietal disease, shared number impairments, and a comparable general level of deficit in both CBS and PCA measured by MMSE [$t(16)=0.27$, $p>0.7$], we investigate these patients together in a single group which we refer to as CBS/PCA (see Morgan et al., 2011 for a similar strategy).

Regardless of the relationship between language and number representations, there may be other number systems that can contribute to number knowledge. One such system in which number-related abilities may be grounded is called the parallel individuation system (PIS) or the object tracking system (OTS) (Pylyshyn, 2001; Revkin, Piazza, Izard, Cohen, & Dehaene, 2008; Scholl, 2001). Parallel individuation is a mechanism that represents objects as single entities and allows humans as well as primates to trace object movements in space and time, thus supporting the fundamental notion of object permanence. One of the limitations of parallel individuation is that it can simultaneously track only up to 3 – 4 entities, similar to the ANS, and it cannot process larger quantities with any precision. One attribute of parallel individuation that can circumvent in part the computational limit of 3 – 4 units involves a “chunking” mechanism where a numerosity like 6 can be represented as 3 clusters of 2 (Feigenson & Halberda, 2004; Le Corre & Carey, 2007).

The existence of parallel individuation has been corroborated by several empirical studies in healthy adults (e.g., Barth et al., 2006; Barth, Kanwisher, & Spelke, 2003; Cordes, Gelman, Gallistel, & Whalen, 2001; Mandler & Shebo, 1982; Mathy & Feldman, 2012). Number vocabularies of isolated communities on Papua/New Guinea also appear to use a parallel individuation-like system (Lean, 1988). Moreover, because this system is evident in young children and infants (e.g., Berteletti, Lucangeli, Piazza, Dehaene, & Zorzi, 2010; Feigenson et al., 2002, 2004; Piazza et al., 2010; Moher, Tuerk, & Feigenson, 2012), linguistically isolated adults such as deaf signers living in remote communities (e.g., Coppola, Spaepen, & Goldin-Meadow, 2013; Frank, Everett, Fedorenko, & Gibson, 2008; Gordon, 2004) and non-human animals (E. M. Brannon, Wusthoff, Gallistel, & Gibbon, 2001; E. Brannon & Terrace, 2000; Cantlon & Brannon, 2006) who have limited access to the precise number system, this has been taken as additional evidence for the dependence of precise number knowledge on language. However, the extent to which chunking abilities are rooted in specific brain networks has not been assessed.

In this report, we examine the contribution of the different number systems to quantity-related deficits in CBS/PCA patients, and we examine the neuroanatomic correlates of their impairment. In addition, we tested to what extent these patients are able to apply heuristics (e.g., Gigerenzer & Gaissmaier, 2011) in order to compensate for their deficit in number processing. An important question thus is whether a mechanism such as chunking is indeed a core number system or represents a general multi-domain processing heuristic that can be applied for efficiently processing numerosities. In other words, to represent the precise cardinality of a number bigger than 3 or 4, we can use a language-based *counting strategy*, a process by which a cardinality in the number system is represented as an augmentation of the preceding number in the sequence by “1” (e.g., (Beller & Bender, 2008; Le Corre & Carey, 2007). Another way in which we can potentially evaluate a numerosity bigger than 3 or 4 involves *chunking* these quantities into several smaller clusters or subsets. For example, a numerosity like 6 can be represented as 3 clusters of 2. The question is whether this is a distinct number system as in parallel individuation because it is evident in individuals with limited language and is associated with precise representations that are larger than about 3 or 4; or whether this is simply a variant process for evaluating numerosities in a more efficient manner regardless of language status, as in counting by two’s and three’s, resembling other heuristic processes for optimizing efficiency known broadly as executive resources (Badre, 2008; Koechlin & Summerfield, 2007). There is, indeed, a long history of chunking as a strategic approach for improving efficiency in a variety of cognitive tasks. In short-term memory (STM), for example, limits are usually expressed in terms of chunks of information that can be stored (e.g., Anderson, Bothell, Lebiere, & Matessa, 1998; Gobet, Lane, & Croker, 2001; Mathy & Feldman, 2012; Simon, 1974). In other words, a single chunk represents a group of entities sharing a salient feature that are treated as a single unit. Classic examples of chunking can be found in consideration of strings of letters like LAXJFKSFO. While it may be difficult to remember this as a random sequence of letters, it is much easier to recall these as a collection of three airport codes —LAX (Los Angeles), JFK (John F. Kennedy), and SFO (San Francisco) (see Moher et al., 2012). Other studies have shown that healthy adults are able to chunk on the basis of chess configurations (e.g., Chase & Simon, 1973), word sequences (e.g., Simon, 1974), and ordinal relations (e.g., Mathy & Feldman, 2012).

