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Synchronization of fronto-parietal beta and theta networks as a signature of visual awareness in neglect

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ABSTRACT

In the neglect syndrome, the perceptual deficit for contra-lesional hemi-space is increasingly viewed as a dysfunction of fronto-parietal cortical networks, the disruption of which has been described in neuroanatomical and hemodynamic studies. Here we exploit the superior temporal resolution of electroencephalography (EEG) to study dynamic transient connectivity of fronto-parietal circuits at early stages of visual perception in neglect. As reflected by inter-regional phase synchronization in a full-field attention task, two functionally distinct fronto-parietal networks, in beta (15–25 Hz) and theta (4–8 Hz) frequency bands, were related to stimulus discrimination within the first 200 ms of visual processing. Neglect pathology was specifically associated with significant suppressions of both beta and theta networks engaging right parietal regions. These connectivity abnormalities occurred in a pattern that was distinctly different from what was observed in right-hemisphere lesion patients without neglect. Also, both beta and theta abnormalities contributed additively to visual awareness decrease, quantified in the Behavioural Inattention Test. These results provide evidence for the impairment of fast dynamic fronto-parietal interactions during early stages of visual processing in neglect pathology. Also, they reveal that different modes of fronto-parietal dysfunction contribute independently to deficits in visual awareness at the behavioural level.

1. Introduction

Neglect is a common syndrome following right hemisphere damage. It is characterized by both a rightward bias in spatial sensory-motor processing and non-lateralized deficits of arousal, attentional capacity, and working memory (Husain and Rorden, 2003; Hillis, 2006; Bartolomeo et al., 2012). Traditionally, neglect has beefn explained in terms of localized damage of specific right-hemisphere brain structures including the inferior parietal lobe (Vallar and Perani, 1986; Mort et al., 2003), superior temporal gyrus (Karnath et al., 2004), and inferior frontal cortex (Husain and Kennard, 1996). Diverse as these sites are, lesions share core symptoms of neglect, consistent with a disconnection syndrome or failure of individual constituent nodes in frontal or parietal lobes to integrate a network-level function (Doricchi and Tomaiuolo, 2003).

Several lines of research provide support to the disconnection hypothesis. First, neuroanatomical studies of the architecture of fronto-parietal networks have shown that the dorsolateral prefrontal cortex and the posterior parietal cortex are directly and extensively interconnected in both monkeys (Petrides and Pandya, 1984; Schmahmann and Pandya, 2006) and humans via three long-distance fasciculi (Thiebaut de Schotten et al., 2011; Bartolomeo et al., 2012). Functional MRI studies have identified two major fronto-parietal networks subserving attention in humans, a bilateral dorsal one and a right-lateralized ventral one (rev. Corbetta and Shulman, 2002, 2011). Second, converging evidence exists for the role of the integrity of fronto-parietal networks in neglect pathology. It has been shown that the functional inhibition of fronto-parietal connections generates an intraoperative neglect-like pattern during a bisection line task in patients undergoing surgery (Thiebaut de Schotten et al., 2005).

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Using lesion-symptom mapping and fractional anisotropy, specific components of fronto-parietal fibers have been isolated that are responsible for the deficits in modulation of attention by task relevance (Ptak and Schnider, 2010) and for severity of chronic symptoms in neglect (Lunven et al., 2015). By measuring hemodynamic coherent fluctuations in the event-related fMRI signal, He et al. (2007) were the first to demonstrate disrupted functional connectivity in fronto-parietal networks in neglect patients, as confirmed recently by analysis of resting state functional connectivity using both MRI (Baldassarre et al., 2014) and high-resolution electroencephalographic (EEG) signals (Fellrath et al., 2016).

From a functional point of view, fronto-parietal networks in healthy subjects have been associated with spatial attention and orienting, with the dorsal network related to the control of spatial and featural attention and stimulus-response mapping, and the right-lateralized ventral network linked to reorienting to unexpected but behaviorally relevant events (rev. Corbetta and Shulman, 2002). However, fronto-parietal networks also are strongly implicated with conscious processing (Dehaene and Changeux, 2011). Neuroimaging and electrophysiological studies of conscious access in humans (e.g., during attention blink, binocular rivalry, inattention blindness, etc.) have revealed that consciously accessed stimuli consistently "ignite" large-scale prefronto-parietal networks, in contrast to events that have remained out of consciousness (rev. Dehaene and Changeux, 2011; Driver and Vuilleumier, 2001; Rees, 2013). Transcranial magnetic stimulation (TMS) inducing transient dysfunction in parietal or prefrontal areas can prevent conscious perception and even trigger sudden subjective disappearance of visual stimuli (Kanai et al., 2008; Beck et al., 2006; Carmel et al., 2010; Babiloni et al., 2007; Kihara et al., 2011), a reduction of subjective visibility (Rounis et al., 2010), or a hemineglect-like profile (Sack, 2010). Fronto-parietal networks have also been demonstrated to subserve executive control and working memory (Egner et al., 2008; Bressler and Menon, 2010; Menon, 2013; Rottschy et al., 2012, 2013), with prominent activations found in the right hemisphere (Hardwick et al., 2013). Hence, pathologies of these networks or their long-distance connections can critically impair conscious visual perception independently of (van Boxtel et al., 2010; Sumner et al., 2006; Tsuchiya and Koch, 2008; Boehler et al., 2008) or in addition to deficits of attention and central executive networks (Chica et al., 2013). However, the role of fronto-parietal networks for deficient conscious perception, a key symptom in neglect, has remained less well explored.

