Galvanic Vestibular Stimulation Induces a Spatial Bias in Whole-body Position Estimates

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Brain Stimulation

DOI:
10.1016/j.brs.2015.07.030

Published: 01/09/2015

this particular recurrence of migraine with aura. Originality of this case report illustrates the complexity of the risk-benefit analysis in the rTMS treatment for patients suffering from chronic pain disorders.

The authors declare no conflict of interest related to this publication.

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Received 30 June 2015
Available online 11 August 2015

http://dx.doi.org/10.1016/j.brs.2015.07.028

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Galvanic Vestibular Stimulation Induces a Spatial Bias in Whole-body Position Estimates

Dear Editor,

Peripheral galvanic vestibular stimulation (GVS) has been shown to temporarily ameliorate left spatial neglect [1]. Specifically, anodal (facilitatory) stimulation over the left mastoid bone coupled with cathodal (inhibitory) over the right mastoid reduces visuospatial-neglect scores in line cancellation [2] and line bisection tasks [3,4]. This montage increases activity in the left vestibular nerve and suppresses activity in the right [5], which has been shown to focally activate vestibular networks that occupy visuospatial attention mechanisms, primarily in the non-dominant hemisphere [5]. Thus, it appears that electrical stimulation of the peripheral vestibular system can shift visuospatial attention to the left side of space [4]. However, whether such a shift of spatial attention in normal subjects can influence perception of spatial position during whole-body spatial translations is unknown. We hypothesized that shifting attention to the left would result in participants underestimating spatial position estimates during rightward whole-body translations and overestimating spatial position estimates during leftward whole-body translations.

12 right-handed healthy males (mean age 21.6 years (SD = 3.1)) participated in this randomized cross-over study. Participants provided written informed consent. The study was approved by the local ethics committee. Participants were blindfolded and stood with their feet shoulder-width apart upon a computer controlled linear sled, running on a level track along the inter-aural axis (Fig. 1A). Participants were asked to stand upright with their head facing straight ahead and hold onto a sled-mounted support to minimize body movement – verified by trunk (C7) position recordings (Fastrak tracking system, Polhemus, VT, USA). Conductive electrode pads (4 cm × 5 cm) were positioned over the right and left mastoid bones. DC Stimulation was delivered at 1 mA [4] either continually during sled movement 'continual stimulation' or for a single brief pulse at the onset of sled movement 'sham stimulation'. The stimulation conditions were: left anode/right cathode (LA/RC), right

