NeuroImage 59 (2012) 3159–3165

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

# Single pulse TMS induced disruption to right and left parietal cortex on addition and multiplication☆

Elena Salillas [a,]*, Carlo Semenza [b,c], Demis Basso [d,e], Tomaso Vecchi [f], Michael Siegal [g,h,]**

[a] Basque Center on Cognition Brain and Language, Donostia, Spain
[b] Department of Neuroscience, University of Padova, Italy
[c] IRCCS Ospedale S Camillo, Lido di Venezia, Italy
[d] Faculty of Education. Free University of Bozen, Italy
[e] CeNCA, Centro di Neuroscienze Cognitive Applicate, Rome, Italy
[f] Department of Psychology, University of Pavia, Italy
[g] Department of Psychology, University of Trieste, Italy
[h] Department of Psychology, University of Sheffield, UK

ARTICLE INFO

*Article history:*
Received 23 June 2011
Revised 15 September 2011
Accepted 31 October 2011
Available online 4 November 2011

*Keywords:*
Mathematics
Intraparietal sulcus
Verbal codes

ABSTRACT

Whether or not mathematical operations are dependent on verbal codes in left hemisphere areas – particularly the left intraparietal sulcus – remains an issue of intense debate. Using single pulse transcranial magnetic stimulation directed at horizontal and ventral regions of the left and right intraparietal sulcus, we examined disruption to reaction times in simple addition and multiplication. Results indicate that these two operations differ in the pattern of lateralization across time for the two areas studied. These show that computational efficiency is not specifically dependent on left hemisphere regions and, in particular, that efficiency in multiplication is dependent on the ventral region of the intraparietal sulcus in the right hemisphere considered to be critical for motion representation and automatization.



## Introduction

In mapping mathematical abilities in the brain, a still very coarse distinction is made, despite recent progress, between the respective functions of the left and of the right hemisphere. Traditionally, since acalculia mostly derives, in several varieties, from left hemisphere lesions, mathematical cognition has been linked in large measure to the left hemisphere and to linguistic functions (Jackson and Warrington, 1986). Number words have been considered to provide a verbal code that facilitates exact calculation (Dehaene et al., 1999; Spelke and Tsivkin, 2001). In this respect, activation in left hemisphere (LH) brain regions has been found in fMRI studies in operations relying on memory retrieval (Dehaene et al., 1999, 2003; Pinel and Dehaene, 2010; Stanescu-Cosson et al., 2000; Zhou et al., 2007). In particular, operations such as addition and multiplication involve activation of the left horizontal portion of the intraparietal sulcus (lHIPS) — an area seen to be critical in the representation of quantities. Although the left angular gyrus (lANG) can also be activated in operations as addition or multiplication, it has been seen to concern linguistic processing more than the specific processing of quantity, and the role of the lANG in calculation appears dependent on the lHIPS (Dehaene et al., 2003, 2004, p. 219). By this account, emphasis has been placed on the predominance of a left hemisphere network for calculation. In sum, although the processing of number magnitude has been proposed to reside bilaterally in HIPS, it has been proposed that the lANG jointly with parietal areas is of prime importance for retrieving results in arithmetic problems. (Dehaene et al., 2003, 2004).

Within this context, our first research question concerns whether *both right and left parietal regions are critical for exact numerical processing*. There are reasons to further explore the contribution of the right hemisphere and non-language-related processing during these tasks. First, not all neuroimaging studies have found more activation in left hemisphere language regions on calculation tasks (Pesenti et al., 2000; Zago et al., 2001). There are investigations that have shown right posterior parietal activations (Dehaene, 2009; Hubbard et al., 2005; Knops et al., 2009a; McCrink et al., 2007) and these activations have been attributed to the need of a visuospatial medium for arithmetic. Second, there is evidence from neuropsychological data

☆ This research was supported by European Union Marie Curie Action Contract "NUMBRA" (504927) and by a MIUR grant 2005 and Italian PRIN 2007 (2007XFM93B_005) to C.S. M.S. is supported by a European Union 6th Framework Marie Curie Chair and a grant from the Fondazione Benefica Kathleen Foreman-Casali. T.V. is supported by the Italian PRIN2006 and in part by Fondazione CARIPLO. D.B. is supported by the fund FIRB RBNE018ET9_003. E.S. is supported by the Marie Curie FP7-PEOPLE-2010-IEF programme.

