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Causal role of the posterior parietal cortex for two-digit mental subtraction and addition: A repetitive TMS study

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A R T I C L E I N F O

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A B S T R A C T

Although parietal areas of the left hemisphere are known to be involved in simple mental calculation, the possible role of the homologue areas of the right hemisphere in mental complex calculation remains debated. In the present study, we tested the causal role of the posterior parietal cortex of both hemispheres in two-digit mental addition and subtraction by means of neuronavigated repetitive TMS (rTMS), investigating possible hemispheric asymmetries in specific parietal areas. In particular, we performed two rTMS experiments, which differed only for the target sites stimulated, on independent samples of participants. rTMS was delivered over the horizontal and ventral portions of the intraparietal sulcus (HIPS and VIPS, respectively) of each hemisphere in Experiment 1, and over the angular and supramarginal gyri (ANG and SMG, respectively) of each hemisphere in Experiment 2. First, we found that each cerebral area of the posterior parietal cortex is involved to some degree in the two-digit addition and subtraction. Second, in Experiment 1, we found a stronger pattern of hemispheric asymmetry for the involvement of HIPS in addition compared to subtraction. In particular, results showed a greater involvement of the right HIPS than the left one for addition. Moreover, we found less asymmetry for the VIPS. Taken together, these results suggest that two-digit mental addition is more strongly associated with the use of a spatial mapping compared to subtraction. In support of this view, in Experiment 2, a greater role of left and right ANG was found for addition needed in verbal processing of numbers and in visuospatial attention processes, respectively. We **also** revealed a greater involvement of the bilateral SMG in two-digit mental subtraction, in response to greater working memory load required to solve this latter operation compared to addition.

Introduction

Mental calculation is a fundamental ability involved in a wide range of daily activities. For this reason, understanding its brain underpinnings is a pivotal topic in cognitive science. However, while it is clear that mental calculation is connected to several cognitive processes, information about cerebral areas involved in different calculation processes is still relatively limited. Indeed, despite several attempts to investigate the causal role of brain regions involved in simple mental calculation (e.g., Andres et al., 2011; Della Puppa et al., 2015b; Maurer et al., 2015; Salillas et al., 2012), few studies have addressed this issue on more complex mental calculation (e.g., De Smedt et al., 2009; Grabner et al., 2015). This issue is particularly important because of a crucial difference between simple and complex mental calculation that is not merely quantitative. Simple mental calculation, in fact, is mostly based on rote verbal memory, underpinned by the left angular gyrus (ANG) associated with the verbal processing of numbers (e.g., Dehaene et al., 2003). In contrast, complex mental calculation is solved via procedures requiring a stronger recruitment of quantity systems (e.g., Fehr et al., 2007; Menon et al., 2000) underpinned by the bilateral horizontal portion of the intraparietal sulcus (HIPS) (Dehaene et al., 2003).

Recently, behavioral studies observed that attentional shifts implied by arithmetic operations influence the speed to detect a target presented on the left or right of the screen, specifically when participants solve one-digit subtractions and two-digit additions, respectively (Masson and Pesenti, 2014, 2015). They have also shown the so-called operational momentum effect, a bias in over- and under-estimating the

Abbreviations: ANG, angular gyrus; IPS, intraparietal sulcus; HIPS, horizontal intraparietal sulcus; LH, left hemisphere; MNL, mental number line; RH, right hemisphere; SMG, supramarginal gyrus; VIPS, ventral intraparietal sulcus

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results of addition and subtraction, respectively, especially for two-digit additions (Lindemann and Tira, 2015). The idea is that ancient neural circuits, such as for example, multimodal parietal areas involved in saccadic and attentional control, are "recycled" for arithmetic calculation (Dehaene and Cohen, 2007). This hypothesis received further support from neuropsychological studies. Importantly, patients with left neglect (and right parietal lesions) present deficits in the mental number line (MNL) (e.g., Vuilleumier et al., 2004; Zorzi et al., 2002; see also Benavides-Varela et al., 2014) consisting of a horizontal representation of numerical magnitude in which larger numbers are associated with the right side of the line and smaller numbers with the left side.

First neuroimaging investigations of mathematical functions (Dehaene et al., 1999; Pesenti et al., 2000) indicated a pivotal role of the left hemisphere (LH) in calculation, with little specification about the contribution of the right hemisphere (RH). However, a recent meta-analysis on functional magnetic resonance imaging (fMRI) studies (Arsalidou and Taylor, 2011) revealed a much more complex story. The meta-analysis revealed that addition, subtraction, and multiplication differentially recruited prefrontal and parietal regions in the LH and RH: neural activity was dominant in the LH for addition, mainly bilateral for subtraction, and in the RH for multiplication. In particular, Rosenberg-Lee et al. (2011) showed that multiplication evoked a greater activation of the right posterior intraparietal sulcus (IPS) compared to addition, suggesting that these operations recruit different brain processes, therefore challenging the idea that both would rely on a strategy based on memory retrieval. In addition, the relative recruitment of the right IPS (including HIPS) was related to the processing of order information in the context of mental arithmetic (Knops and Willems, 2014). More importantly, fMRI studies have demonstrated that bilateral frontal and parietal regions are differently engaged during simple and complex calculation operations (Fehr et al., 2007, 2008; Hamid et al., 2011; Menon et al., 2000; Zhang et al., 2005). In particular, the inferior parietal lobule, including the ANG, the supramarginal gyrus (SMG), and the IPS, shows stronger activation in response to increasing calculation difficulty (Vansteensel et al., 2014; Wu et al., 2009). Moreover, an involvement of the right ANG and SMG has been observed in visuospatial attention and working memory in complex calculation (Zago et al., 2001).