In the present study, we focused on two tasks that target the precise number system and parallel individuation. In the first task, CBS/PCA participants were asked to perform precise calculations, namely addition and subtraction. The cardinality of the numbers involved in the calculations progressively increased over the course of the trials. Tasks involving precise calculation such as these should heavily engage the precise number system, and these non-aphasic patients should be able to perform these tasks if precise number depends on language. However, previous results (e.g., Halpern et al., 2007; Halpern et al., 2004) have shown that CBS/PCA patients are impaired in arithmetic when compared with healthy controls. If this is related to degraded representations of number knowledge, then we should observe a magnitude effect, that is, greater difficulty with numerosities larger than about 4, the limit for representing exact cardinalities in the ANS. From this perspective, since number representations depend on the integrity of IPL, we expected the magnitude effect (great

difficulty with larger numbers than smaller numbers) to be associated in part with gray matter atrophy in the IPL that characterizes both groups of patients.

In the second task, we focused on the ability of CBS/PCA patients to match the numerosity of an array of dots (filled, 1 cm circles) with an Arabic numeral using a multiple-choice format. Half of the time, the dot arrays were presented in a random spatial configuration; and half of the time, the dot arrays were presented in a spatial distribution that clustered the dots to facilitate chunking the total number of dots. A discrepancy in numeral-dots matching accuracy for clustered and randomly distributed arrays should emerge only in individuals with a deficit in the verbally-mediated precise number system. However, we expected CBS/PCA patients to show a discrepancy between clustered compared to random dot arrays, despite the absence of aphasia, because of their degraded representations of number knowledge. In addition, if chunking is a number-independent resource strategy, then these patients should be able to take advantage of the clustered configuration of dots in order to improve the accuracy of dot enumeration for arrays larger than about 4.

2. Methods

2.1 Participants

We studied 19 non-aphasic native English-speakers with CBS ($n = 12$) or PCA ($n = 7$). CBS patients were diagnosed according to published criteria (Armstrong et al., 2013) and clinical–pathological studies of patients with autopsy-proven corticobasal degeneration (CBD; e.g., Boeve et al., 1999; Grimes, Lang, & Bergeron, 1999; Murray et al., 2007). These patients had an asymmetric extrapyramidal syndrome involving features such as limb rigidity, dystonia and “alien limb” phenomena, together with progressive ideomotor apraxia and cortical sensory loss, but there was no aphasia. There are no published clinical consensus criteria for PCA, and we based the diagnosis on clinical–pathological cases in our lab and elsewhere emphasizing the presence of progressive visuospatial difficulty without memory or language impairment (e.g., Alladi et al., 2007; Crutch et al., 2012, 2013). We measured overall dementia severity with the Mini Mental State Exam (MMSE). In order to quantify language performance in these patients, and because general processing efficiency may play a role in performance, we also measured Boston Naming Test (BNT) and category naming fluency (FAS test). Patients with other cognitive deficits such as progressive aphasia or an amnesic syndrome were excluded, and patients with a neurologic condition such as stroke or hydrocephalus, a primary psychiatric disorder or a medical condition causing cognitive difficulty were excluded. We also assessed 15 community-dwelling healthy seniors with comparable age and education who scored 28 or higher (out of 30) on the MMSE and underwent a screening procedure to ensure absence of any condition or medication that could compromise cognitive performance. Clinical, demographic, and neuropsychological information is summarized in Table 1. All subjects participated in an informed consent procedure approved by the University of Pennsylvania Institutional Review Board.

