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The role of the right frontal eye field in overt visual attention deployment as assessed by free visual exploration

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A B S T R A C T

The frontal eye field (FEF) is known to be involved in saccade generation and visual attention control. Studies applying covert attentional orienting paradigms have shown that the right FEF is involved in attentional shifts to both the left and the right hemifield. In the current study, we aimed at examining the effects of inhibitory continuous theta burst (cTBS) transcranial magnetic stimulation over the right FEF on overt attentional orienting, as measured by a free visual exploration paradigm.

In forty-two healthy subjects, free visual exploration of naturalistic pictures was tested in three conditions: (1) after cTBS over the right FEF; (2) after cTBS over a control site (vertex); and, (3) without any stimulation. The results showed that cTBS over the right FEF–but not cTBS over the vertex–triggered significant changes in the spatial distribution of the cumulative fixation duration. Compared to the group without stimulation and the group with cTBS over the vertex, cTBS over the right FEF decreased cumulative fixation duration in the left and in the right peripheral regions, and increased cumulative fixation duration in the central region.

The present study supports the view that the right FEF is involved in the bilateral control of not only covert, but also of overt, peripheral visual attention.

1. Introduction

The visual exploration of our environment by means of eye movements is an omnipresent behaviour during the activities of our everyday life (e.g., Land, 2006). Our visual processing system includes a complex neural network that allows to displace the fovea (the retinal region with highest receptor density and thus best resolution) and align it with visual targets. There is consensus that–at least when the eyes are free to move–eye movements and visual attention move together across the visual space (e.g., Hunt and Kingstone, 2003), a phenomenon often referred to as overt attentional orienting.

Situations requiring spatial shifts of visual attention have been shown to engage a fronto-parietal cortical network in both hemispheres. Key nodes of this network are the frontal eye field (FEF) and areas of the posterior parietal cortex (PPC; in the superior parietal lobule and around the intraparietal sulcus) (e.g., Corbetta and Shulman, 2002). These areas strongly overlap with the cortical representation of oculomotor processes (e.g., Ignashchenkova et al., 2004; Nobre et al., 2000; Corbetta et al., 1998).

The spatial distribution of cumulative fixation duration during visual exploration has thus often been used as a reliable indicator of the allocation of visual attention in space, both in healthy individuals and in patients with attentional disorders. For instance, the impairment in directing visual attention towards the contralesional side of space observed in patients suffering from hemispatial neglect is closely reflected in a significant ipsilesional bias in the spatial distribution of visual fixations during visual exploration (e.g., Müri et al., 2009; Malhotra et al., 2006; Pflugshaupt et al., 2004; Sprenger et al., 2002; Karnath et al., 1998).

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Transcranial magnetic stimulation (TMS) is a non-invasive method that is able to temporarily interfere with the activity of a given cortical region, thereby allowing to establish causal relationships between the affected cortical region and its contribution to behaviour (e.g., Pascual-Leone et al., 2000). Recent developments in the repetitive TMS (rTMS) stimulation protocols, such as continuous theta burst stimulation (cTBS; e.g., Nyffeler et al., 2006; Huang et al., 2005), led to short stimulation times and long-lasting behavioural effects, allowing offline testing (i.e., after stimulation application).

Several studies in the visual attention domain have been conducted applying TMS over parietal and frontal areas in healthy participants. TMS applied over the right PPC usually led to a neglect-like behavioural performance (e.g., Cazzoli et al., 2009a,b; Nyffeler et al., 2008; Dambeck et al., 2006; Ellison et al., 2004; Bjoertomt et al., 2002; Müri et al., 2002; Hilgetag et al., 2001; Fierro et al., 2000; Pascual-Leone et al., 1994). In particular, it was shown that the application of cTBS over the right PPC could induce offline a neglect-like rightward shift in the spatial distribution of visual fixations during free visual exploration for 30 min after stimulation (Cazzoli et al., 2009b; Nyffeler et al., 2008).

