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The influence of current direction on phosphene thresholds evoked by transcranial magnetic stimulation

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Abstract

Objectives: To quantify phosphene thresholds evoked by transcranial magnetic stimulation (TMS) in the occipital cortex as a function of induced current direction.

Methods: Phosphene thresholds were determined in 6 subjects. We compared two stimulator types (Medtronic-Dantec and Magstim) with monophasic pulses using the standard figure-of-eight coils and systematically varied hemisphere (left and right) and induced current direction (latero-medial and medio-lateral). Each measurement was made 3 times, with a new stimulation site chosen for each repetition. Only those stimulation sites were investigated where phosphenes were restricted to one visual hemifield. Coil positions were stereotactically registered. Functional magnetic resonance imaging (fMRI) of retinotopic areas was performed in 5 subjects to individually characterize the borders of visual areas; TMS stimulation sites were coregistered with respect to visual areas.

Results: Despite large interindividual variance we found a consistent pattern of phosphene thresholds. They were significantly lower if the direction of the induced current was oriented from lateral to medial in the occipital lobe rather than vice versa. No difference with respect to the hemisphere was found. Threshold values normalized to the square root of the stored energy in the stimulators were lower with the Medtronic-Dantec device than with the Magstim device. fMRI revealed that stimulation sites generating unilateral phosphenes were situated at V2 and V3. Variability of phosphene thresholds was low within a cortical patch of 2×2 cm^2. Stimulation over V1 yields phosphenes in both visual fields.

Conclusions: The excitability of visual cortical areas depends on the direction of the induced current with a preference for latero-medial currents. Although the coil positions used in this study were centered over visual areas V2 and V3, we cannot rule out the possibility that subcortical structures or V1 could actually be the main generator for phosphenes.

Keywords: Human visual cortex; TMS; Phosphenes; Threshold; Functional magnetic resonance imaging; Retinotopic map

1. Introduction

The excitatory effect of transcranial magnetic stimulation (TMS) allows us to determine thresholds of cortical excitability in individual subjects. This is a standard procedure in the motor cortex, as motor output can be assessed by the compound muscle action potential (cMAP). More recently, there has been growing interest in thresholds within the visual system. Stimulating the occipital pole of the brain causes the perception of a light flash, i.e. a phosphene (Barker et al., 1985; Meyer et al., 1991). Thresholds of phosphenes were measured quantitatively for the first time within a pathophysiological framework. In patients suffering from migraine, Aurora et al. (1998) found lower thresholds for phosphene induction than in normal volunteers. In contrast, Afra et al. (1998) found no difference in phosphene thresholds between normal volunteers and migraine patients.

The controversial results have been attributed to methodological differences (Aurora and Welch, 1999; Mulleners et al., 1999; Schoenen et al., 1999). Indeed, it is not yet clear which conditions are best suited to eliciting the perception of phosphenes and reproducibly determining phosphene thresholds.

Effects of TMS depend on the direction of the induced current, which is opposite to the current direction in the coil. In the first systematic study of phosphenes, Meyer et al. (1991) mentioned a preferential current direction for the excitation of the visual cortex. Using a round coil and a monophasic pulse, they found that currents passing the occipital cortex from lateral to medial to evoke stronger phos-

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phenes than currents flowing in the opposite direction. The same directional preference was reported by Amassian et al. (1994) for the visual extinction effect. An induced current passing the occipital pole from left to right disturbed the perception of visual stimuli in the right visual hemifield and therefore, seemed to preferentially stimulate the left hemisphere. The opposite was found to be true for currents flowing from right to left: they affected perception predominantly in the left visual hemifield. In the motor cortex, a similar phenomenon is well known. Greater excitability of the corticospinal motor system is found with monophasic currents passing through the precentral gyrus from posterior to anterior, than with a current direction from anterior to posterior (Brasil-Neto et al., 1992; Mills et al., 1992; Niehaus et al., 2000). We recently quantified motor threshold differences for both of these current directions. (Kammer et al., 2001).

The aim of the present study was to quantify the differences in phosphene thresholds with different current directions. Furthermore, we asked how reliable the determination of phosphene thresholds is. In addition we compared thresholds measured with two different stimulator types. Finally, we identified the areas in the occipital lobe where the center of the coil was placed during the threshold measuring procedures. To that end we first identified the borders of visual areas with functional magnetic resonance imaging (fMRI) and then used a stereotactic positioning system to project the position of the coil onto the corresponding cortical surface of the subject.

