Neuroscience 311 (2015) 484–489

RIGHT HEMISPHERE DOMINANCE DIRECTLY PREDICTS BOTH BASELINE V1 CORTICAL EXCITABILITY AND THE DEGREE OF TOP-DOWN MODULATION EXERTED OVER LOW-LEVEL BRAIN STRUCTURES

Q. ARSHAD,[†] S. SIDDIQUI,[†] S. RAMACHANDRAN, U. GOGA, A. BONSU, M. PATEL, R. E. ROBERTS, Y. NIGMATULLINA, P. MALHOTRA AND A. M. BRONSTEIN [*]

Division of Brain Sciences, Charing Cross Hospital Campus, Imperial College, Fulham Palace Road, London W6 8RF, UK

Abstract—Right hemisphere dominance for visuo-spatial attention is characteristically observed in most right-handed individuals. This dominance has been attributed to both an anatomically larger right fronto-parietal network and the existence of asymmetric parietal interhemispheric connections. Previously it has been demonstrated that inter-hemispheric conflict, which induces left hemisphere inhibition, results in the modulation of both (i) the excitability of the early visual cortex (V1) and (ii) the brainstem-mediated vestibular–ocular reflex (VOR) via top-down control mechanisms. However to date, it remains unknown whether the degree of an individual's right hemisphere dominance for visuospatial function can influence, (i) the baseline excitability of the visual cortex and (ii) the extent to which the right hemisphere can exert top-down modulation. We directly tested this by correlating line bisection error (or pseudoneglect), taken as a measure of right hemisphere dominance, with both (i) visual cortical excitability measured using phosphene perception elicited via single-pulse occipital trans-cranial magnetic stimulation (TMS) and (ii) the degree of trans-cranial direct current stimulation (tDCS)-mediated VOR suppression, following left hemisphere inhibition. We found that those individuals with greater right hemisphere dominance had a less excitable early visual cortex at baseline and demonstrated a greater degree of vestibular nystagmus suppression following left hemisphere cathodal tDCS. To conclude, our results provide the first demonstration that individual differences in right hemisphere dominance can directly predict both the baseline excitability of low-level brain structures and the degree of top-down modulation exerted over them.

Key words: right hemisphere dominance, visual cortical excitability, vestibular–ocular reflex, line bisection, top-down modulation.

[*]Corresponding author.
E-mail address: a.bronstein@imperial.ac.uk (A. M. Bronstein).
[†] Both authors contributed equally.
Abbreviations: tDCS, trans-cranial direct current stimulation; TMS, trans-cranial magnetic stimulation; VOR, vestibular-ocular reflex.

INTRODUCTION

Disrupting the right lateralized fronto-parietal attentional network to induce interhemispheric competition has previously been shown to modulate low-level brain function. Specifically, these modulatory effects have been shown to influence both visual cortex excitability and the brainstem-mediated vestibular–ocular reflex (VOR) (Silvanto et al., 2009; Arshad et al., 2013b) Such modulation was suggested to occur due to left hemisphere inhibition (Silvanto et al., 2009; Arshad et al., 2013b), owing in part to the fact that the right hemisphere is dominant for visuospatial function in right-handed individuals (Kinsbourne, 1977).

Right hemisphere dominance for spatial functions has been attributed to the existence of an anatomically larger right parieto-frontal network that correlates with visuo-spatial ability (De Schotten et al., 2011) and the presence of asymmetric parietal interhemispheric connections, which allows for the right hemisphere to exert a greater degree of inhibition (Koch et al., 2011). However to date, it remains unknown whether individual differences in the degree of right hemispheric dominance can influence (i) the baseline excitability of the visual cortex and (ii) the extent to which top-down modulation can be exerted over the brainstem-mediated VOR.

Herewith, we directly tested for this by correlating line bisection error (sometimes referred to as 'pseudoneglect'), taken as a measure of right hemisphere dominance, with (i) baseline visual cortical excitability and (ii) the degree of vestibular nystagmus suppression following left hemisphere cathodal trans-cranial direct current stimulation (tDCS).

EXPERIMENTAL PROCEDURES

Subjects

Twenty-eight right-handed subjects (Handedness score over 40 (Oldfield, 1971) participated in the study (15 female, age range 19–24 years, mean age 22 years). Note, our power calculation revealed that in order to achieve a correlation coefficient of 0.65 and above, at an alpha value of 0.05 (two tails) and power of 0.9, would require 28 participants. All subjects were naive to the purpose of study and had no history of otological, ophthalmological, psychiatric or neurological disorders. All subjects

http://dx.doi.org/10.1016/j.neuroscience.2015.10.045
0306-4522/© 2015 The Authors. Published by Elsevier Ltd. on behalf of IBRO.

provided written informed consent as approved by the local ethics research committee.