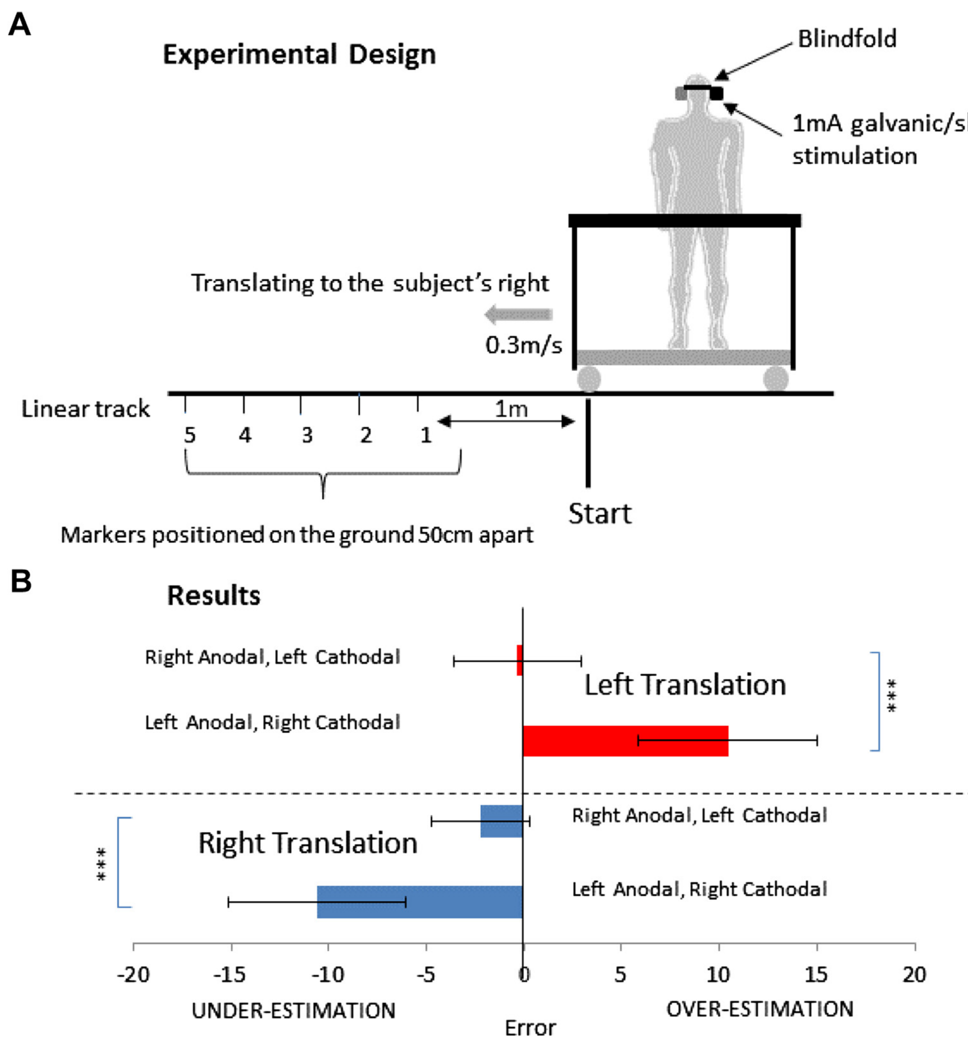

Figure 1. (A). Experimental design. Subjects were blindfolded and stood on a linear sled. Electrode pads were fixed over the mastoid bones on the right and left side which delivered either RA/LC, LA/RC or sham galvanic stimulation. The sled was translated rightwards or leftwards and participants were asked to estimate how far they thought the sled had moved, providing a number in the numerical experiment or a letter in the alphabetic experiment. The figure represents a rightward translation. (B). Mean error scores (±SD) for the numerical interval experiment. The numerical experiment showed that subjects underestimated the distance moved less for rightward translations and overestimated for leftward translations during left anodal/right cathodal stimulation.

anode/left cathode (RA/LC) or sham, performed in a randomized order.

Each trial began with the sled at position zero (start) and then translated either leftward or rightward at a constant velocity of 0.3 m/s [6], ramp up/ramp down time: 1.0 s; well above translational thresholds [7]. Possible stopping positions were a series of five equally spaced positions beginning 1 m from the start position, labeled "1 to 5" separated by 50 cm intervals along the same path as the linear track, akin to a ruler on the floor (Fig. 1A). Participants performed five practice runs through the positions 1–5 with visual feedback (raising the blindfold).

For each stimulation condition, participants were translated to each of the five possible stopping positions in each direction four times in a randomized order, giving a total of 40 trials (4 repeats × 5 positions × 2 directions) per stimulation condition (LA/RC, RA/LC or sham). For each trial participants estimated the position number they thought they had stopped at. To control for possible numerical biasing, we performed the same experiment using letters of the alphabet as markers (A–G) [8] in five naive right-handed males.

In each condition, we summed the error from each trial for each subject taking into account the polarity of each error as positive (overestimate) or negative (underestimate). The total error during the sham condition was subtracted from the total error in the galvanic condition, thus controlling for baseline performance.

