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Waves of awareness for occipital and parietal phosphenes perception

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ABSTRACT

Transcranial magnetic stimulation (TMS) of the occipital cortex is known to induce visual sensations, i.e. phosphenes, which appear as flashes of light in the absence of an external stimulus. Recent studies have shown that TMS can produce phosphenes also when the intraparietal sulcus (IPS) is stimulated. The main question addressed in this paper is whether parietal phosphenes are generated directly by local mechanisms or emerge through indirect activation of other visual areas. Electroencephalographic (EEG) signals were recorded while stimulating left occipital or parietal cortices inducing phosphene perception in healthy participants and in a hemianopic patient who suffered from complete destruction of the early visual cortex of the left hemisphere. Results in healthy participants showed that the onset of phosphene perception induced by occipital TMS correlated with differential cortical activity in temporal sites while the onset of phosphene perception induced by parietal TMS correlated with differential cortical activity in the stimulated parietal site. Moreover, IPS-TMS of the lesioned hemisphere of the hemianopic patient with a complete lesion to V1 showed again that the onset of phosphene perception correlated with differential cortical activity in the stimulated parietal site. The present data seem thus to suggest that temporal and parietal cortices can serve as different local early gatekeepers of perceptual awareness and that activity in the occipital cortex, although being relevant for perception in general, is not part of the neural bases of the perceptual awareness of phosphenes.

1. Introduction

A central question in consciousness studies is to reveal which brain regions, and in what order of activation, critically determine specific conscious percepts. Several models have been proposed in order to find the brain areas ("where") correlating with visual awareness and to determine the time-course of neural activation in interconnected areas ("when/how") needed for awareness to emerge. With respect to the "where" question, one of the most influential models in visual processing, the so-called two-streams hypothesis (Goodale and Milner, 1992; Milner and Goodale, 2008), states that visual awareness is restricted to the ventral stream (Milner, 2012). The dorsal stream, instead, is thought not to be "in the business of providing any kind of a visual representation of the world" (Goodale and Milner, 2004, p. 114). With respect to the "when/how" question, another very influential model, Lamme's model (Lamme et al., 1998), states that recurrent processing feeding back to occipital cortex is necessary for awareness to emerge. On the basis of these two models, it can be predicted that the neural correlates of visual awareness can only be found along the ventral stream (comprising the occipital and temporal cortices) and that the integrity of the primary visual cortex (V1) is needed. Recent findings have challenged both of these statements. It has indeed been found that, at least under certain circumstances, the dorsal stream can generate visual awareness (Hesselmann and Malach, 2011; Koivisto et al., 2010; Mazzi et al., 2014) and that recurrent processing feeding back to V1 is not necessary for visual awareness (Zeki and ffytche, 1998; ffytche and Zeki, 2011; Mazzi et al., 2014).

In the present paper we further tested the contribution of the dorsal stream and V1 in the emergence of awareness by combining transcranial magnetic stimulation (TMS) and electroencephalography (EEG), two modern methodologies which can provide information both with respect to the "where" and the "when/how" questions.

TMS, by being a non-invasive direct stimulation method, is one

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of the state of the art methodologies used to study whether a specific neural area plays a crucial role in cognitive processes. The logic is the following: if TMS of a specific cortical area has a specific effect on performance, this area and the network associated to it are crucial for the studied function. In this respect, for example, if TMS is applied to the portion of the primary motor cortex (M1) representing the contralateral hand, a motor twitch of the hand contralateral to the stimulation is elicited, thus making it possible to conclude that activity within the stimulated area (M1) has a causal role in eliciting the motor twitch. Moreover, TMS can be useful not only for the localization of eloquent cortical areas but it can also determine the intensity needed to evoke a specific effect. For instance, by stimulating M1, one can determine the minimal TMS pulse intensity (the so-called motor threshold) needed to evoke a motor potential; this intensity is considered to directly reflect the level of excitability of the stimulated cortex.