Line bisection task

Each subject performed 10 line bisection trials. For each trial a single centralized 20-cm long and 1-mm wide black line was presented to the subject on a horizontally orientated A4 paper sheet. Subjects were required to bisect the line at the perceived mid-point with a red ballpoint pen. Five trials were performed with the right hand and the remaining five trials were performed with the left hand (randomized order). In each trial we calculated the deviation in mm from the true center (De Schotten et al., 2011). For each subject we summed the 10 individual deviation values and calculated the mean deviation. A positive line bisection error denoted a bias to the right of the true center, whereas a negative error denoted a bias to the left.

Threshold measurement of visual cortical excitability

Application of single-pulse trans-cranial magnetic stimulation (TMS) over the occipital cortex elicits the illusionary percept of a brief flash of light. This illusionary percept is termed a phosphene and the intensity of TMS required to elicit these percept's are suggested to reflect the underlying excitability of the visual cortex (Boroojerdi et al., 2002). That is, if low intensities of TMS (i.e. a low % of the total maximum stimulator output) can elicit phosphenes, it implies that the underlying cortical excitability is high and vice versa.

Biphasic TMS pulses were administrated with a Magstim 200 stimulator (Magstim Co, UK). We used a 70-mm figure of an eight-shaped coil, always held with the handle turned laterally. For V1 the coil was placed centrally over the inion until the brightest stationary phosphene was reported in the central visual field (Arshad et al., 2014a). For V5, TMS was applied 3 cm vertically up and 5 cm laterally (either right or left) from the inion until the brightest moving phosphene was detected (Seemungal et al., 2013). The participants were asked to verbally describe the phosphene and its perceived location in terms of its position superimposed upon an imagined clock face. Initially, the intensity of the stimulation was set at 68% of the maximum stimulator output, but this was increased if the participants did not perceive a phosphene.

Visual cortical thresholds were established by implementing a modified binary search (MOBS) paradigm. Adopting this paradigm allowed for us to determine the intensity of TMS required to elicit a phosphene 50% of the time (i.e., threshold). This paradigm utilizes an adaptive procedure, whereby the initial stimulus value (TMS pulse) is presented at a value which represents the bisection of an initial upper and lower boundary pair. These boundary pairs are continually updated based upon the subject's prior response to each TMS pulse (e.g. a positive subjective response will shift the boundary downward and vice versa). The actual threshold was determined after subjects made three consecutive alternate choices in order to minimize variability. Once, we had established the threshold we ascertained whether it was correct by applying a trial sequence of 20 TMS pulses. Each of the 20 TMS pulses were separated by 6 s and the subject had to respond verbally with either a "yes" or "no" response to whether they had perceived a phosphene following each TMS pulse. If the established threshold was correct then we observed 10 (+ or − 2 i.e. between 8 and 12) yes responses (Arshad et al., 2014a). If the number of "yes" responses was outside this range, the threshold was re-established.

Vestibular stimulation and eye movement recording

Following otoscopy to exclude local contra-indications, subjects underwent caloric stimulation to elicit the vestibular-ocular reflex (VOR). Participants lay supine on a couch with the head tilted up by 30° in order to obtain maximal horizontal semi-circular canal activation. Caloric irrigations were performed with cold water (i.e. 30 °C; 7 °C below core body temperature) with a flow rate of 500 ml/min for 40 s (CHARTR VNG; ICS medical). In response to the caloric stimulation an oculomotor response is elicited in the form of 'vestibular nystagmus'. The onset of nystagmus and the perceptual state of vertigo typically begins approximately 20 s after the start of the irrigation reaching a peak at around 60 s. The total duration of the response lasts on average 3 min in total (Fitzgerald and Hallpike, 1942).

Right cold caloric irrigations induce left-beating vestibular nystagmus (i.e. beating toward the non-stimulated ear) with a rightward slow phase component. Conversely, left cold caloric irrigations elicit a right-beating vestibular nystagmus. Eye movements were recorded using a head-mounted infra-red binocular video-oculography (VOG) system (CHARTR VNG; ICS medical). Eye movements were analyzed using a computerized automatic analysis program (CHARTR VNG; ICS medical) that removed the fast phases of the nystagmus and plotted each individual slow phase velocity over a period of 100 s. The response intensity was determined by identifying the peak slow phase eye velocity.

tDCS

Stimulation was applied using a battery-driven stimulator (neuroConn GMBH, ilmenau, Germany). We applied either unipolar cathodal (test condition) or anodal (control condition) tDCS, over the left hemisphere (P3: international 10–20 system for EEG electrode placement; electrode placement area 25 cm^2). The reference electrode was always placed over the ipsilateral shoulder, with a larger electrode placement area of 35cm^2 in order to maximize subject comfort. This specific stimulation montage was employed as our previous work has shown that left hemisphere cathodal stimulation induces vestibular nystagmus suppression. Left hemisphere anodal stimulation has previously been shown to have no modulatory effect upon the VOR; thereby implementing this condition allowed for us to control for non-specific effects that could be attributed to electrical stimulation. The current had a ramp-up time of 10 s at which point a