Brain and Cognition 98 (2015) 27–34

Contents lists available at ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c

# The time course for visual extinction after a 'virtual' lesion of right posterior parietal cortex

Michael Vesia [a,b], Matthias Niemeier [c,*], Sandra E. Black [a], W. Richard Staines [a,b]

[a] Heart and Stroke Foundation Centre for Stroke Recovery, Sunnybrook Health Sciences Centre, Toronto, ON, Canada
[b] Department of Kinesiology and Faculty of Applied Health Sciences, University of Waterloo, Waterloo, ON, Canada
[c] Department of Psychology, University of Toronto Scarborough, Toronto, ON, Canada

ARTICLE INFO

*Article history:*
Accepted 19 May 2015
Available online 5 June 2015

*Keywords:*
Posterior parietal cortex
Theta burst stimulation
TMS
Visuospatial attention

ABSTRACT

Our understanding of the attentional networks in the human brain largely relies on neuropsychological studies in patients with lesions to the posterior parietal cortex (PPC), particularly in the right hemisphere, that may cause severe disruptions of attentional functions. However, lesion studies only capture a point in time when the dysfunctions caused by the damage have triggered a chain of adaptive responses in the brain. To disentangle deficits and ensuing cortical plasticity, here we examined the time course for one's ability to detect objects in the visual periphery after an inhibitory continuous theta-burst stimulation (cTBS) protocol to the left or right PPC. Our results showed that cTBS of right PPC caused participants to be less sensitive to objects appearing on the left side as well as to objects appearing on both sides at the same time, consistent with an overall shift of attention to the right side of space. In addition, we found that participants missed more objects during bilateral presentations similar to patients with visual extinction. Critically, extinction evolved over time; that is, visual extinction for ipsilateral objects improved after 10 min whereas contralateral extinction peaked around 15–25 min after cTBS. Our findings suggest that lesions to the PPC impair competition between the two visual hemifields, resulting in contralateral extinction as a secondary response, arguably due to ensuing disruptions in interhemispheric balance.



## 1. Introduction

Cognitive neuropsychology is an important source of knowledge about the mechanisms of the human brain, relating functional deficits in patients to acquired lesions. An influential view is to assume that behavioral impairment and the site of damage directly relate to each other. By corollary, lesions in a particular region can affect the functions associated with that region, but maintain other functions, subserved by unaffected regions, unchanged (Caramazza, 1984). This assumption is difficult to defend given what is now known about the complex interplay between injury-related deficits and widespread, compensatory brain plasticity evolving after an insult (Pascual-Leone, Amedi, Fregni, & Merabet, 2005).

Extensively studied are lesions to the right posterior parietal cortex (PPC) that can cause severe attentional deficits (Driver & Mattingley, 1998; Leibovitch et al., 1998; Milner & Mcintosh, 2005; Mort et al., 2003; Vallar, 1998; but also see Karnath, Ferber, & Himmelbach, 2001; Karnath, Fruhmann Berger, Kuker, & Rorden, 2004; Karnath, Himmelbach, & Küker, 2003). Importantly, these deficits have been shown to reflect disruptions in activity throughout the parietofrontal networks for attention beyond the lesion sites themselves (Corbetta, Kincade, Lewis, Snyder, & Sapir, 2005; Corbetta & Shulman, 2011; He, Shulman, Snyder, & Corbetta, 2007), including imbalanced competition between hemispheres and suppression of the lesioned side (Hilgetag, Théoret, & Pascual-Leone, 2001; Kinsbourne, 1977; Koch et al., 2008).

Important cues to disentangle the blend of deficits and secondary effects could arise from studies that trace how dysfunctions evolve at different rates immediately after a lesion. However, systematic patient studies can rarely begin earlier than days after an insult and seldom test behavioral changes at multiple points in time after the insult. To examine the development of attentional deficits immediately after an insult, here we produced 'virtual' lesions in healthy participants using transcranial magnetic stimulation (TMS). TMS provides a unique opportunity to causally

* Corresponding author at: Department of Psychology, University of Toronto Scarborough, 1265 Military Trial, Toronto, ON M1C 1A4, Canada. Fax: +1 (416) 287 7642.
*E-mail address:* niemeier@utsc.utoronto.ca (M. Niemeier).

http://dx.doi.org/10.1016/j.bandc.2015.05.003
0278-2626/

examine the neural mechanisms of selective spatial attention in the healthy brain (Chambers & Heinen, 2010; Chambers & Mattingley, 2005) in an experimentally controlled manner, following one of two general approaches. One is an online approach that delivers single-pulses or a short train of stimulations (repetitive TMS or rTMS) to perturb activity in a brain region during task performance. This approach is thought to interfere with function by silencing neurons and adding neural noise to ongoing information processing and can produce results that are highly time- and task-dependent (Siebner, Hartwigsen, Kassuba, & Rothwell, 2009). However, an alternative, offline approach mimics brain lesions more closely, possibly producing short-term plastic changes in synaptic organization (Chen & Udupa, 2009; Ziemann et al., 2008). It applies rTMS for several seconds or minutes to modulate cortical excitability beyond the duration of the applied stimulation and then tests the resulting transient effects on task performance (Bolognini & Ro, 2010).

Both online and offline TMS approaches have implicated the PPC in spatial attention, consistent with patient studies. Examples include TMS-induced attentional biases in line bisection judgments and visual search difficulties similar to the pathological rightward biases and exploratory deficits found in patients with spatial neglect (Ashbridge, Walsh, & Cowey, 1997; Bjoertomt, Cowey, & Walsh, 2002; Ellison, Schindler, Pattison, & Milner, 2004; Fierro, Brighina, Piazza, Oliveri, & Bisiach, 2001; Kim et al., 2005; Muggleton et al., 2006). Another example is a TMS-induced impairment in the detection of visual objects appearing contralateral to the stimulation site during bilateral stimulus presentation, similar to the contralesional visual extinction often observed in patients with visual neglect (Bien, Goebel, & Sack, 2012; Dambeck et al., 2006; Hilgetag et al., 2001; Jin & Hilgetag, 2008; Meister et al., 2006; Pascual-Leone et al., 1994).

