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Research report

Re-assessing acalculia: Distinguishing spatial and purely arithmetical deficits in right-hemisphere damaged patients

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ABSTRACT

Arithmetical deficits in right-hemisphere damaged patients have been traditionally considered secondary to visuo-spatial impairments, although the exact relationship between the two deficits has rarely been assessed. The present study implemented a voxelwise lesion analysis among 30 right-hemisphere damaged patients and a controlled, matched-sample, cross-sectional analysis with 35 cognitively normal controls regressing three composite cognitive measures on standardized numerical measures. The results showed that patients and controls significantly differ in Number comprehension, Transcoding, and Written operations, particularly subtractions and multiplications. The percentage of patients performing below the cutoffs ranged between 27% and 47% across these tasks. *Spatial* errors were associated with extensive lesions in fronto-temporo-parietal regions -which frequently lead to neglect- whereas *pure arithmetical* errors appeared related to more confined lesions in the right angular gyrus and its proximity. Stepwise regression models consistently revealed that *spatial* errors were primarily predicted by composite measures of visuo-spatial attention/neglect and representational abilities. Conversely, specific errors of *arithmetic* nature linked to representational abilities only. Crucially, the proportion of *arithmetical* errors (ranging from 65% to 100% across tasks) was higher than that of *spatial* ones. These findings thus suggest that unilateral right hemisphere lesions can directly affect core *numerical/arithmetical* processes, and that right-hemisphere acalculia is not only ascribable to visuo-spatial deficits as traditionally thought.

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1. Introduction

Is there a calculation impairment typical of lesions to the right hemisphere? If so, to what extent such deficit should be considered secondary to non-numerical/spatial cognitive functions? For many years the notion of "spatial acalculia" was generally applied to any calculation deficit emerging after right-hemisphere brain lesions. However, a detailed description of the right-hemisphere damaged (RHD) patients' errors and its association with specific cognitive functions and brain regions was rarely attempted.

A number of studies investigated different aspects of number and calculation processing by focusing on lateralisation, i.e., whether they related to functions or lesions of one of the two hemispheres, and on the comparison between left brain damaged patients, right brain damaged patients, and a control group of healthy participants (Basso, Burgio, & Caporali, 2000; Dahmen, Hartje, Büssing, & Sturm, 1982; Hécaen, 1962; Hécaen & Angelergues, 1961; Jackson & Warrington, 1986; Rosselli & Ardila, 1989). Most of these studies converged on the fact that patients with lesions to the left hemisphere have greater overall impairment than the right hemisphere lesion group and the controls. Importantly, they also reported that right-hemisphere damaged patients present deficits in specific numerical and calculation domains.

What is the primary cause of these numerical deficits? Since the earliest report from Henschen (1926), most studies seem just to have assumed that acalculia from a right-hemisphere lesion was secondary to spatial disorders or to a generalized reduction of cognitive resources (see, for reviews Hartje, 1987; Micelli & Capasso, 1999). Subsequently, in describing right hemisphere acalculia, some authors -almost accidentally- reported the presence of errors of non-spatial nature (Basso et al., 2000; Grafman, Passafiume, Faglioni, & Boller, 1982). While these authors acknowledged no correspondence between numerical and visuo-spatial deficits, they did not discuss the nature of such errors any further and did not venture in any theoretical interpretation about what the right hemisphere may do in calculation. A study by Ardila and Rosselli (1994) proposed for the first time that numerical deficits in RHD patients were due to proper numerical deficits (e.g., inability to evoke mathematical facts and remember their appropriate uses) however their conclusions were based on anecdotic descriptions: they did not include a control group and no statistical analyses were performed.

Recent studies, using different approaches have obtained similar conclusions, namely that the causal relation between visuo-spatial and numerical deficits might not be so straightforward. Granà and colleagues, for instance, reported the case of a patient who displayed difficulties in retaining the visuo-spatial layout necessary for dealing with multidigit multiplication. In particular, the patient, while knowing what, when, and how to carry out the various steps, did not know where to place the results of the intermediary and final steps of the calculation. Crucially, the pattern of errors could not be adduced to neglect deficits (Granà, Hofer, & Semenza, 2006).

In another study, a group of 24 RHD patients with and without unilateral left-neglect was examined in order to explore whether basic calculation and number processing would be affected by the presence of neglect. The results showed that measures of neglect did not relate with errors in mental calculation tasks, suggesting that visuo-spatial and arithmetical deficits are partially independent (Benavides-Varela et al. 2014). Still, the restricted number of items of the battery used in this study, which was appropriately designed for basic clinical screening, did not allow further correlations with specific error categories, and the relation between numerical impairment and other general-purpose cognitive processes was not explored.

Neglect undoubtedly influences some errors, however. An interesting, effect was shown, for example, by Dormal, Schuller, Nihoul, Pesenti, and Andres (2014) who compared right hemisphere patients with and without neglect on mental addition and subtraction of two-digit numbers. They found that neglect patients performed worse in subtracting large numbers while they were still able to solve large addition problems matched for difficulty and magnitude of the answer. They interpreted such results as demonstrating a causal relationship between the ability to attend the left side of representational space and the solving of large subtraction problems. Such interpretation would be in keeping with the idea (Hubbard, Piazza, Pinel, & Dehaene, 2005) that subtracting or adding a number would shift attention to the left or to the right of a mental space continuum: this shift would help localizing the position of the answer.

The role of the right hemisphere is not just limited to calculation but extends to processing of long numbers. Another study by Benavides-Varela et al. (2016) recently highlighted the role of the right hemisphere for transcoding complex digits, particularly those containing *zeros*. The study showed that processing *zeros* requires specific mechanisms mainly grounded in the right insula and possibly also the right parieto-frontal connections. Lesions to these regions impaired the operation of overwriting *zeros*, which relies in turn on the capacity to merge the information derived from a previous intermediary process of transcoding (see Power & Dal Martello, 1990). Moreover, right hemisphere-damaged patients struggled with the transcoding of *zeros* in complex numbers due to their difficulties in setting-up appropriate empty-slot structures, and in the parsing and mastering of the categorical spatial relations between digits. These functions stand apart from other mechanisms necessary for completing transcoding tasks with other numbers, do not seem to be totally reduplicated in the left hemisphere (otherwise there would not be errors in such patients), and do not entirely depend on generic processing resources. Moreover, the investigation showed that the processes required for dealing with *zeros* do not relate to neglect deficits.

Overall, these studies indicate that the right-hemisphere supports certain numerical abilities independently of other general-purpose mechanisms, which is in line with several studies using transcranial magnetic stimulation (Andres, Pelgrims, Michaux, Olivier, & Pesenti, 2011; Maurer et al., 2015; Salillas, Semenza, Basso, Vecchi, & Siegal, 2012), neuroimaging findings (Price, Mazzocco, & Ansari, 2013; Rosenberg-Lee, Chang, Young, Wu, & Menon, 2011), and intraoperative functional mapping of numerical functions (Della Puppa et al., 2014, 2013; Semenza, Salillas, De Pellegrin, & Della Puppa, in press; Yu et al., 2011). In particular, a meta-