2.2 Materials

We performed an *arithmetic task* and a *numeral-dots transcoding task* to measure CBS/PCA patients' number-related abilities. The tasks were administered in an untimed, "paper-and-pencil" manner.

2.2.1 Arithmetic calculations—In this task, participants were asked to compute 16 simple mathematical problems (8 addition problems and 8 subtraction problems) involving two Arabic numerals (e.g. $2 + 5$; $8 - 3$). The problems were presented in writing blocked by arithmetic calculation, involved pairs of single digits and two digits, and the magnitude of the numbers involved in the calculations was manipulated in order to increase over the course of the trials (range = 2 to 66). This also allowed us to test to what extent previously reported CBS and PCA difficulties in calculation depend on the mathematical algorithm for addition and subtraction, or on difficulties in manipulating precise numbers of different magnitudes.

2.2.2 Numeral-dots transcoding task—For the numeral-dots transcoding task (illustrated in Figure 1), participants were presented with two, equally-sized complementary runs totaling 16 trials. During the first run, subjects matched a dot array to one of four Arabic numeral choices. During the second run, subjects matched an Arabic numeral to one of four dot array choices. Half of the items in each run were presented with randomly distributed dot arrays, and the other half were presented with dot arrays ordered in lines of three or four dots displayed in parallel to each other. The cardinality of the Arabic numerals as well as the number of dots in the arrays ranged between 6 and 9, and the same numerosities was presented in both random and ordered arrays in both runs. Choices were displayed vertically in the center of the page to minimize biases due to spatial neglect, and the correct choice occupied each of the four available locations equally often. The clustered and random arrays were presented in a pseudo-random, counterbalanced order across subjects. Performance in the numeral-dots transcoding task was averaged across the two runs because there was no statistical difference between the two, but we analyzed separately the items with clustered dot arrays and the arrays with randomly distributed dots.

Behavioral performance did not significantly differ between CBS patients and PCA patients [Arithmetic task: $F(1,19) = 0.99$, $p > .7$; Transcoding task: $F(1,19) = 0.82$, $p > .3$ (both statistical tests are corrected for the age of the subjects that shows a significant difference between the two subgroups [$t(17) = 2.2$, $p = .044$)] . Performance was compared across healthy controls and CBS/PCA patients using non-parametric tests due to a ceiling effect in the control group.

2.4 Imaging procedure and analysis

High-resolution volumetric T1-weighted MRI was obtained within 12 months of behavioral testing for 14 CBS/PCA patients (CBS: $n = 7$; PCA: $n = 6$). These patients matched the overall group of patients in age, education and MMSE (all p -values $> .1$). Reasons for exclusion from the MRI study included issues related to health and safety (e.g., metallic implants, shrapnel, claustrophobia), intercurrent medical illness, and lack of interest in participating in an imaging study. MRI volumes were acquired using an MPRAGE sequence

from a SIEMENS 3.0T Trio scanner with an 8-channel head coil and the following acquisition parameters: repetition time=1620 msec; echo time=3.87 msec; slice thickness=1.0 mm; flip angle=15°; matrix=192×256, and in-plane resolution=1.0×1.0 mm. Whole-brain MRI volumes were preprocessed using PipeDream (<https://sourceforge.net/projects/neuropipedream/>) and Advanced Normalization Tools (<http://www.picsl.upenn.edu/ANTS/>) using a state-of-the-art procedure described elsewhere (Avants, Epstein, Grossman, & Gee, 2008; Klein et al., 2010). Briefly, PipeDream deforms each individual dataset into a standard local template space. A diffeomorphic deformation was used for registration that is symmetric to minimize bias toward the reference space for computing the mappings, and topology-preserving to capture the large deformation necessary to aggregate images into a common space. Template-based priors are used to guide GM segmentation and compute GM probability, which reflects a quantitative measure of GM density. Resulting images were warped into MNI space, smoothed using a 5 mm full-width half-maximum Gaussian kernel and downsampled to 2 mm³ resolution.

