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Research report

Two distinct neural mechanisms in early visual cortex determine subsequent visual processing

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ABSTRACT

Neuroscience research has conventionally focused on how the brain processes sensory information, after the information has been received. Recently, increased interest focuses on how the state of the brain upon receiving inputs determines and biases their subsequent processing and interpretation. Here, we investigated such 'pre-stimulus' brain mechanisms and their relevance for objective and subjective visual processing. Using non-invasive focal brain stimulation [transcranial magnetic stimulation (TMS)] we disrupted spontaneous brain state activity within early visual cortex (EVC) before onset of visual stimulation, at two different pre-stimulus-onset-asynchronies (pSOAs). We found that TMS pulses applied to EVC at either 20 msec or 50 msec before onset of a simple orientation stimulus both prevented this stimulus from reaching visual awareness. Interestingly, only the TMS-induced visual suppression following TMS at a pSOA of −20 msec was retinotopically specific, while TMS at a pSOA of −50 msec was not. In a second experiment, we used more complex symbolic arrow stimuli, and found TMS-induced suppression only when disrupting EVC at a pSOA of ~ −60 msec, which, in line with Experiment 1, was not retinotopically specific. Despite this topographic unspecificity of the −50 msec effect, the additional control measurements as well as tracking and removal of eye blinks, suggested that also this effect was not the result of an unspecific artifact, and thus neural in origin. We therefore obtained evidence of two distinct neural mechanisms taking place in EVC, both determining whether or not subsequent visual inputs are successfully processed by the human visual system.

1. Introduction

The occipital lobe of the human brain is dedicated to the processing of visual inputs. Early cortical stages of visual information processing occur approximately 60–100 msec after stimulus presentation in visual areas V1, V2 and V3 of the occipital brain, together commonly referred to as early visual cortex (EVC). Much research has focused on the specific

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visual properties these early visual areas process, their neuronal tuning to these properties, and the information flow within and/or between these regions of EVC (e.g., Cardin, Friston, & Zeki, 2011; Downing, Chan, Peelen, Dodds, & Kanwisher, 2006; Nandy, Sharpee, Reynolds, & Mitchell, 2013). These are examples of how research conventionally focuses on the brain's response to inputs from the environment. Yet, how inputs are processed may depend not only on nature of the information, but also on the prior state of the brain (Arieli, Sterkin, Grinvald, & Aertsen, 1996; Busch, Dubois, & VanRullen, 2009; Hesselmann, Kell, Eger, & Kleinschmidt, 2008; Mathewson, Gratton, Fabiani, Beck, & Ro, 2009).

Recent studies have addressed the potential modulatory role of neural state *prior* to visual input. Electrophysiological studies have shown, for example, that under conditions of near-threshold stimulus visibility, the variability in stimulus perception is indeed reflected in pre-stimulus brain activity (Busch, et al., 2009; van Dijk, Schoffelen, Oostenveld, & Jensen, 2008; Dugue, Marque, & VanRullen, 2011; Hanslmayr et al., 2007; Mathewson, et al., 2009; Romei et al., 2008; Romei, Gross, & Thut, 2010; Toscani, Marzi, Righi, Viggiano, & Baldassi, 2010). So far, the power (van Dijk, et al., 2008; Romei, et al., 2008; Romei, et al., 2010; Toscani, et al., 2010) and phase (Busch, et al., 2009; Dugue, et al., 2011; Mathewson, et al., 2009) of pre-stimulus parieto-occipital oscillations in the alpha frequency band (i.e., 8–12 Hz), and phase-locking in the beta (16–30 Hz) and gamma (>30 Hz) frequency bands (Hanslmayr, et al., 2007) have been related to this perceptual modulation. Next, researchers reversed the line of reasoning and showed that they could affect stimulus visibility by externally manipulating parieto-occipital alpha oscillations (e.g., de Graaf et al., 2013; Mathewson et al., 2012; Romei, et al., 2010), establishing a causal relation between stimulus visibility and pre-stimulus neural state. Together, these studies demonstrate that neural processing that occurs prior to sensory input can play a functional role in perception.