The present study aimed at evaluating the dynamic functional connectivity of fronto-parietal networks during conscious visual perception in neglect. This objective was approached by employing a task that specifically assessed the ability to integrate information from the two hemi-fields, and by applying an electrophysiological measure that specifically assesses integration between cortical areas. In our task, two squares with vertical or horizontal gratings were simultaneously presented in the left and right hemi-fields. Stimuli were non-targets when the two gratings were equal (vertical or horizontal) and were targets when the two gratings differed. The key feature of the task was that both the left and right hemi-fields were stimulated, but stimuli could be classified as targets or non-targets only by integrating information from the two hemi-fields (full-field attention task). Thus, visual awareness was challenged both in a bottom-up way, by stimulating simultaneously the two hemi-fields, and in a top-down way, by attributing task relevance to the information from the two hemi-fields (Vuilleumier et al., 2008; Ptak and Schnider, 2010; Ptak, 2012).

Our electrophysiological measures were applied to cover the temporal scales of conscious visual perception, the correlates of which emerge within 500 ms after stimulus presentation (Tononi and Koch, 2008; Roelfsema et al., 2004; Wyart and Tallon-Baudry, 2008; Dehaene and Changeux, 2011; Melloni et al., 2011; Koivisto and Grassini, 2016). Previously, disrupted functional connectivity of fronto-parietal networks in neglect has been established by analysis of MRI BOLD signals (He et al., 2007; Baldassarre et al., 2014) and resting-state EEG (Fellrath et al., 2016). However, fast dynamic coupling during perception may not be captured by the low time resolution of the fMRI and resting-state EEG signals. Instead, fast and transient network fluctuations can be reflected by the inter-regional synchronization of neuroelectric signals with high time resolution (Rodriguez et al., 1999; Fries et al., 2001; Fries, 2005; Bressler and Tognoli, 2006; Bressler and Menon, 2010). Therefore, the spatial phase synchronization of event-related EEG oscillations was analyzed, to assess fast dynamic interactions of frontal and parietal regions. EEG was recorded in patients with right-hemisphere lesions during full-field visual task processing. Depending on the presence of neglect symptoms, patients were divided into a group with neglect and a group without neglect and were compared to age-matched healthy controls. It was expected that if dynamic fronto-parietal connectivity contributes to hemi-field perceptual deficits, the synchronization between frontal and parietal regions during visual perception would be specifically altered in patients with neglect.

2. Materials and methods

2.1. Participants

Three groups of participants were formed according to neurological examination directed to detect neglect symptoms by means of application of the German version of the Behavioral Inattention Test (BIT, Wilson et al., 1987). BIT consists of six paper-and-pencil tests (line bisection, line cancellation, star and letter cancellation, figure and shape copying) and nine behavioral tests (e.g. telephone dialing, reading, visual exploration of natural scenes, telling and setting the time on a clock face). The three groups were (Table 1):

(1) Patients with neglect (N+): 9 patients aged 35–78 years (median 60 years; 4 females) with right-hemisphere ischemia or hemorrhage (confirmed in CT and/or MRI, at temporo-parietal, posterior parietal, fronto-precentral, or basal ganglia locations, lesion-to-test interval 1–29 weeks, median 14 weeks) and left visual hemineglect syndrome (score below 166 in BIT, measured on-site immediately after the experiment; median 149; range 84–160). Mean lesion size was 7.6% (SD ± 1.2%, range 1.2–17.4%) of estimated brain volume, based on manual reconstruction of lesions from CT images using templates from Damasio and Damasio (1989).

(2) Patients without neglect (N-): 11 patients aged 50–72 years (median 60 years; 5 females) with right-hemisphere ischemia or hemorrhage. Lesions were at prefrontal, (centro-)temporal, anterior temporal, striato-lenticular, or capsular locations, sparing the classical neglect-inducing lesion sites, such as the posterior parietal lobe, the temporo-parietal junction, and in most cases also the fronto-precentral region around the frontal eye fields (confirmed in CT and/or MRI, lesion-to-test interval 5 weeks to 4.5 years, median 13 weeks). In these patients there was no hemineglect syndrome at the time of investigation (BIT score: median 169; range 167.5–170) and no history of a past hemineglect syndrome. Mean lesion size was 2.2% (SD ± 1.9%, range 0.3–6.3%), being significantly smaller than in N+ patients ($F(1/19) = 6.7$, $p=0.02$). However, lesion size did not correlate with BIT scores across all patients (Pearson correlation coefficient, $r=-0.08$, $p > 0.7$) nor separately in either the N– ($p > 0.7$) or the N+ group ($p > 0.2$).

(3) Control group: 14 persons aged 52–76 years (median 60.5 years; 8 females) without any history of neurological disorders.

Four other N+ patients and four other control subjects had participated but had to be excluded from data analysis because of insufficient number of artefact-free trials for EEG analysis.

In all participants, visual acuity was measured immediately before the experiment and found to be better than 0.7. All subjects who took part in the study gave informed written consent according to the Declaration of Helsinki. The experiment was approved by the local ethics committee.