Permutation-based imaging analyses were performed with threshold-free cluster enhancement (Smith & Nichols, 2009) using the randomise tool in FSL (<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki>). GM density was compared in patients relative to healthy seniors (an independent group of 28 healthy seniors with imaging who matched the patient group for education [$t(23) = -0.11$; $p > 0.9$], age [$t(39) = 0.11$; $p > 0.8$] and gender [$X^2 = .08$, $p > 0.3$]). Analyses were run with 10,000 permutations and restricted to voxels containing GM using an explicit mask generated from the average gray matter probability map of all groups. We report clusters that survived a threshold of $p < 0.0005$ with family-wise error (FWE) correction for multiple comparisons and contained a minimum of 200 adjacent voxels.

To relate behavioral performance to regions of significant GM disease, we used the randomise tool of FSL as described above. An explicit mask restricted the analyses to voxels of GM atrophy in the patients as defined in the group comparison. Permutations were run exhaustively up to a maximum of 10,000 for each analysis. We report clusters surviving a height threshold of $p < 0.05$ (uncorrected) and a minimum of 10 adjacent voxels.

3. Results

3.1 Behavioral results

3.1.1 Arithmetic calculations—Overall, CBS/PCA patients were significantly less accurate than healthy controls in arithmetic calculations [Overall performance: $U(33)=36.5$; $Z = -3.7$; $p < 0.001$]. Deficits were present for both addition [$U(33)=53$; $Z = -3.2$; $p < 0.005$] and subtraction: [$U(32)=42.5$; $Z = -3.4$; $p < 0.001$; see figure 2]. In order to investigate whether patients' poor performance was modulated by a number magnitude effect, we correlated mean accuracy in the calculation task with the magnitude of the numbers involved into the calculation. This revealed a highly significant negative correlation [$r = -.952$, $p < 0.001$]. In other words, CBS/PCA patients were significantly worse in performing simple arithmetic calculations with relatively larger numerosities. In addition, patients' performance on the arithmetic task did not correlate with a measure of their linguistic skills, i.e. the Boston Naming Test [$r = -0.09$, $p > 0.7$].

3.1.2 Numeral-dots transcoding task—As summarized in Figure 3, CBS/PCA patients were more impaired than healthy seniors in their overall numeral-dots transcoding performance [$U(34)=65$; $Z = -3.1$; $p < 0.01$, see Figure 3]. Moreover, CBS/PCA patients' performance significantly differed from controls' performance for clustered trials of dots and trials with random dot spatial configurations [clustered arrays: $U(34)=67.5$; $Z = -3.2$; $p < 0.01$; random arrays: $U(34)=73.5$; $Z = -2.9$; $p < 0.01$]. Most importantly, a comparison between items with clustered arrays and spatially random arrays within the CBS/PCA patient group revealed that participants are significantly less accurate with random arrays compared to clustered arrays [$Z(19) = -2.2$; $p < 0.03$]. By comparison, controls' performance did not differ across arrays [$Z(19) = -1$; $p > 0.3$] (see Figure 3). Patients' performance correlated neither with the Boston Naming Test nor with FAS test [all measures: $p > 0.1$].

3.2 Imaging results

We found similar behavioral findings in the subset of patients with available imaging. Thus, we observed a significant difference between the control group and the imaged subgroup of CBS/PCA patients in the arithmetic tasks [overall performance: $U(28)=16.0$; $Z = -3.9$; $p < 0.001$; addition: $U(28)=28.5$; $Z = -3.4$; $p < 0.002$; subtraction: $U(28)=17.5$; $Z = -3.4$; $p < 0.001$] as well as for the overall score and for the subsets of trials with clustered and random arrays in the numeral-dots transcoding task [Overall score: $U(28)=41$; $Z = -3.1$; $p < 0.01$; ordered arrays: $U(28)=45$; $Z = -3.2$; $p < 0.05$; random arrays: $U(28)=49$; $Z = -2.8$; $p < 0.05$]. Thus, the imaged subgroup of CBS/PCA patients is representative of the entire patient sample.

