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Seeing in the dark: Phosphene thresholds with eyes open versus closed in the absence of visual inputs

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ABSTRACT

Background: Voluntarily opening or closing our eyes results in fundamentally different input patterns and expectancies. Yet it remains unclear how our brains and visual systems adapt to these ocular states. Objective/Hypothesis: We here used transcranial magnetic stimulation (TMS) to probe the excitability of the human visual system with eyes open or closed, in the complete absence of visual inputs.
Methods: Combining Bayesian staircase procedures with computer control of TMS pulse intensity allowed interleaved determination of phosphene thresholds (PT) in both conditions. We measured parieto-occipital EEG baseline activity in several stages to track oscillatory power in the alpha (8–12 Hz) frequency-band, which has previously been shown to be inversely related to phosphene perception.
Results: Since closing the eyes generally increases alpha power, one might have expected a decrease in excitability (higher PT). While we confirmed a rise in alpha power with eyes closed, visual excitability was actually increased (PT was lower) with eyes closed.
Conclusions: This suggests that, aside from oscillatory alpha power, additional neuronal mechanisms influence the excitability of early visual cortex. One of these may involve a more internally oriented mode of brain operation, engaged by closing the eyes. In this state, visual cortex may be more susceptible to top-down inputs, to facilitate for example multisensory integration or imagery/working memory, although alternative explanations remain possible.

Introduction

Most of the time, opening our eyes opens the floodgates of sensation, preparing and allowing us to interact with the environment. Conversely, closing our eyes means that we shut the world out. With closed eyes, we can turn inwards, focusing on our other senses or our thoughts, memories, and mental images. It seems plausible that our brains would have evolved distinct modes of operation for these two ocular states. But it is not immediately clear what exactly this might mean. In the current study, we focused on a brain system very likely to be affected by eye closure; early visual cortex.

One reflection of brain state is the excitability, or reactivity, of a cortical region. Concerning early visual cortex, *a priori* one might have opposing hypotheses about the effect of eye closure on visual excitability. Perhaps visual cortex becomes more excitable when opening the eyes, since this act enables the arrival of visual inputs. Conversely, excitability might rather increase with eye closure, since it could be ecologically useful to be sensitive to dark moving shapes even with eyes closed. Approaching the issue from a different perspective, one established consequence of eye closure is an increase in oscillatory power in the alpha (~10 Hz) frequency band [1]. Moreover, alpha power has been shown to be inversely related to visual excitability [2]. Combining these insights, eye closure could reduce visual excitability. But from a neurocognitive perspective one might again intuit the opposite: Eye closure, by diminishing the likelihood of bottom-up inputs, could free up early visual cortex for top-down inputs, facilitating such faculties as cross-sensory integration, imagery, or working memory (see e.g. Ref. [3]. In sum, the effect of eye closure on visual excitability is not obvious *a priori*.

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Neuroimaging studies have investigated which brain regions [4–9] and dynamics [3,10–13] behave differently depending on whether our eyes are open or closed. Without any external inputs in either case, these ocular states have been associated with distinct patterns of neural activation. Generally, *closing* the eyes changed activity in multiple regions of the brain, including early sensory and multisensory regions, while *opening* the eyes rather increased activity in attentional and oculo-motor regions [3,4,6,7,14–16]. For instance, recent findings by Xu et al. [17] support two distinct networks underlying these two states, demonstrating increased cross-sensory connectivity and highly integrated information processing for eyes closed, while ascribing a highly specialized mode of information processing to the eyes open state. Following Marx et al. [3], we will refer to these functional states as 'exteroceptive', for eyes open, and 'interoceptive', for eyes closed. The exteroceptive state is characterized by overt attention, while the interoceptive state was associated with multisensory integration, recall of sensory experiences and imagination [3,6,15,18].

Focusing again on early visual cortex, blood oxygen level dependent (BOLD) signal increases when closing the eyes, except for congenitally blind participants [15]. But while such neuroimaging results are interesting, important, and suggestive, they remain at the same time inevitably limited. Non-invasive brain stimulation techniques can provide complementary insights [19–21]. Transcranial magnetic stimulation (TMS) involves magnetic pulses administered at the scalp that enter and excite the brain. Such pulses can disrupt visual processing if applied over occipital cortex at certain delays to a visual stimulus [22–26], but can also induce transient visual experiences called 'phosphenes' [27–30]. The strength of stimulation required to elicit phosphenes on a predetermined proportion of trials (conventionally 0.5) is the 'phosphene threshold' (PT): An established measure of cortical excitability of the visual system.