* Correspondence to: E. Salillas, Basque Center on Cognition, Brain and Language (BCBL), Paseo Mikeletegi 69 2°, 20009 Donostia, Spain.
** Correspondence to: M. Siegal, Department of Psychology, University of Sheffield, Western Bank, Sheffield S10 2TP, UK.
*E-mail addresses:* e.salillas@bcbl.eu (E. Salillas), m.siegal@sheffield.ac.uk (M. Siegal).

1053-8119/$ – see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.neuroimage.2011.10.093

showing dissociations between linguistic and mathematical abilities in developmental and acquired language disorders (Landerl et al., 2004; Varley et al., 2005), and patient studies have documented that acalculia can occur without damage to LH language areas (Granà et al., 2006; Hartje, 1987) or that simple calculation can be preserved in persons with aphasia (Rossor et al., 1995; Warrington, 1982; Whalen et al., 2002).

Lesion studies are indeed important for discovering whether a given anatomical structure is necessary to carry over a given task. However, a structure may contribute to performing a task and yet be not strictly necessary. Results from the use of TMS techniques imply causal relationships, overcoming the limitations of correlation approaches in neuroimaging and the lack of clearly identifiable neural loci in the study of patients. The virtual lesion approach provided by TMS can therefore help to establish the importance of left and right parietal areas in calculation. Use of these techniques should facilitate investigation of the extent to which both left and right IPS are fundamental for addition and/or multiplication.

Therefore the present study used single-pulse TMS to explore the role of bilateral IPS in calculation. Our focus was on two areas: *HIPS* and *VIPS*. Stimulation was directed at the *right and left HIPS* in order to compare whether interference to operations of addition and multiplication would be confined to the lHIPS in a LH network dedicated to calculation, as consistent with a verbally-mediated account (Dehaene et al., 2003, 2004), or to the HIPS bilaterally as would be consistent with an account in which verbal mediation is not specifically necessary and sufficient to calculation (Bloom and Keil, 2001; Campbell and Epp, 2004; Gelman and Butterworth, 2005).

We also examined the effects of TMS on the *ventral portion of the intraparietal sulcus* bilaterally (rVIPS and lVIPS). Recently, fMRI activation accompanying numerical processing in adults in the HIPS has been reported to extend adjacently to the rVIPS region (Cantlon et al., 2006). Moreover, applying TMS to the ventral portion of the rIPS (mean Talairach coordinates, $x=22.0$, $y=68.6$, $z=39.8$) impairs processing of number magnitude (Cohen Kadosh et al., 2007). Although this location differs from the posterior superior parietal lobe studied by Andres et al. (2011) in a TMS study of calculation, it is in the region studied by Salillas et al. (2009) who showed that TMS inhibition of VIPS results in impaired efficiency in both motion perception and number comparison. As Salillas et al. (2009) have suggested, VIPS may be recruited within a network sustaining number comparison to complement HIPS by facilitating use of a mental number line. In order for a person to decide whether a number is higher or lower than a reference number, the focus of attention has to "move" along the mental number line in a way similar to that in which sensory motion is computed. This process may be carried by adjacent motion sensitive areas such as VIPS forming the basis of visuospatial operations implied in arithmetic (Knops et al., 2009b; Salillas et al., 2009). Therefore, concerning our first research question, if right IPS is essential for efficiency in exact calculation, then no differences across hemispheres should be obtained. Only a main effect of site of stimulation or visual field should be found. In this regard, we predicted a joint involvement of ventral and horizontal IPS in calculation as shown through TMS induced disruption to these regions.