An analysis of GM atrophy in CBS/PCA patients relative to healthy seniors revealed significant atrophy in bilateral parietal, occipital and frontal cortex, including inferior parietal and dorsolateral prefrontal regions (Figures 4 and 5; Appendix).

3.2.1 Arithmetic calculations—We divided the trials into three levels (small, medium and large) according to the size of the numbers which were used in the calculations, and for each individual patient we conducted a Spearman correlation reflecting performance accuracy on these levels of magnitude. For example, a value close to -1 for a patient reflects that the patient's performance became worse as the magnitude of the numbers became bigger. In contrast to that, a value close to 0 reflects that the patient's accuracy in the task was independent of the magnitude of the numbers involved. We related these values reflecting the magnitude effect to GM atrophy with a regression analysis. This revealed a significant association of the magnitude effect with right superior and inferior parietal cortex (around the intraparietal sulcus; see Table 2 and Figure 4).

3.2.2 Numeral-dots transcoding task—First, we calculated the difference between the mean patient's accuracy with random versus clustered arrays of dots involving the same numerosity (e.g., 6). For example, we calculated the mean accuracy of a patient for random arrays containing 6 dots and we subtracted this value from the mean accuracy of the same patient for clustered arrays containing 6 dots. We repeated the same operation for each of the distinct magnitudes of dots we employed. Then we computed a Spearman correlation for each subject between this score and the target number of dots (for brevity purposes, we refer

to this rho-value as the *clustering-gradient*). In other words, a negative correlation indicates that the participant is getting worse in chunking as the numerosity of the dots increases. We related this clustering-gradient to GM atrophy with a regression analysis. We looked for a negative correlation between the chunking gradient and GM atrophy, which should indicate a relation between GM atrophy and decrease in chunking ability. This revealed significant associations of the clustering-gradient with left inferior parietal cortex and right dorsolateral prefrontal cortex (see Table 3 and Figure 5).

4. Discussion

In the present study we investigated the nature of number processing difficulties in non-aphasic patients with CBS/PCA. Deficits in number knowledge as well as in other forms of manipulation of quantities (e.g., quantifiers in language) have been demonstrated in CBS/PCA patients in previous work (e.g., Halpern et al., 2007; Halpern et al., 2004; Koss et al, 2010; Morgan et al., 2011). We found that non-aphasic patients with CBS/PCA have difficulty with simple calculations, showing greater difficulty on larger numbers than smaller numbers, consistent with a magnitude effect. Histopathologic burden accumulates significantly in parietal cortex in CBS and PCA (Murray et al., 2007; Pantelyat et al., 2011; Renner et al., 2004; Tang-Wai & Graff-Radford, 2004; Victoroff, Ross, Benson, Verity, & Vinters, 1994), and there is agreement that parietal regions play a critical role in number processing (e.g., Danker & Anderson, 2007; Nieder & Dehaene, 2009; Piazza & Dehaene, 2004; Pinel et al., 2004). We related CBS/PCA patients' calculation deficit to parietal atrophy. We also found that these patients benefit from clustered compared to random arrays in a numeral-dots transcoding task. Performance on this task was associated with parietal and frontal atrophy. We discuss below the role of language in number processing, and the nature of number systems from the perspective of adults with focal disease affecting the parietal lobe.

4.1 Approximate vs precise calculation

The results of the *arithmetic task* support the claim that CBS/PCA patients have a specific impairment of the precise number system while the analog magnitude system appears to be relatively spared. These patients were severely impaired in simple mathematical calculations that require a precise number as output. This was characterized by increasingly prominent difficulties as the size of the precise number increased. This is consistent with a number magnitude effect, which has been previously reported to be strongly associated with the precise number system (e.g., Stanescu-Cosson et al., 2000).