Similarly, TMS of visual areas induces conscious visual percepts, or phosphenes, i.e. the experience of flashes of light in the absence of an external stimulus. Additionally, akin to the motor threshold, cortical excitability can be measured with the phosphene threshold. Typically, phosphene perception has been studied by stimulating areas within the occipital cortex. However, recent findings (Marzi et al., 2009; Mazzi et al., 2014; Fried et al., 2011) have shown that phosphenes can be elicited also along the dorsal stream (Goodale and Milner, 1992; Milner and Goodale, 2008), specifically in the intra-parietal sulcus (IPS). Interestingly for the purposes of the present paper, Mazzi and collaborators (2014) tested both healthy participants and hemianopic patients with a complete lesion of V1 and asked them to report the presence/absence of phosphenes while their occipital or parietal cortex was stimulated (only the parietal cortex was stimulated in hemianopic patients). The authors reported that, in healthy participants, IPS-phosphenes have a higher phosphene-threshold and different phenomenical characteristics than those elicited by occipital TMS. Importantly, they showed that parietal phosphenes can be obtained also in patients with a complete lesion to the ipsilateral V1 and that their conscious visual percepts were undistinguishable from those obtained with healthy participants. The authors concluded that (1) neural activity in V1 is not necessary for visual awareness and (2) that IPS is an independent generator of the awareness of phosphenes. As a note of caution, one should consider the possibility that the awareness of phosphenes generated by TMS of IPS could result from a spread of activity towards other visual areas (i.e. extrastriate areas and the temporal cortex). Although the involvement of V1 seems unlikely given the results with hemianopic patients, the awareness of IPS phosphenes could be induced by a "third visual area", or a network subtending connections with IPS, that could be in charge of providing access to visual awareness (Fried et al., 2011; Mazzi et al., 2014). A likely candidate for this hypothesis, as suggested by the previously described models (Goodale and Milner, 1992; Lamme et al., 1998) could be found along the ventral stream, e.g., in the temporal cortex which is known to play an important role in visual awareness (Goodale and Milner, 1992).

In order to test the contribution of such a "third area" in the generation of phosphenes, TMS-evoked potentials (TEPs) can be acquired by co-registering EEG signals while the cortex is stimulated. TEPs represent a clear and direct measure of cortical excitability and can be used to assess the state of cortical reactivity and connectivity also in the so-called silent-areas that do not produce a peripheral marker (Ilmoniemi et al., 1997). Here, we adopted an interactive approach (Miniussi and Thut, 2010) by using EEG–TMS co-registration while the participant performed a task. This approach consists in the stimulation of a circumscribed cortical area with TMS and to monitor, with EEG, the induced electrical changes in the whole cortex. EEG–TMS co-registration conceives the tracing of the time course of functionally relevant activity in distant but functionally connected areas relevant for the task at hand (i.e. effective connectivity). The relevance of this approach is twofold: (1) it provides an empirical measure of the network of areas implicated in a specific task as the activation induced by TMS of the targeted area propagates to functionally connected areas and (2) it provides information on the causal relationship in the connections across the network of activated areas. Given the high temporal resolution of EEG and the properties of the spreading of activity induced by TMS, if an area X results to be active prior to area Y it can be assumed that the activity in area X causes a change in the activity of area Y through effective connections between the two areas.

Thanks to these characteristics, TEPs are ideal to gather information on the time-course and spatio-temporal dynamics of the emergence of phosphene perception. Despite the relative crudeness of spatial topography of EEG, its temporal resolution is very high (in the range of milliseconds) and this is the most crucial characteristic for the purposes of the present paper. The logic is the following: if TEPs detect an electrical difference at the stimulated area (e.g. IPS) between phosphene-present and phosphene-absent trials in a specific time window after TMS, to be considered crucial for this effect, a "third area" (e.g. temporal cortex) should display a comparable effect (phosphene-present different than phosphene-absent) in the same or earlier time windows. If such a differential effect cannot be found, no causal role of the supposed "third area" (e.g. temporal cortex) can be advocated for the perception of phosphenes elicited by TMS of the stimulated area (e.g. IPS).

The main purpose of the present paper is to uncover the spatio-temporal dynamics of the onset of the phosphene perception as induced by occipital and parietal TMS. To do this, healthy participants and one hemianopic patient was asked to report the presence/absence of a phosphene induced by stimulation of a specific occipital and parietal site by means of TMS while monitoring and recording TEPs. On the basis of the results of this EEG–TMS interactive co-registration approach, we could draw some conclusions both on the role of V1 in perceptual awareness and on whether or not other functionally interconnected areas are playing some role in the emergence of awareness after stimulation of the occipital and parietal cortex.

2. Experiment 1

2.1. Materials and methods

2.1.1. Healthy participants

Sixteen healthy volunteers (9 females) were recruited to participate in the study. Their ages ranged between 22 and 28 years (mean 25 years, sd 1.90) and they were all right handed, as assessed with the Edinburgh Handedness Inventory (Oldfield, 1971). They all had normal or corrected-to-normal visual acuity and no history of neurological or psychiatric disorders. All participants gave their written informed consent prior to participation. The experiment was carried out according to the principles laid down in the 1964 Declaration of Helsinki and approved by the local Ethics Committee. As assessed by a safety screening questionnaire (adapted from Rossi et al., 2011), participants were negative for all risk factors associated with TMS: none reported neurological disorders, cardiac pacemaker, any history of epilepsy or migraine, current treatment with any psychoactive medication and pregnancy. One participant could not perceive reliable phosphenes after either occipital or parietal sites and four participants dropped out and did not perform the second session. These participants were thus excluded from the sample.