Online TMS approaches as well as most offline protocols, are limited in the duration of induced effects or require extended stimulation times. However, one exception is a recently introduced offline protocol, called continuous theta-burst stimulation (cTBS), that produces a consistent, long-lasting, and powerful depression (LTD)-like effect in cortical activity (Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005; Huang & Sommer, 2009). From a methodological perspective, cTBS has the advantage of yielding longer inhibitory neural effects with much shorter conditioning time than other offline protocols (Huang & Sommer, 2009; Nyffeler et al., 2006). Previous work in healthy humans has reported that cTBS over the right PPC causes visual exploration behavior to shift to the right side (Nyffeler et al., 2008), similar to what is observed in right-brain damaged patients with spatial neglect (i.e., Karnath, Niemeier, & Dichgans, 1998; Niemeier & Karnath, 2002). Additionally, 'neglect-like' deficits could be corrected with subsequent stimulation of the left PPC (Cazzoli, Wurtz, Muri, Hess, & Nyffeler, 2009), and similar to this, in patients with right-brain damage and neglect cTBS to the left unaffected hemisphere has shown promising, long-lasting therapeutic potential (Cazzoli et al., 2012; Koch et al., 2012; Müri et al., 2013; Nyffeler, Cazzoli, Hess, & Muri, 2009). However, to our knowledge no study to date has tested in detail how TMS-induced deficits of attention evolve over time (c.f., Thut, Nietzel, & Pascual-Leone, 2005, tested three 10 min blocks using 1 Hz rTMS train for 25 min, but found no extinction).

Here our aim was to use cTBS to produce transient 'virtual' lesions of the PPC in healthy participants, by suppressing cortical activity for about an hour, to examine the time course of this region's contribution to spatial attention (i.e., trace chronometry of participants' ability to detect visual objects presented in the left, right or both visual fields at specific time points over a period of an hour). We hypothesized that cTBS, particularly to the right PPC, would induce visual extinction-like deficits, varying as a function of time.

## 2. Materials and methods

### 2.1. Subjects

Eleven right-handed (Oldfield, 1971) volunteers (5 females; 19–45 years old) with normal or corrected to normal vision participated in the study. All subjects were screened for adverse reactions to TMS (Keel, Smith, & Wassermann, 2001) and gave informed consent before participation. Seven individuals were tested on both parietal TMS sites. All experimental procedures were approved by the Office of Research Ethics at the University of Waterloo and conformed to the Declaration of Helsinki.

### 2.2. Theta-burst stimulation

Magnetic stimulation was delivered using a 90-mm outer diameter figure-of-eight coil with a MagPro stimulator (MCF-B65; Medtronic, Minneapolis, Minnesota, USA). First, we defined the hand motor area (motor hotspot) of each hemisphere as the point where stimulation evoked the largest motor evoked potential in the contralateral first dorsal interosseous (FDI) muscle. Surface electromyographic (EMG) was recorded from FDI muscle using 9-mm diameter Ag–AgCl electrodes. EMG recordings were amplified (2000×), band-pass filtered (DC – 200 Hz), digitized with a sample frequency of 1 kHz, using customized LabVIEW software (National Instruments; Austin, TX, USA). Next, we determined the active motor threshold (AMT) at the motor hotspot for each hemisphere. AMT was defined as the lowest intensity required to elicit a motor-evoked potential of 200 μV or greater in five out of ten trials from the contralateral FDI while the participants maintained about 10% of their maximum voluntary contraction using visual feedback. We then adjusted the intensity of the experimental stimulation to 80% of the individual AMT for each participant and hemisphere. The average AMT was 39% (SD = 5.36) of maximum stimulator output for left and 35% (SD = 5.15) for right hemisphere (no significant difference was found between hemispheres, $t(16) = 1.57$, $p = 0.14$). Finally, we applied continuous theta burst stimulation (cTBS; 3-pulse burst at 50 Hz repeated every 200 ms) over either left or right posterior parietal cortex (600 pulses) (Huang et al., 2005). Parietal targets were defined according to P3 (left PPC) and P4 (right PPC) electrode positions on the 10–20 electroencephalogram (EEG) coordinate system (Herwig, Satrapi, & Schönfeldt-Lecuona, 2004; Okamoto et al., 2004) using commercially available 10–20 EEG stretch caps for 20 channels (Electro-Cap International) in each participant. These electrode positions have been reported previously to include a site situated over the inferior parietal lobule close to a posterior part of the adjoining intraparietal sulcus (Herwig et al., 2004; Okamoto et al., 2004; Vesia, Monteon, Sergio, & Crawford, 2006; Vesia, Prime, Yan, Sergio, & Crawford, 2010; Vesia, Yan, Henriques, Sergio, & Crawford, 2008) and validated in a participant using BrainSight *Neuronavigation* (Rogue Research, Canada; *see* Fig. 1). For parietal stimulation, the center of the coil was positioned tangentially to the skull with the handle pointing downward and slightly posteriorly.

### 2.3. Procedure and apparatus

Participants performed a visual stimulus detection task used previously elsewhere (Hilgetag et al., 2001) and were randomly assigned to one of two stimulation groups: (1) left parietal cTBS ($n = 9$) or (2) right parietal cTBS ($n = 9$). Two separate experimental sessions were performed for each parietal stimulation condition. The order of the sessions was randomized and separated by a minimum of two weeks. For each experimental session, we obtained