Both CBS and PCA are rare neurodegenerative syndromes with overlapping loci of disease in the parietal lobe. There is also clinical evidence of number impairments in both CBS and PCA. Therefore, we considered it appropriate to investigate these patients together in a single group in order increase the power of our analysis. However, further work will be needed to investigate possible differences between groups of the CBS and PCA participants.

In contrast to previous claims, the present data do not support the hypothesis that precise calculations strongly depend upon language-related abilities (e.g., Stanescu-Cosson et al 2000; Dehaene et al 2003). This is because the patients in our cohort do not have language-

related deficits. Moreover, patients' calculation accuracy did not correlate with a common language measure, the BNT. Previous work supported the dissociation between mathematical and linguistic abilities, showing that calculation is preserved in patients with severe aphasia and semantic dementia (e.g., Varley, Klessinger, Romanowski, & Siegal, 2005; Zamarian, Karner, Benke, Donnemiller, & Delazer, 2006; Halpern et al, 2004). In addition to that, a TMS study by Salillas and colleagues (Salillas, Semenza, Basso, Vecchi, & Siegal, 2012) revealed that a temporary disruption of a critical node of the language network, such as the left intraparietal sulcus, does not affect computational efficiency during additions and multiplications.

The laterality of our imaging results also reflects the neuropsychological profile of the patient group since the CBS/PCA patients we selected have spared linguistic abilities and the structural MRI did not find significant atrophy in the left angular gyrus. Additional work will be needed to establish that performance corresponds to Weber's Law reflecting use of an approximate number system in the face of a compromised precise number system, and to investigate to what extent patients with linguistic deficits and more extensive atrophy in the left parietal regions also have limitations in calculation.

4.2 Chunking abilities

In the present study we also investigated the ability of patients with CBS and PCA to take advantage of an alternative approach to their precise number processing difficulties. We focused our attention on *chunking*. We found that CBS/PCA patients are significantly more successful with systematically clustered numerosities than stimuli distributed in a spatially random manner. We do not believe that this pattern of impairment can be explained entirely by the visuospatial nature of the materials since previous work has shown a similar deficit with numerosities tested entirely with Arabic numerals (Koss et al, 2010). Moreover, since both types of arrays rely on perceiving the spatial distribution of stimuli, a spatial deficit presumably would have compromised both types of arrays equally, and we did not observe this.

Consider the basis for the discrepancy we observed between randomly distributed and clustered arrays. The numeral-dots transcoding task requires precise computations that go beyond the limit of the analog number system. One possibility is that an intact parallel individuation number system can at least partially support patients' difficulties by allowing them to enumerate clustered arrays in multiples up to about 4×4 . Thus, CBS/PCA patients should be able to reliably appreciate that 2 clusters of 4 is the equivalent of 8. Clusters involving 5 (e.g. 5 clusters of 5) may be too difficult to appreciate reliably in a precise manner since the magnitude of 5 is beyond the approximate number system. Even though a precise computation of numerosities like 8 and 12 is beyond the limit of the analog magnitude system, the parallel individuation system can extend CBS/PCA patients' number processing as long as the clustering feature of parallel individuation can be implemented and is not overwhelmed by the numerosity of one of the dimensions of the clustered array.

However, the extent to which chunking is a specific feature of a parallel individuation number system is unclear. Chunking may instead represent a general purpose heuristic to optimize efficient information processing that can be applied to any domain of knowledge.

