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Research report

# Cortical control of inhibition of return: Causal evidence for task-dependent modulations by dorsal and ventral parietal regions

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ABSTRACT

Inhibition of return (IOR) reflects a bias to preferentially attend to non-previously attended or inspected spatial locations. IOR is paramount to efficiently explore our environment, by avoiding repeated scanning of already visited locations. Patients with left visual neglect after right parietal damage or fronto-parietal disconnection demonstrated impaired manual, but not saccadic, IOR for right-sided targets (Bourgeois et al., 2012). Here we aimed at investigating in healthy participants the causal role of distinct cortical sites within the right hemisphere in manual and saccadic IOR, by evaluating the offline effects of repetitive Transcranial Magnetic Stimulation (rTMS) on the right intra-parietal sulcus (IPS) and the right temporo-parietal junction (TPJ). Our results show that rTMS over both sites lastingly interfered with manual but not saccadic IOR for right-sided targets. This behavioral pattern closely mimicked the performance of neglect patients evaluated with the same paradigm. In contrast, for left-sided targets, rTMS over the right IPS impaired both manual and saccadic IOR, while rTMS over the right TPJ produced no modulation in either task. We concluded that distinct parietal nodes of the dorsal and ventral spatial attention networks of the right hemisphere make different contributions to exogenous orienting processes implicated in IOR, and that such effects are hemifield- and task-dependent.



## 1. Introduction

Our visual system is constantly overloaded with information from the environment. Hence, when several events compete for limited perceptual resources, selective attention mechanisms are necessary to efficiently devote processing to relevant objects and respond to them appropriately. Activity within fronto-parietal orienting systems allows us to drive

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spatial attention to an object either voluntarily (endogenously) or involuntarily (exogenously) (Chica et al., 2011, 2013; Corbetta and Shulman, 2002; Indovina and Macaluso, 2007; Nobre et al., 1997; Perry and Zeki, 2000; Rosen et al., 1999). The sudden appearance of a peripheral stimulus often triggers an exogenous attentional capture, which facilitates the early processing of a subsequent target, increasing accuracy and reducing response times (RTs) of targets presented at the attended or inspected location. However, after 100–400 msec, depending on the task at hand (Chica et al., 2006; Lupiáñez et al., 1997), responses to previously attended or inspected locations are slower and/or less accurate, as compared to responses to non-previously attended or inspected locations (Berlucchi, 2006; Klein, 2000; Lupiáñez et al., 2006; Posner and Cohen, 1984; Posner et al., 1985). This phenomenon is known as inhibition of return (IOR); it is generated under both overt and covert orienting, that is when gaze moves to a peripheral stimulus (saccadic IOR), or has to remain on central fixation while participants respond manually (manual IOR) (Posner et al., 1985).

Psychophysical observations from a single brain-damaged patient (Sapir et al., 1999), neuroimaging data obtained in intact humans (Anderson and Rees, 2011), and neurophysiological evidence in monkeys (Dorris et al., 2002), indicate that the superior colliculus (SC), a structure of the midbrain tectum involved in sensory-guided eye and upper trunk movements, critically contributes to IOR. The SC contribution to IOR could be developed in concert with up-stream cortical structures such as the posterior parietal cortex (Dorris et al., 2002). Consistent with this notion, event-related Transcranial Magnetic Stimulation (TMS) over areas of the right posterior parietal cortex has proven able to disrupt manual IOR (Chica et al., 2011), and IOR spatial remapping (Van Koningsbruggen et al., 2010).

Also consistent with the hypothesized importance of right posterior parietal cortical sites in IOR, patients with right hemisphere damage and signs of left visual neglect demonstrated facilitation, instead of IOR, for the detection of consecutive right-sided targets using manual responses (Bartolomeo et al., 1999; Bourgeois et al., 2012; see also Vivas et al., 2003, 2006). In contrast, patients with right hemisphere damage but no signs of visuo-spatial neglect seem to display normal manual IOR for stimuli presented in both the right and the left hemi-spaces (Bartolomeo et al., 1999).

We have recently demonstrated that unlike manual IOR, saccadic IOR for right-sided targets was preserved in the same group of neglect patients (Bourgeois et al., 2012) (see Table 1). Moreover, in this study, disruption of manual IOR was associated with cortical lesions involving areas of the right postero-inferior parietal cortex or their white matter connections with prefrontal regions. Unfortunately, the extension of the brain lesions made it difficult to establish whether right parietal structures pertaining to the dorsal attentional network, such as the intra-parietal sulcus (IPS), or to the ventral attentional network, such as the temporo-parietal junction (TPJ) (Corbetta and Shulman, 2002), or both, could be causally implicated in the modulation of IOR, and whether such modulation would also be present in the intact human brain.

To address these issues, we applied inhibitory patterns of focal repetitive TMS (rTMS) on these two areas of the right parietal cortex (right IPS and right TPJ) to induce transient lasting interference of local and connectivity-mediated brain activity, which we hypothesized would mimic the behavioral effects observed in our population of neglect patients (Valero-Cabré et al., 2011; Wagner et al., 2007). To establish causality, we then gauged the impact that such disruption on either cortical site would exert on manual and saccadic IOR for ipsilateral (right-sided) and contralateral (left-sided) visual targets.

## 2. Methods

### 2.1. *Participants*

Twenty-two participants (12 women, all right-handed, mean age 25 years, range 18–36 years) with normal or corrected-to-normal vision and no history of neurological or psychiatric disorders participated in this study. A control group of sixteen age- and sex-matched participants (8 women, all right-handed, mean age 22 years, range 19–30 years, $t > 1$ for mean age and sex comparisons) was also included. This study was reviewed by the INSERM ethical committee and received the approval of an Institutional Review Board (CPP *Ile de France* 1). Written informed consent was obtained from each participant. In addition, participants filled in a safety-screening questionnaire to rule out risk factors for magnetic resonance imaging (MRI) and TMS interventions. Before the experiment, all participants underwent structural high-definition MRI, which was then 3D-reconstructed and served to navigate the position of the TMS coil in native brain space.

**Table 1 – Summary table indicating the presence of an IOR effect or a facilitatory effect, in healthy participants, and right brain-damaged patients with and without neglect, for left and right-sided targets, under manual or saccadic responses (Bartolomeo et al., 1999; Bourgeois et al., 2012).**

| | Manual | | Saccadic | |
|---|---|---|---|---|
| | Left targets | Right targets | Left targets | Right targets |
| Healthy participants | IOR | IOR | IOR | IOR |
| RBD patients without neglect | IOR | IOR | IOR | IOR |
| RBD patients with neglect | IOR | Facilitation | No IOR[a] | IOR |

a Bourgeois et al.'s (2012) study did not find a significant IOR effect for left-sided targets under saccadic responses in patients with left visual neglect, although no strong conclusions were extracted at this point, because the authors were not confident on this newly observed result, which might have been explained by the increased RT variability often observed in neglect patients' performance for left-sided targets.