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Subliminal galvanic-vestibular stimulation recalibrates the distorted visual and tactile subjective vertical in right-sided stroke

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ABSTRACT

Stroke of the right cerebral hemisphere often causes deficits in the judgement of the subjective visual vertical (SVV) and subjective tactile vertical (STV) which are related to central vestibular functioning. Clinically, deficits in the SVV/STV are linked to balance problems and poor functional outcome. Galvanic Vestibular Stimulation (GVS) is a non-invasive, save stimulation technique that induces polarity-specific changes in the cortical vestibular systems. Subliminal GVS induces imperceptible vestibular stimulation without unpleasant side effects. Here, we applied bipolar subliminal GVS over the mastoids (mean intensity: 0.7 mA, 20 min duration per session) to investigate its online-influence on constant errors, difference thresholds and range values in the SVV and STV. 24 patients with subacute, single, unilateral right hemisphere stroke were studied and assigned to two patient groups (impaired vs. normal in the SVV and STV) on the basis of cut-off scores from healthy controls. Both groups performed these tasks under three experimental conditions on three different days: a) sham GVS where electric current was applied only for 30 s and then turned off, b) left-cathodal GVS and c) right-cathodal GVS, for a period of 20 min per session. Left-cathodal GVS, but not right-cathodal GVS significantly reduced all parameters in the SVV. Concerning STV GVS also reduced constant error and range numerically, though not significantly. These effects occurred selectively in the impaired patient group. In conclusion, we found that GVS rapidly influences poststroke verticality deficits in the visual and tactile modality, thus highlighting the importance of the vestibular system in the multimodal elaboration of the subjective vertical.

1. Introduction

The human brain constructs verticality perception by integrating vestibular, somatosensory and visual information. The correct perception of verticality is an important requirement for efficiently moving and acting in the world. An impairment of this ability frequently follows stroke as indicated by deviations of the patients' subjective visual vertical (SVV) larger than $\pm 2°$ from the earth vertical (Bender and Jung, 1948; Kerkhoff, 1999; Yelnik et al., 2002; Utz et al., 2011b). In this task patients have to judge when a rod, that is rotated mostly in the frontal (roll) plane, is aligned with the earth vertical. In addition to the visual domain, disturbed perception of verticality after stroke has been observed in the haptic modality. In the haptic variant of the task a rod has to be adepted with one hand (typically the nonparetic, ipsilesional hand) to the earth vertical (subjective tactile vertical = STV) while blindfolded. Tilts in these two sensory verticals are significantly associated with impairments in other perceptual tasks (i.e. line orientation judgments, constructional apraxia, visual neglect (Funk et al., 2013; Kerkhoff, 1999), balance problems (Bonan et al., 2007), a tilted subjective postural vertical (Perennou et al., 2008), and a poor functional outcome of the individuals with stroke (Funk et al., 2013). Those results have been interpreted in favor of a multimodal, graviceptive–vestibular pathway proceeding from the brainstem via the thalamus to temporoparietal multisensory cortical areas, and in case of a lesion leading to perturbations of the visual vertical (Brandt et al., 1994; Baier et al., 2012) or the tactile vertical (Funk et al., 2010a, 2010b). Moreover, some researchers postulate, that the right cerebral hemisphere elaborates an *integrated* verticality representation across different modalities (Perennou et al., 2008). As a consequence, lesions of the right hemisphere, i.e. due to stroke, might compromise perception of the vertical in a multimodal way.

Abbreviations: GVS, galvanic-vestibular stimulation; SVV, subjective visual vertical; STV, subjective tactile vertical

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As the vestibular system plays a significant role in the computation of the subjective vertical, its activation may modulate the verticality perception. For this purpose electrical stimulation of the vestibular system can be induced by placing one electrode behind each ear over the left and right mastoid respectively (termed galvanic vestibular stimulation or GVS, for review see Utz et al., 2010). Underneath the mastoids the vestibular nerve projects from the inner ear to the vestibular brain stem nuclei, over thalamic nuclei to a number of distributed cortical vestibular areas including area 2cv near the central sulcus, area 3a, b in the somatosensory cortex, parietal area 7a, and the parieto-insular-vestibular-cortex (PIVC). Although there is no primary vestibular cortex as in the visual, auditory or tactile modality, the above mentioned array of multiple, interconnected vestibular cortical areas is thought to be under the control of the PIVC (Guldin and Grüsser, 1998). Practically, GVS consists of applying direct current to the mastoids – usually delivered by a small battery-driven constant current stimulator. The positive electrode is termed the anode, the negative the cathode. Consequently, the two following electrode combinations are typically used for GVS: left-cathodal/right-anodal (CL) and right-cathodal/left-anodal (CR) GVS. Subliminal GVS can be administered by adjusting the current intensity below an individual's sensory threshold. This has the methodological advantage that different GVS protocols and polarities can be manipulated elegantly without the patient's knowledge (whether real current is flowing or not) that might otherwise influence his/her performance due to "spatial cueing" effects induced by a tingling sensation under one electrode. Furthermore, GVS is painless, easily applicable, safe, and induces minimal side effects when used in accordance with standard safety guidelines (Utz et al., 2011c).