In the present paper, we tested whether CBS/PCA patients can take advantage of a chunking heuristic in order to perform a numeral-dots transcoding task. Chunking, as defined by Mathy and Feldman (2012), can be considered a process that can be recruited whenever our cognitive system can decode regularities in a set of data to help solve a cognitive challenge. Our observations thus are not incompatible with the notion of chunking as a cognitive heuristic that allows CBS/PCA patients to simplify the computational load of a numerosity task. CBS/PCA patients can be easily overwhelmed by tasks involving cardinalities bigger than 3 or 4 (e.g., Halpern et al., 2004) and here we showed that their performance is significantly more accurate when the dot arrays are presented in clusters. This improvement may have been due in part to chunking. It should be kept in mind that CBS/PCA patients did not obviously develop a spontaneous chunking strategy for the randomly distributed dot arrays, even though they were given many examples of clustering. Moreover, there was no correlation between FAS and chunking performance. Additional work is needed to determine the basis for chunking.

Neuroimaging results nevertheless appear to be consistent with the possibility that the improvement of patients' performance with ordered arrays may be due in part to a chunking heuristic rather than preservation of a quantity-specific number system. We found that the *chunking-gradient* is related to GM atrophy in frontal regions including bilateral dIPFC which have previously been associated with increased capacity of working memory (e.g., Botvinick, Braver, Barch, Carter, & Cohen, 2001), and with strategic manipulation of materials in working memory (e.g., Smith et al., 2001). In addition, temporary disruption of dIPFC by Transcranial Magnetic Stimulation (TMS) seems to compromise working memory performance (e.g., Bilek et al., 2013; Mottaghy, Gangitano, Sparing, Krause, & Pascual-Leone, 2002). While these results are consistent with a crucial role for dIPFC in supporting a chunking process that allows individuals to facilitate the representation of information, we cannot rule out the possibility that dIPFC encodes number-specific information or that disease in this anatomic distribution can compromise chunking as a domain-specific process for number-related problems.

5. Conclusion

Taken together, the results of impairments in CBS/PCA patients in the present study provide a fine-grained picture of the specific features of number knowledge in the setting of a compromised precise number system. Overall, those patients were impaired in their performance on simple arithmetic and transcoding tasks. These data support the claim that the precise number system is compromised in non-aphasic patients with CBS/PCA. The pattern of impairment is consistent with a magnitude effect, apparently leaving intact the analog number system. Moreover, we found that these non-aphasic patients are able to capture the structure of a set of objects and to take advantage of this regularity in order to compensate at least in part for their number processing difficulties. This may be due in part to the relative preservation of a chunking heuristic that can take advantage of perceived clusters to support relatively precise numerosity beyond the limitation of the approximate number system. Neuroimaging analyses highlighted the contribution of IPL and dIPFC to CBS/PCA patients' processing of number knowledge.

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Appendix

Main clusters of reduced gray matter density in patients with CBS/PCA relative to healthy seniors.

Neuroanatomic Region	L/R	MNI Coordinates			Peak voxel p value
		x	y	z	
Dorsolateral prefrontal cortex		30	48	30	
extended in the temporal lobe	R	50	–54	20	< .001

Neuroanatomic Region	L/R	MNI Coordinates			Peak voxel p value
		x	y	z	
Medial temporal gyrus extended into the parietal lobe	L	40	8	24	< .001
		-50	-58	14	
		-42	-56	24	
		-48	-60	24	
Dorsolateral prefrontal cortex extended in the inferior frontal gyrus	L	-56	-40	46	< .001
		-34	20	26	
		-38	20	30	
		-46	44	6	
Precentral gyrus extended into the superior prefrontal cortex	L	-36	-10	48	< .001
		-16	22	60	
		-16	46	42	

Note. MNI, Montreal Neurological Institute

Highlights

- CBS/PCA patients have relatively preserved chunking abilities.
- Chunking abilities depends upon the fronto-parietal network.
- Chunking is a cognitive heuristic and not a number-specific ability.
- CBS/PCA patients' deficit in numbers processing is strongly affected by numbers size.
- CBS/PCA patients' deficit in precise calculations appears to be independent from linguistic skills.

Figure 1.

Examples of Numeral-Dots Transcoding Task. Panel A: Example of an item trial with a random spatial configuration of dots. Panel B: Example of an item trial with a clustered spatial configuration of dots.

Figure 2.