The role of the FEF in visual exploration has been less intensively investigated with TMS. Recent studies applying brain stimulation (e.g., Lane et al., 2013; Ellison et al., 2014) investigated the role of the FEF in visual search tasks. However, the influence of the modulation of the FEF activity on eye movements during these tasks was not assessed. In particular, to the best of our knowledge, no previous study has assessed whether and how TMS over the right FEF influences the spatial deployment of visual overt attention (i.e., by means of eye movements) in free visual exploration. This question is relevant for several reasons. First, evidence coming from patient studies suggests that–although hemispatial neglect can result from both parietal and frontal lesions (e.g., Husain and Kennard, 1996; Heilman and Valensetin, 1972)–the resulting patterns of deficits in visual exploration may be different depending on lesion location (Heide and Kömpf, 1998). Second, studies investigating the effects of TMS over the FEF on attentional orienting mostly applied covert attentional shifting paradigms (i.e., where attention has to be displaced without eye movements, by maintaining central fixation; e.g., Ronconi et al., 2014; Duecker et al., 2013; Grosbras and Paus, 2002; Smith et al., 2005; O'Shea et al., 2004; Muggleton et al., 2003) or saccadic paradigms (i.e., where saccades have to be produced towards given target locations or opposite to target locations; e.g., Walker et al., 2009; Jaun-Frutiger et al., 2013), rather than using overt attentional shifting with eye movements and with no pre-defined target locations as in free visual exploration. Third, the role of the FEF seems to be context-dependent, i.e., different stimuli (e.g., different paradigms) may elicit different behavioural results in conjunction with TMS application (see for an overview Vernet et al., 2014). Fourth, unlike the lateralized, contralateral effects after right PPC stimulation, previous research suggests that the application of TMS over the right FEF has bilateral effects, at least on the above-mentioned covert attentional shifting or saccadic paradigms (e.g., Duecker et al., 2013; Walker et al., 2009; Grosbras and Paus, 2002; see for an overview Vernet et al., 2014). Moreover, it has been shown that TMS over the right FEF can modulate visual perception differentially in the central an the peripheral visual field, in terms of behavioural performance and BOLD activity in retinotopic visual cortical areas (Ruff et al., 2006).

The aim of the present study was thus to assess the role of the right FEF on the overt spatial deployment of visual attention as measured by visual exploration. We applied cTBS in a causal, interference approach. Healthy participants performed a free visual exploration task of naturalistic pictures, and their eye movements were thereby measured. The spatial distribution of visual fixations, as well as several basic parameters pertaining to saccades and visual fixations, were assessed as a function of cTBS applied over the right FEF and, in turn, against cTBS applied over a control site (vertex) and no stimulation. We hypothesized that–analogously to the results obtained with covert attentional shifting paradigms–cTBS over the right FEF would have bilateral effects on overt visual attention deployment as assessed by free visual exploration. Moreover, we aimed at testing whether overt visual attention deployment after cTBS over the FEF would be differentially affected centrally and peripherally, analogously to the results obtained with visual perceptual paradigms.

2. Materials and methods

2.1. Participants

Forty-two healthy subjects participated in the study. The participants were assigned to three groups: (1) FEF stimulation group: Sixteen participants (7 men, 3 left-handed), with a mean age of 31 years (SD: 6 years, range: 25–48 years); (2) Vertex stimulation group: Ten participants (8 men, 4 left-handed), with a mean age of 31 years (SD: 7 years, range: 23–47 years); (3) Control group without stimulation: Sixteen participants (7 males, 2 left-handed), with a mean age of 31 years (SD 6 years, range: 25–49 years). All participants had normal or corrected-to-normal vision.

The study was approved by the Ethical Committee of the State of Bern and was consistent with the latest Declaration of Helsinki. All subjects gave written informed consent prior to participation.

2.2. Visual stimuli and procedure

Forty-two naturalistic colour photographs of everyday scenes were displayed in a dimly lit room on a cathode ray tube computer display (Samsung SyncMaster 959NF), with 24 bit colour depth and a refresh rate of 85 Hz. Images were presented with a resolution of 800×600 pixels and in full-screen size (36×27 cm), resulting in a viewing angle of $29° \times 22°$. Two examples of images are presented in Fig. 1.

A central fixation point was presented for 1.5 s, followed by the image for 5.5 s. Subjects were instructed to fixate the central fixation point between image presentations and to freely explore the images. The 42 images were shown twice in random order.

For the two groups undergoing stimulation (over the FEF or the vertex), cTBS was applied over the respective location prior to the beginning of the free visual exploration paradigm, in an offline approach. The whole experiment lasted about 30 min.

2.3. Transcranial magnetic stimulation procedure

The region of stimulation was either the right frontal eye field (FEF stimulation group) or the vertex (vertex stimulation group). Repetitive, biphasic magnetic pulses were generated by a TMS stimulator (MagPro, Medtronic Functional Diagnostics, Skovlunde, Denmark).

For the stimulation of the FEF, a figure-eight-coil with an outer radius of 50 mm (Magnetic Coil Transducer MC-B70, MagVenture, Farum, Denmark) was used. The FEF was localized according to previously described procedures (Ro et al., 1999; Müri et al., 1991). In brief, the individual resting motor threshold was first determined, and was defined as the minimum stimulator output of TMS single pulses that was able to consistently elicit twitches in the small hand muscles of the left relaxed hand. The coil was then moved anteriorly to the hand area, 2 cm on average. The handle of the coil pointed backwards, in a 45° angle with respect to the sagittal plane.