In contrasting addition and multiplication, our study was intended to address a second research question concerning *whether multiplication is more verbally-mediated than addition*. We examined the neural basis of computations involving simple addition and multiplication — operations that have both been considered to be especially dependent on verbally-coded facts (Lemer et al., 2003). Nevertheless, simple addition is usually done with the use of procedural strategies whereas multiplication is thought to rely more in memorization (e.g., Dehaene and Cohen, 1997; Roussel et al., 2002). These strategies may lead to differences in the form of final representations (e.g., Siegler and Shipley, 1995; Siegler and Shrager, 1984). Thus as has often been reported (e.g. Cohen et al., 2000; Dehaene and Cohen, 1997; Delazer and Benke, 1997; Lemer et al., 2003; Pesenti et al., 1994; van Harskamp et al., 2002), mental representations of multiplication facts may have greater reliance on verbal memory and hence greater left hemisphere involvement than those for addition facts.

A third research question involved examination of *the temporal pattern of left and right parietal contributions to calculation*. The study of the time course of IPS involvement in calculation can be achieved using single pulse TMS while targeting left or right parietal areas. However, to date, research has been limited to studies of repetitive TMS effects on number processing that have mainly concerned magnitude comparisons (Andres et al., 2005; Cohen Kadosh et al., 2007; Göbel et al., 2001; Knops et al., 2006; Sandrini et al., 2004). Recently, Andres et al. (2011) have used rTMS to address lateralization effects in the HIPS during simple arithmetic. They have reported that rTMS directed at the bilateral HIPS during simple subtraction and multiplication influences calculation, thus questioning the proposal of a left lateralized network for exact arithmetic.

The use of single pulse TMS at different stimulus onset asynchronies (SOAs) in our investigation was aimed to determine whether lateralization is constant across time or whether left and right IPS areas are necessary at different moments (i.e. visuospatial processes are used before a left lateralized verbal recovery of the answer occurs). Stimulation was delivered at one of four SOA intervals (150, 200, 250 and 300 ms). These SOAs were chosen because they have been shown to be critical time points where arithmetic processes are detected in ERP studies. Specifically, similar arithmetic problems elicit ERP components starting as soon as 250 ms after problem presentation, and this effect lasts until 280, 350 or 400 ms (e.g., Galfano et al., 2009; Stanescu-Cosson et al., 2000). Since no study has addressed the time course in lateralization due to restrictions in the imaging techniques used, our investigation of SOA effects was exploratory.

In the two experiments reported here, lateralization was examined in two ways: through the presentation of lateralized stimuli and through the selective stimulation of a hemisphere at a time. In Experiment 1, we compared stimulation in the contralateral visual field to TMS stimulation with the interhemispheric sulcus as the control site. In Experiment 2, stimulation in the contralateral field was compared to ipsilateral stimulation as the control site. These two approaches allowed us to give consistency to the results and a more fine grained timing of processes could be observed in Experiment 2. Lateralized presentation was intended to maximize the projections of the stimuli contralaterally and the involvement of the TMS stimulation to each hemisphere. In Experiment 1, the critical comparison concerned RTs after contralateral stimulation vs. central stimulation. Therefore, maximal effects were expected since disruption was compared against a neutral condition. As in Experiment 2, the critical comparison concerned the visual field that was ipsilateral vs. contralateral to the stimulated hemisphere in tracking how and when ipsilateral stimuli presentation differs with the maximum expected disruption after contralateral presentation. Thus this experiment was expected to yield weaker effects due to inter-hemispheric transfer although the comparison between visual fields entailed a finer investigation of interhemispheric differences.

## Experiment 1

### *Method*

The procedure was approved by the Ethics Committee of the Department of Psychology of the University of Pavia.

### *Participants*

Twelve right-handed undergraduates participated in the study (mean age: 23 yrs. range 21 to 26; 3 males and 9 females; average + 91% laterality index scores as indicated from the Oldfield (1971)). All of them provided informed consent before the experiment.