Mean ($\pm$ SEM) accuracy of responses provided for addition and subtraction by Healthy Seniors (CNTRL, in gray) significantly differ from patients (CBS/PCA, in white). Please see text for details.

Figure 3.

Mean ($\pm$ SEM) accuracy of responses provided in the trials of Numeral-Dots Transcoding task with clustered arrays (dotted) and in the trials with random arrays (diagonal lines). Healthy Seniors (CNTRL) significantly differ from patients (CBS/PCA) on this task, and the within-group comparison between ordered and random arrays revealed a significant difference only in the patient group.

Figure 4. Regions of gray matter atrophy (colored areas) in patients with CBS/PCA relative to healthy seniors, and regions related to the score reflecting the magnitude effect (red). The red clusters are around the intraparietal sulcus; peaks: 30 –56 50; 32 –48 46.

Figure 5.

Regions of gray matter atrophy in patients with CBS/PCA relative to healthy seniors (colored areas) and regions related to the *chunking gradient* (red). Panel A: the red clusters are in right and left inferior parietal cortex; peaks: 52 -38 48; -62 -32 36. Panel B: the red clusters are in right and left dorsolateral prefrontal cortex; peaks: -46 40 22; 44 40 14.

Table 1

Mean ($\pm$ SEM) demographic and neuropsychological data for patients and control groups.

Demographic/Clinical Measure	Patients (N=19)	Healthy Seniors (N=15)
Age (years)	62 (2.0)	64 (2.0)
Education (years)	14.9 (0.5)	16.2 (0.6)
Gender (female / male)	16 / 8	10 / 6
MMSE score (max = 30) ^{I*}	24 (1.0)	29.3 (0.2)
Boston Naming Test (max = 30) ^I	27.3 (0.4)	27 (3.0)
FAS (total) ^{I*}	28 (4)	43 (2)
Disease duration (years)	2.3 (0.5)	--

Note:

* significant difference between the two groups: $p < .001$;

^I Data for some or the neuropsychological measures were available only for a subgroup of patients due to limited patient availability or technical difficulty: MMSE was administered to 18 out of 19 patients; BNT score was available for 17 out of 19 patients; FAS test was available for 16 out of 19 patients.

Patients and control groups did not significantly differ in age [$t(31) = .42$; $p > .6$], gender [$X^2 = .045$; $p > .8$], and education level [$t(34) = 1.61$; $p > .1$]. The patient groups differed from controls in their MMSE score and FAS [MMSE: $t(31) = 4.07$; $p < .001$; FAS: $t(29) = 3.52$; $p < .001$]. CBS/PCA patients did not differ from controls in BNT [BNT: $t(30) = .30$; $p > .7$].

Table 2
Regions of reduced gray matter density in patients with CBS/PCA that relate to the *number-size effect*.

Neuroanatomic Region (BA)	MINI Coordinates			Peak voxel p value
	X	y	z	
Superior parietal cortex (7)	R 30	-56	50	.007
Inferior parietal cortex (40)	R 32	-48	46	.02
Medial occipital cortex (18)	R 40	-88	8	.03

Note. BA, Brodmann area; MNI, Montreal Neurological Institute

Table 3
Regions of reduced gray matter density in patients with CBS/PCA that relate to the *chunking gradient*.

Neuroanatomic Region (BA)	L/R	MNI Coordinates			Peak voxel p value
		x	y	z	
Dorsolateral prefrontal cortex (46)	L	-46	40	22	.001
Dorsolateral prefrontal cortex (46)	R	44	40	14	.002
Inferior frontal gyrus (44/45)	R	56	14	24	.003
Precentral gyrus (6)	R	52	8	14	.005
Medial prefrontal cortex (10)	L	-24	60	10	.001
Inferior parietal cortex (40)	R	52	-38	48	.009
Inferior parietal cortex (40)	L	-62	-32	36	.01
Superior parietal cortex (7)	R	26	-48	56	.02
Inferior parietal cortex (40)	R	56	-44	36	.02

Note. BA, Brodmann area; MNI, Montreal Neurological Institute