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Cortical excitability and the shape of the haemodynamic response

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ABSTRACT

Individual differences in the temporal dynamics of the haemodynamic response can reflect cortical excitation and can reveal underlying cortical physiology. Here, we show differences in the shape of the haemodynamic response that are dependent on stimulus parameters. Two sets of visual stimuli were used varying in parameters that are known to manipulate the haemodynamic response in the visual cortex. We measured the oxyhaemoglobin response using near infrared spectroscopy. The first set of stimuli comprised chromatic square-wave gratings that varied with respect to the separation in the CIE UCS chromaticities of the alternating bars. The gratings with large separations in chromaticity evoked an oxyhaemoglobin response with greater amplitude, consistent with greater activation of the visual cortex. The second set of stimuli comprised horizontal achromatic gratings that (1) were static, (2) drifted at a constant velocity towards fixation, or (3) reversed direction every half spatial cycle to create a vertical vibrating motion. Although the three types of grating had a similar effect on the amplitude of the oxyhaemoglobin response, the moving gratings (2 and 3) evoked a steeper decrease in oxyhaemoglobin concentration after stimulus-offset. The steeper slope appears to reflect the post-stimulus undershoot and the slope may provide a correlate of cortical excitability when the amplitude of the haemodynamic response has saturated.

Introduction

Near-infrared spectroscopy (NIRS) uses light to measure changes in spectral reflectance of oxygenated and deoxygenated blood in the cortex (Villringer et al., 1993). The temporal resolution of NIRS is higher than that of fMRI (although its spatial resolution is much poorer) and NIRS offers the opportunity for closer interrogation of the temporal properties of the haemodynamic response.

The relationship between haemodynamic changes and neural excitation is complicated but is related to local field potentials (Logothetis et al., 2001). The haemodynamic response can therefore be used as a surrogate measure of neural activation. Comparisons of fMRI/NIRS responses to visual stimuli and findings from electroencephalography (EEG) studies to the same stimuli explicitly test the relationship between the haemodynamic and the neural response. Visual stimuli that evoke a strong neural response also produce a large change in the haemodynamic response in visual cortex. For example, the fMRI BOLD signal increases linearly with log contrast (Olman et al., 2004; Vazquez and Noll, 1998), and high log contrast produces greater oxyhaemoglobin responses measured using NIRS (Rovati et al., 2007). Higher contrast grating patterns also increase the amplitude of visual evoked potentials and increase gamma activity in visual cortex (Schadow et al., 2007). However, there is some debate over the sensitivity of the haemodynamic response to changes in spatial frequency (compare Swettenham et al., 2013, with Huang et al., 2003). Tong et al. (2005) measured NIRS and EEG responses to an auditory stimulus in an odd-ball paradigm, and found an increase in oxyhaemoglobin a few seconds after the presence of a P300 component in an ERP response. Simultaneous NIRS and EEG recordings have also been used to measure the relationship between haemodynamic responses and alpha activity (Moosmann et al., 2003) and epileptogenic activity (for example, see Gallagher et al., 2008; Lareau et al., 2011; Roche-Labarbe et al., 2008).

There are several independent indications of a cortical hyperexcitability in migraine (see Aurora and Wilkinson, 2007 for a review). For example, Huang et al. (2003) found that patients with migraine showed larger BOLD responses to grating stimuli than controls. It is therefore of interest that Coutts et al. (2012) using NIRS found that patients with migraine showed shorter oxyhaemoglobin responses compared to healthy controls, suggesting that the shape of the haemodynamic response can also be related to cortical excitability. This suggestion is consistent with the findings of Muthukumaraswamy et al. (2012) that individuals with lower concentrations of GABA produced taller and thinner BOLD responses in the visual cortex, compared to individuals with higher concentrations of GABA. GABAergic mechanisms affect local cortical excitability (Semyanov et al., 2003). It is therefore possible that the shape of the haemodynamic response, as well as its amplitude, can reflect cortical excitability. Consequently we wanted to test the relationship between the

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amplitude and shape of the oxyhaemoglobin response to different visual stimuli.

Here we present two experiments in which we measured the relationship between the amplitude and the shape of the oxyhaemoglobin response using NIRS. We manipulated stimulus parameters that have been shown to affect viewing comfort and to influence the probability of paroxysmal EEG activity in patients with photosensitive epilepsy. Following the findings reported by Muthukumaraswamy et al. (2012) and Coutts et al. (2012), we chose to focus on the effect of the stimulus parameters on the oxyhaemoglobin response during stimulus presentation and immediately after stimulus presentation, and the effect on the size of the post-stimulus undershoot (PSU). Our aim was to measure the haemodynamic response in relation to cortical excitation.

In the first experiment, we presented isoluminant chromatic square-wave gratings that varied in the separation between the chromaticities of the component bars. Gratings with large chromaticity separation are uncomfortable to view and can produce a large haemodynamic response (Haigh et al., 2013a, b). Flicker in which two coloured lights alternate can evoke paroxysmal EEG activity in patients with photosensitive epilepsy (Parra et al., 2007), and the probability of paroxysmal activity increases with the separation in chromaticity. For the second experiment, we presented achromatic square-wave gratings that were (1) static (2) drifted at a constant (10 Hz) velocity, or (3) drifted at the same velocity but reversed direction every half spatial cycle causing the stripes to vibrate. 10 Hz vibrating frequency was associated with the highest probability of a photoparoxysmal response in patients with photosensitive epilepsy (Binnie et al., 1985). Achromatic gratings with a drifting or vibrating motion are particularly uncomfortable to view, when compared to a static grating (Haigh et al., 2012), and the vibrating motion is epileptogenic (Binnie et al., 1985). These stimuli vary in their 'strength' which should offer a range of cortical stimulation sufficient to measure any relationship between the amplitude and the shape of haemodynamic responses.