By means of Transcranial Magnetic Stimulation (TMS), a brain interference tool that allows temporal disruption of neuronal activity, the contribution of pre-stimulus EVC state to visual perception can be investigated. If applied over occipital cortex, TMS can lead to a complete abolishment of conscious perception of suprathreshold visual stimuli. This effect is well-established for TMS applied at stimulus onset asynchronies (SOAs) around 70–130 msec (e.g., Amassian et al., 1989; Corthout, Uttl, Ziemann, Cowey, & Hallett, 1999; Sack, van der Mark, Schuhmann, Schwarzbach, & Goebel, 2009, see Kammer, 2007, for review). Several chronometric TMS studies investigating the temporal profile of EVC involvement in visual perception have revealed additional time windows prior to stimulus onset at which TMS over EVC disrupts multiple aspects of visual perception: visual discrimination (Corthout, Hallett, & Cowey, 2003; Corthout, Uttl, Juan, Hallett, & Cowey, 2000; Laycock, Crewther, Fitzgerald, & Crewther, 2007), subjective visibility, and priming (Jacobs, de Graaf, Goebel, & Sack, 2012).

The problem with pre-stimulus masking is that TMS pulses prior to visual stimuli may elicit all kinds of non-neural or non-specific effects, such as attentional priming, multisensory priming/integration (due to the ‘click’ of the pulse), and most importantly the induction of eye blinks. In previous work, we already addressed several of these alternative explanations of pre-stimulus masking effects, for instance by removing trials with eye blinks (Jacobs, Goebel, & Sack, 2012), controlling for sound with Sham TMS (de Graaf, Cornelsen, Jacobs, & Sack, 2011; Jacobs, Goebel, et al., 2012), and controlling for sensory stimulation of the skin with vertex TMS (Jacobs, Goebel, et al., 2012). Therefore, we concluded that a neural mechanism underlies (at least part of) the obtained pre-stimulus TMS masking effects. We proposed that pre-stimulus TMS exerts its effects by putting EVC in a suboptimal state (de Graaf, Cornelsen, et al., 2011), perhaps one of rhythmic neuronal firing at an ineffective frequency and/or phase, thereby hampering subsequent visual processing (Jacobs, Goebel, et al., 2012).

In Jacobs, Goebel, et al. (2012), we reported a rather broad time interval in which TMS could negatively influence visual perception of symbolic arrow stimuli ranging from −80 to −40 msec at group level, but showing more narrow effective time windows in single participants. Another study by our group showed impaired visual discrimination and subjective visibility of bar stimuli for high-intensity (>65% maximal stimulator output) EVC-TMS at −25 msec (de Graaf, Cornelsen, et al., 2011). Since the latter was not a chronometric TMS study, we cannot exclude the possibility that both pre-stimulus time windows are part of a broader period of EVC relevance that stretches from −25 to −80 msec. Yet, other studies have reported multiple, separate time windows of visual suppression by TMS within the pre-stimulus time frame (Corthout, et al., 2003; Corthout, et al., 1999).

The identification of two distinct time periods of EVC perceptual relevance leaves room for multiple interpretations: it could imply a single neural mechanism that comes into play repetitively, or two separate neural mechanisms which independently occur in EVC, but which are both necessary for accurate visual perception. Here, our aim is to investigate these two alternatives, and as such, to shed new light on the role of pre-stimulus processes in EVC for visual perception.

In the current project, we investigated the relevance of pre-stimulus brain state in EVC in two separate experiments. In Experiment 1, we used a paradigm of increasing magnetic stimulation strength (de Graaf, Cornelsen, et al., 2011) to test possible TMS masking effects at −50 msec, and at −20 msec. In contrast to our previous explorations, we presented stimuli at the TMS-targeted visual field location and in a control location, allowing us to evaluate retinotopic specificity of potential masking effects. Moreover, we compared these results to the pattern of masking effects for two post-stimulus masking windows (+90 and +120 msec), always measuring both objective (forced-choice stimulus orientation determination) and subjective (stimulus visibility rating) visual processing. Looking ahead, we found retinotopic TMS masking at −20 msec and non-retinotopic TMS masking at −50 msec, supporting a separation of two pre-stimulus masking windows with fundamentally different underlying mechanisms.

Previous work using symbolic arrow stimuli (Jacobs, Goebel, et al., 2012) indeed found masking effects at −50 msec, but found no suppression at −20 msec. To elucidate these matters, in Experiment 2 we measured a range of SOAs, using symbolic arrow stimuli. Moreover, we measured EoG simultaneously, to later evaluate the influence of eye blinks