GVS as a stimulation method has significant effects on a wide variety of cognitive and perceptual tasks, both in healthy persons and neurological patients (for review see Utz et al., 2010). For example, Wilkinson and co-workers found that GVS facilitated visual memory recall in healthy persons (Wilkinson et al., 2008) and improved visuo-constructive deficits in a right-hemisphere lesioned patient (Wilkinson et al., 2010, 2014). Similar studies showed modulatory effects of GVS on somatosensory deficits (Schmidt et al., 2013a) and different components of visual neglect (Utz et al., 2011a, 2011b; Oppenländer et al., 2014) thus demonstrating multifaceted effects on neuropsychological functions or deficits.

The first study that assessed the influence of GVS on verticality perception in healthy subjects found a shift of the visual and tactile vertical towards the anode (Mars et al., 2001). In a recent study (Volkening et al., 2014) the SVV and STV shifted towards the anode during GVS, whereas this shift was reversed towards the cathode in both modalities once stimulation was turned off. Overall, the effects were strongest for the haptic modality. Evidence from a recent clinical study (Saj et al., 2006) in right-hemisphere lesioned patients with vs. without visual neglect showed that left-cathodal GVS reduced the constant error in the SVV. Whether GVS also affects performance in the STV is unknown, to the best of our knowledge. Moreover, performance of impaired persons in both sensory verticals (visual, tactile) is most often characterized by two features: a frequently observed directional error (= the counterclockwise or clockwise tilt in the frontal or roll plane) and/or a reduced precision or pathologically increased variability as indicated by raised difference thresholds or huge ranges in these tasks (Kerkhoff, 1999; Utz et al., 2011a). These latter types of errors are frequently observed in patients with a tilted SVV or STV (Funk et al., 2010b, 2013) and are significantly related to disturbed spatial behavior as well (i.e. line orientation judgments, Funk et al., 2013) or balance problems (Bonan et al., 2007). Hence, both from a theoretical and a clinical viewpoint, it would be important to know whether GVS modulates not only the constant (directional) errors but also those parameters that indicate a reduced precision and higher variability in the SVV and STV. Finally, we sought to analyze whether modulatory GVS effects occur *selectively* in patients with disturbed SVV/STV or are also found in those patients without a deficit in these sensory axes.

Our research questions for this study were hence threefold: 1) Does GVS modulate constant/directional errors in the SVV and STV? 2) Does GVS modulate the precision in the SVV/STV as expressed by difference thresholds and range of performance? 3) Are the modulatory effects induced by GVS specific for patients with an impaired SVV/STV or do significant effects also occur in patients who are unimpaired in these tasks?

2. Methods

2.1. Patients

The study was approved by the local ethics committee (Ärztekammer des Saarlandes, Nr. 147/08, 16.9.2008) and included 24 patients with unilateral right-sided stroke (Table 1). Inclusion criteria were right-handedness and a single right hemisphere infarction or hemorrhage. Exclusion criteria were other neurological or psychiatric diseases, epilepsy, a sensitive scalp skin and metallic brain implants (Iyer et al., 2005). The participants were 9 women and 15 men with a median age of 63.6 years (range 42–84 years), and a median time since lesion of 2 months (range: 1–84 months). Patients were allocated into an "impaired" or "unimpaired" group depending on their performance in the SVV or the STV tasks (described below) separately. Normative data for both tasks had already been collected in a previous study (Kerkhoff, 1999). The cut-off-score for the constant error was 2.0° for the SVV and 2.5° for the STV. Healthy controls did not participate in the present study (see Table 1).

For both the SVV and STV the patients were allocated to a patient group *with or without a spatial deficit in the SVV or STV* (termed impaired or unimpaired) depending on their performance in the sham condition in both tasks. Further information about the patient sample and additional clinical assessments (i.e. visual neglect, visual field, motor status) can be found in the companion paper in this special issue on "Brain stimulation and Attention" (see Oppenländer et al., 2014). The sample studied in the present study was identical to that in the companion paper. All patients had a corrected visual acuity for the near distance (0.4 m) of at least 0.7 (=70%, 7/10).

2.2. Experimental procedures

In the first session the stimulation threshold for GVS was determined in all subjects. After fixing the electrodes, galvanic bipolar stimulation was delivered by a constant direct current (DC) stimulator (9 voltage battery, Type: ED 2011, manufacturer: DKI GmbH, DE-01277 Dresden). The carbon-rubber electrodes (50 mm × 35 mm) were fastened on the skin over each mastoid (binaural stimulation), in order to activate the peripheral vestibular organs. The conditions were termed Cathode Left (CL) when the cathode was placed over the left mastoid and the anode on the right, and Cathode Right (CR) when polarization was inversed. Similar to others (Rorsman et al., 1999) we stimulated below the sensation threshold (subliminal) in order to prevent awareness of any electrical stimulation in the 3 experimental conditions. A switch on the stimulation device delivered current at individually adjusted levels for each patient. This threshold was individually determined in this first session by slowly increasing current intensity in steps of 0.1 mA until the participant indicated a tingling sensation (first threshold). The current was subsequently reduced