However, it should be noted that the results from both neuropsychological and neuroimaging studies cannot definitely clarify the causal role of the LH and RH in mental calculation. On the one hand, most of neuropsychological studies have a limited spatial resolution since cerebral lesions are usually wider compared to the cerebral areas revealed by neuroimaging studies. On the other hand, neuroimaging studies adopt a correlational approach and, thus, they do not provide proof of the causal role of a specific cerebral region in the process.

In order to overcome these drawbacks, transcranial magnetic stimulation (TMS) would be a more appropriate approach, because it can be used to investigate the causal role of specific areas in mental arithmetic with high spatial resolution. TMS studies have shown that specific RH areas are involved in specific simple mental arithmetic operations (for a review see Salillas and Semenza, 2015). For example, it has been shown that the efficiency in performance for simple multiplications not only involves HIPS but also depends on a motion-sensitive area, i.e., the ventral region of the intraparietal sulcus (VIPS) of the RH (Salillas et al., 2009, 2012). Using navigated repetitive TMS (rTMS) for preoperative mapping of calculation function, a more recent study found that one-digit addition-related areas were predominantly localized in the LH, while one-digit subtraction-related ones were localized in the RH (Maurer et al., 2015).

With the same goal, recent studies conducted with direct cortical electrostimulation (DCE) found a role of specific RH areas in simple addition and multiplication (Della Puppa et al., 2013, 2015a, 2015b; Duffau et al., 2002; Roux et al., 2009; Semenza et al., 2016) and subtractions (Yu et al., 2011). Finally, by means of a technique similar to rTMS and DCE (i.e., transcranial direct current stimulation, tDCS) and focusing on the acquisition of mathematical knowledge, Grabner et al. (2015) demonstrated that the left posterior parietal cortex is causally involved in arithmetic learning of two-digit operations.

In the present study, we aimed to test the causal role of specific LH and RH parietal areas in two-digit mental addition and subtraction using rTMS. In particular, unlike Grabner et al. (2015), the present study evaluated not only the left, but also, crucially, the right posterior parietal cortex. Furthermore, rTMS stimulation, which has a higher spatial resolution than tDCS (Priori et al., 2009), allowed us to disentangle the contribution of the specific areas within the posterior parietal cortex of both hemispheres. More importantly, the present study and the Grabner et al. (2015) one investigate different cognitive processes. Indeed, in our case, rTMS stimulation was administered to interfere with the genuine calculation process of complex operations, while in Grabner et al.'s (2015) study, tDCS stimulation was administered to modulate the learning process of complex operations.

We performed two rTMS experiments, which differed only for the target sites stimulated, on independent samples of participants who resolved mentally complex additions and subtractions and provided the result verbally. In Experiment 1, rTMS was delivered over HIPS and VIPS of each hemisphere. After having tested the role of the HIPS and VIPS in the two-digit mental arithmetic, a second experiment was carried out in order to evaluate the causal role of ANG and SMG of each hemisphere. We predict a bilateral contribution of the posterior parietal cortex, with some specialization. Consistently with the idea that two-digit additions determine attentional shift along the MNL compared to two-digit subtraction (Masson and Pesenti, 2014; 2015; Lindemann and Tira, 2015), we expect to find a greater rightward asymmetry for the involvement of HIPS, especially during complex additions, due to the fact that the right HIPS is involved not only in the quantity system (e.g., Fehr et al., 2007; Menon et al., 2000), but also in processing the order information along the MNL (Knops and Willems, 2014). We also expect to find the involvement of VIPS, especially during complex additions, as this area underpins the use of the MNL (Salillas et al., 2009, 2012). On the contrary, finding particular functional asymmetries for the involvement of ANG and SMG in both operations would not be expected, given the contribution of these two areas to more general cognitive processes involved in the calculation (Dehaene et al., 2003; Zago and Tzourio-Mazoyer, 2002). However, given the importance of left and right ANG in verbal processing and visuospatial attention, respectively, and the fact that addition is a more automatic operation than subtraction, we expect to find the involvement of ANG especially for additions. Opposite hypotheses can be made for the lateralization of ANG involvement in solving complex operations: leftward and rightward asymmetries for the involvement of ANG in solving complex operations would indicate the importance of verbal processing and visuospatial attention mediated by this area, respectively. Moreover, a greater involvement of SMG might be predicted for subtractions, given the higher cognitive demands posed by solving complex subtractions compared to additions.

Experiment 1

Method

Participants

Ten native Italian participants (three males; mean age=25.27 years, *SD*=4.79 years) took part in this study. The sample size was chosen based on an a-priori power analysis (G*Power 3 software; Faul et al., 2009) for *F* tests (see Ambrosini et al., 2013; Montefinese et al., 2015a, 2015b). This analysis revealed that our sample size was large enough to detect a significant (α=.05) interaction corresponding to an effect size of ≈.1 (η_p^2) with a statistical power (1− β) of .80. Participants had normal or corrected-to-normal vision and reported no history of neuropsychiatric illness or epilepsy, and had no contraindication to