2. Methods

2.1. Subjects and setup

Six healthy subjects (age 21–37 years, 4 males, two females) participated in the study after giving their written informed consent. The study was approved by the local internal review board of the Medical Faculty, University of Tübingen.

Subjects were stimulated either with a Medtronic-Dantec Magpro stimulator (Skovlunde, Denmark) in the monophasic mode (maximal rate 0.33 Hz) or with a Magstim 200 stimulator (Whitland, Dyfed, UK, maximal rate 0.2 Hz). Both stimulators were fitted with the standard figure-of-eight coil. The Medtronic-Dantec coil (MC-B70) is angled 140°. The two windings each have a diameter of 24–96 mm and a mean diameter of 60 mm (as measured by X-ray). They overlap by 38 mm. The Magstim coil (P/N 9790) is not angled. The two windings each have a diameter of 56–91 mm and a mean diameter of 74 mm. They are arranged adjacent to each other and do not overlap. In the experiment the coil was fixed on a tripod. Coil position in relation to the head was monitored and registered continuously in all 6 degrees of freedom – 3 translational and 3 rotational – with a custom-made positioning system (Kammer et al., 2001). Current directions were described for the initial fast rising phase of the monophasic current pulse induced in the brain (Kammer et al., 2001). In the Medtronic-Dantec stimulator current directions were controlled with a dedicated switch. When the switch was set to 'normal' and the coil handle pointed to the left, the induced current direction in the brain was right to left. With the same coil orientation, the 'backward' position of the switch resulted in an induced current direction from left to right. With the Magstim stimulator the orientation of the coil handle to the left resulted in an induced current direction from left to right. To flip current direction to right–left the orientation of the coil handle had to be flipped 180°.

2.2. Phosphene thresholds

Phosphene thresholds at the occipital pole were measured separately for each hemisphere and current direction. The coil handle was oriented horizontally. First, a stimulation site was determined as follows: position of the coil was moved step by step while the subject looking at a computer screen (21″, observer distance 57 cm, visual field 36° × 28°, background intensity 0.5 cd/m^2) was stimulated with a suprathreshold intensity until he or she observed a sharply delineated phosphene clearly restricted to the contralateral visual field. At this coil position 10 different stimulator intensities (step size 2%) were tested 10 times in a randomized order. Coil position was continuously monitored and kept constant. After each stimulation the subject reported the presence or absence of a phosphene. Using the Boltz-

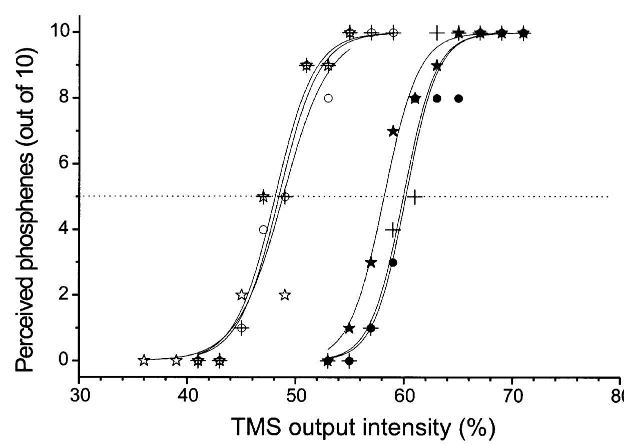

Fig. 1. Example for phosphene threshold measurements and Boltzmann fits (subject MV, right hemisphere, stimulator: Medtronic-Dantec). On the abscissa, stimulus intensity is given in percent of maximal output. The ordinate depicts the number of phosphenes perceived out of 10 stimulations. Open symbols indicate the induced current direction right–left, filled symbols left–right. Sigmoidal functions were fitted to the data using the Boltzmann equation. Thresholds were defined as the half-maximal value (5/10) of the respective function (dashed line). Measurements were performed 3 times per current direction. For each measurement a new stimulation site was determined first. The stimulation sites for these measurements are shown in Fig. 5, upper right (right hemisphere).