As shown in Fig. 1B, LA/RC GVS modulated perceived spatial position estimates in a direction specific manner. A 2 × 2 repeated-measures ANOVA, with factors stimulation side (2 levels: LA/RC, RA/LC) and translation direction (2 levels: right, left), revealed a significant main effect of direction ($F[1,11] = 91.3$; $P < 0.001$) but not stimulation side ($F[1,11] = 0.73$; $P = 0.41$), and a significant Stimulation side × Direction interaction ($F[1,11] = 52.1$; $P < 0.001$). That is, GVS influenced the polarity of errors for leftward and rightward translations. Post-hoc paired *t*-tests showed that LA/RC GVS produced a significantly *smaller* estimate of distance moved during rightward translations ($P < 0.001$) and a significantly *larger* estimate during leftward translations ($P < 0.001$) compared to RA/LC stimulation (Fig. 1B). The same pattern of responses was found in the alphabetic experiment (Direction effect ($F[1,4] = 18.4$;

$P < 0.001$); Stimulation side × Direction interaction ($F[1,4] = 9.5$; $P = 0.02$)).

We provide the first demonstration that LA/RC GVS shifts estimates of whole-body spatial position. A possible explanation for this finding is an altered gain of the peripheral vestibular system. However, for this explanation to hold we would expect to observe biases for both active stimulation conditions, which we do not. Eye movements could also have influenced position estimates. GVS at around 1 mA is known to produce both torsional and weak horizontal eye movements toward the anode [9]. However, the fact that we did not observe position biases in both active stimulation conditions also rules out the possibility of a gaze-shift mediated effect.

The most parsimonious explanation for our results is that LA/RC GVS biased spatial attention during the position task. Previous studies have shown that this montage biases visuospatial attention to the left space [1,2,4]. We show that when participants perform a whole-body spatial position task, LA/RC stimulation induces a relative spatial bias toward left space which results in participants underestimating spatial position estimates during rightward whole-body translations, and overestimating spatial position estimates during leftward whole-body translations. Further, these biases are not secondary to numerical biasing as the alphabetical control experiment yielded identical results.

To conclude, our data indicates that LA/RC GVS induces hemispheric biases in spatial attentional networks which subsequently disrupts position estimates.

Acknowledgments

We acknowledge the technical assistance from Mr David Buckwell (Imperial College London).

We are supported by the UK Medical Research Council (MR/J004685/1).

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Received 10 July 2015
Available online 11 August 2015

http://dx.doi.org/10.1016/j.brs.2015.07.030

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Deep Brain Stimulation in a Dopaminergic Non-responsive Patient With Parkinson's Disease: Case Report and Systematic Review

Dopaminergic responsiveness is defined as a clinically relevant decrease in the Unified Parkinson's Disease (PD) Rating Scale (UPDRS) part III score after administration of a supra-threshold dose of levodopa or other dopamine agonists [1]. Dopaminergic responsiveness is generally considered related to the expected efficacy of Deep Brain Stimulation (DBS) and therefore a critical requirement in the selection of DBS-candidates [2–4].

In this letter we present a typical PD-patient who had an excellent response to DBS of the subthalamic nucleus (STN) despite profound unresponsiveness to dopaminergic medication. Intrigued by this apparently controversial experience, an extensive literature search was performed on this topic.

A 57-year-old male was referred to our university PD-clinic with a 10-year history of a progressive hypokinetic-rigid syndrome. The diagnosis idiopathic PD was made based on the patients history, neurological examination, and a series of additional diagnostic tests (Table 1). Nevertheless, the patient had no improvement of PD motor symptoms on levodopa/benserazide and dopamine agonists. Because of ongoing clinical deterioration in the absence of alternative treatment options, our multidisciplinary team ultimately decided to offer the patient DBS treatment. Quadripolar DBS-electrodes (model 3389; Medtronic) were bilaterally implanted in the STN and connected to a subcutaneous pulse generator (Activa; Medtronic). The surgical procedure was uneventful. At seven months follow-up, the patient is doing well without medication. With the stimulator off his UPDRS part III score is 35; with the stimulator on the UPDRS-score is 17.

An individual patient data meta-analysis based on original data from reports across all studies concerning all variables of interest was performed. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was used [5]. The literature databases MEDLINE, PubMed, EMBASE, and ISI Web of Science were screened with the search terms "Parkinson's disease" AND "DBS" AND "STN." All papers until November 2014 in the English literature were considered. Reference lists of selected papers were checked for related articles. The resulting