In the current study we directly tested visual excitability under conditions of open versus closed eyes, in the complete absence of visual inputs. We determined PT for both ocular states in a controlled, interleaved, within-subject paradigm, letting a Bayesian staircase algorithm (QUEST, see Methods) control the intensity of TMS pulses on a trial-by-trial basis. Considering the relation between PT and alpha oscillatory power, we placed electroencephalography (EEG) electrodes over parietal and occipital cortex to take into account the classical eye closure effect on alpha power. Looking ahead, parieto-occipital alpha power was indeed higher with closed eyes. At the same time, PT was significantly lower with closed eyes, indicating increased visual excitability.

Methods

Participants

Nineteen participants, including two authors (T.G., S.O.), indicated perception of phosphenes and were selected for the experiment. All were screened for TMS safety and provided written informed consent, receiving monetary compensation for participation. Procedures were approved by the local ethics committee.

TMS and EEG parameters

Single biphasic TMS pulses were applied to occipital cortex using a MC-B70 figure-of-eight coil connected to a MagPro X100 stimulator (MagVenture, Farum, Denmark). The coil handle was oriented laterally to the right, but the exact coil position on the scalp depended on an idiosyncratic phosphene hotspot. In a localization procedure, participants viewed a fixation point on a computer monitor (57 cm viewing distance) while the TMS coil was moved over right occipital regions, administering TMS pulses until participants indicated perceiving a peripheral phosphene in the lower left quadrant relative to fixation. If the reported phosphene retinotopically followed a shift in gaze, the coil location was accepted and fixed by use of a mechanical arm. During the main experiment, TMS intensity was variable, determined per trial by the staircase procedure (see below). A test range was enforced on the staircase algorithm, however, to the effect that pulses were maximally at 70% of maximum stimulator output, with a lower bound adapted from 25% to 20% to finally 10%, as we noted that some participants' PTs were lower than originally anticipated.

We applied four EEG electrodes to locations on the international 10–20 coordinate system [31], attaching them using conductive gel (Ten20®, DO Weaver, Aurora, CO, USA) and leading into a headbox connected to BrainVision amplifiers (BrainProducts GmbH, Munich, Germany). A parietal electrode was placed at P3, an occipital electrode was placed at O1, a ground to Cz and a reference electrode to the left mastoid. No EEG data were recorded for one participant due to time constraints, resulting in 18 full EEG datasets. In a subsample of participants (N = 9) electrooculography (EOG) was also acquired, with two electrodes (HEOG/VEOG) attached near the left eye. EEG/EOG signals were recorded using VisionRecorder software (BrainProducts GmbH, Munich, Germany), with a sampling frequency of 2500 Hz, a notch filter at 50 Hz, and filtered with high and low cut-off values of 250 Hz (100 Hz for EOG channels) and 0.1 Hz, respectively.

Design and task

The experimental session contained several stages, after application of EEG electrodes and fixation of the TMS coil. We asked participants to relax for 90 s while we acquired *baseline EEG signals* at different moments throughout the experimental session. We also determined *phosphene thresholds (PT)* several times under different conditions. These conditions included wearing a blindfold or not, with opened or closed eyes. If not wearing the blindfold, participants were looking at a fixation cross on a computer monitor in a darkened but not pitchblack room. The blindfold (Mindfold Inc., Tucson, AZ) was used to create a condition of absolute darkness. It is a fully darkening mask that does not directly touch the eyes, allowing participants to comfortably open or close their eyes underneath. Once participants were wearing the blindfold, we switched the lights in the room fully on or off and asked whether participants could tell the difference, which they reportedly could not. One participant did report a shift in the blindfold during the experiment so that some light penetrated the blindfold for part of the measurement, this participant was marked as having Grounds for Exclusion (GfE; see below). Though the blindfold in all other cases provided perfect darkness, redundantly we nevertheless turned off the lights in the room during the measurements. Under these various conditions, the full sequence of measurements was as follows:

- baseline EEG, eyes open without blindfold (normalization target 'EEGstart')
- PT staircase, eyes open without blindfold (normalization target 'PTstart')
  (participant starts wearing the blindfold)
- baseline EEG 'EEG pre', eyes open (or closed)
- baseline EEG 'EEG pre', eyes closed (or open)
- **interleaved PT staircases for eyes open and closed**
- baseline EEG 'EEG post', eyes closed (or open)
- baseline EEG 'EEG post', eyes open (or closed)
  (participant stops wearing the blindfold)