General methods

Participants

Nineteen females and three males from the University of Essex participated in the study; mean age 21.2 (range 18–54). All had a minimum of 6/6 visual acuity (Lighthouse Test for Near and Far Visual Acuity), a minimum stereo acuity of 60 s·arc (Titmus test; Stereo Optical Co. In., Chicago, IL, USA), and showed no red–green colour deficiencies (Ishihara plates). This study complied with the Code of Ethics of the World Medical Association (Declaration of Helsinki), and was approved by the University of Essex Review Board. All participants gave their informed consent.

Apparatus

The stimuli were displayed on a 24″ LCD screen (Dell corporation model 2408) with a backlight modulation frequency of 162.5 Hz. The Michelson contrast of the modulation was 0.86. For the chromatic gratings, the screen was powered by a Mac G4 Powerbook. For the moving gratings, the screen was powered by a Dell Precision M4500 laptop. A photo diode and associated electronics provided a trigger for the NIRS system.

Stimuli for experiment 1 — static chromatic gratings

Gratings were displayed using SuperLab version 4.0.7b. To select the chromaticities, the three extremes of the screen gamut (red pixels only, green only and blue only) were measured using a telespectroradiometer (model PR-670®, Photo Research®, Chatsworth, CA, USA). The isoluminant midpoints (29 cd/m^2) between each of the three extremes were calculated. Chromaticities equidistant from either side of the midpoint were then used in alternating stripes to create red–green (RG), green–blue (GB) and red–blue (RB) grating patterns. The spatial frequency of the patterns was 2 cpd at a viewing distance of 1 m. Three colour pairs were created for each gamut extreme: a small separation of chromaticities in the CIE UCS diagram (mean separation of the chromaticities = 0.03), a medium separation (mean separation of the chromaticities = 0.19) and a large separation (mean separation of the chromaticities = 0.43). The gratings were circular in outline, subtended 10°, and were surrounded by a grey field of similar luminance. A central black fixation cross was shown throughout the trial (subtending 1.3° of visual angle). The order of the stimuli was randomized and each pattern was presented twice.

Stimuli for experiment 2 — static and moving achromatic gratings

Horizontal gratings were created and presented in MATLAB® using the PsychToolbox extension (Brainard, 1997; Pelli, 1997; Kleiner et al., 2007). All the gratings were achromatic (CCT 4000 K) and had a square-wave luminance profile. The contrast of the gratings was vignetted with a Gaussian filter to reduce edge effects. At half-contrast the gratings subtended 9.1° of visual angle. The gratings had a spatial frequency of 2 cpd. Vibrating and drifting gratings moved vertically with a contour velocity of 5°/s (10 Hz), and to prevent optokinetic nystagmus, they moved symmetrically in opposite directions either side of a horizontal midline (upwards in the upper field and downwards in the lower). The profile of motion for the vibrating grating was a triangle wave: the grating drifted vertically at a constant velocity either up or down through one half spatial cycle before abruptly reversing direction. The stimuli were presented in the following order: drifting, vibrating, static, static, vibrating, drifting, static, drifting, vibrating, vibrating, drifting, static, vibrating, static, drifting, static, vibrating, and drifting.

Procedure

The haemodynamic response was measured using a 10 channel split-receiver near infrared spectroscopy (NIRS) system (Oxymon Mk II Artinis Medical Systems BV Zetten, Netherlands). The optode placement is shown in Fig. 1. Two receivers were placed symmetrically 20 mm above the inion and 30 mm either side of the midline. Two transmitters were then placed vertically 30 mm from the receiver, covering

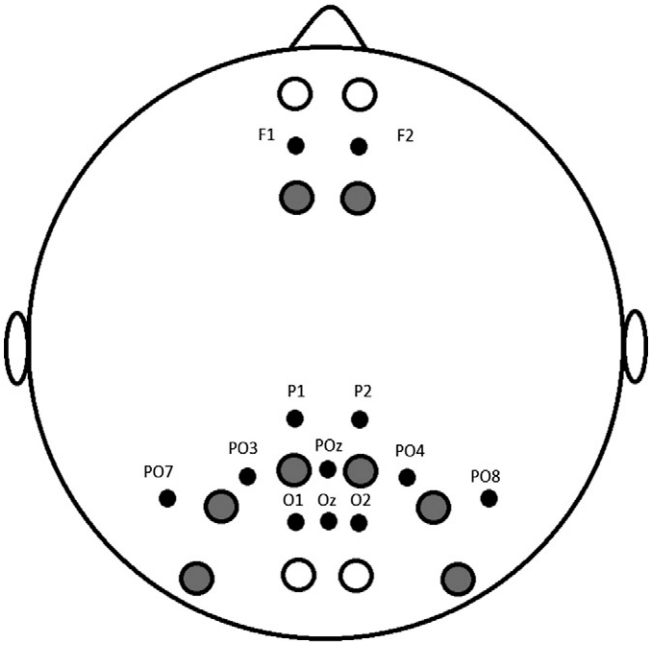

Fig. 1. The layout of the NIRS optodes. The grey circles show the NIRS transmitters, the white circles show the NIRS receivers, and the black circles show the 10–20 EEG electrode locations that were used as a guide for optode placement.