Heliyon 9 (2023) e22194

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Modification of cortical electrical activity in stroke survivors with abnormal subjective visual vertical: An eLORETA study

Meymaneh Jafari [a], Moslem Shaabani [a], Seyed Ruhollah Hosseini [b], Hassan Ashayeri [c], Enayatollah Bakhshi [d], Hojjat Allah Haghgoo [e,*]

[a] *Department of Audiology, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran*
[b] *Department of Psychology, Faculty of Education Sciences and Psychology, Ferdowsi University of Mashhad, Mashhad, Iran*
[c] *Rehabilitation Research Center, Department of Basic Sciences, School of Rehabilitation Sciences, Iran University of Medical Sciences, Tehran, Iran*
[d] *Department of Biostatistics, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran*
[e] *Department of Occupational Therapy. University of Social Welfare and Rehabilitation Sciences, Tehran, Iran*

ARTICLE INFO

Keywords:
Stroke
Subjective visual vertical (SVV)
Vertical perception
EEG
eLORETA
Resting-state network

ABSTRACT

Objectives: Balance impairment is among the main complications of stroke. The gravity-based subjective vertical (SV) is considered an important reference for upright posture and navigation affected by stroke. The correlation between injury location and pathological perception of verticality remains controversial. This study aimed to evaluate the cortico-cortical network of vertical perception among patients with the right hemisphere stroke and abnormal visual-vertical perception compared with healthy individuals.

Materials and methods: This observational cross-sectional study included 40 patients with the right hemisphere stroke and 35 healthy participants. All patients had abnormal visual-vertical perception. The EEG connectivity analysis was conducted through the exact low-resolution brain electromagnetic tomography analysis (eLORETA).

Results: Stroke survivors manifested a power spectral density that reduced within the beta-2 frequency band in the left hemisphere and increased within the beta-3 frequency band in the right hemisphere compared with controls ($p < 0.01$). The lagged-phase synchronization was increased within alpha-1, beta-2, and beta-3 bands and decreased in stroke survivors compared with controls in the vestibular network involved in visual-vertical perception ($p < 0.01$).

Conclusion: The results of this study demonstrated variations in the function and functional connectivity of cortical areas involved in the visual-vertical perception that are mainly located in the vestibular cortex.

1. Introduction

The vestibular system provides information regarding the translation, rotation, and orientation of the head in a gravitational environment [1]. With this information, the gravity-based subjective vertical (SV) is considered an important reference for upright posture and navigation. This reference helps maintain the position of the body and move the body relative to the surrounding

---

[*] Corresponding author. Department of Occupational Therapy, The University of Social Welfare and Rehabilitation Sciences, Kodakyar St, Daneshjo Blvd, Evin, Tehran, 1985713831, Iran.

E-mail address: haghgooh@gmail.com (H.A. Haghgoo).

https://doi.org/10.1016/j.heliyon.2023.e22194
Received 31 May 2022; Received in revised form 16 September 2023; Accepted 6 November 2023

environment by combining vestibular, visual, and proprioception information and vertical representations [2,3]. Constant central nervous calculations and representations of signals provided by peripheral vestibular organs are the prerequisites for an individual's ability to stand upright and perform bi-pedal moves [4].

Brain injuries such as strokes can damage these representations. With the rapid growth in the elderly population and considering genetic factors, the number of stroke patients will increase [5,6]. Having severe impacts on an individual's gait or ability to perform daily activities independently, balance impairment is among the main complications of stroke [7]. Subjective verticality (SV) is also affected in stroke by rotating in the opposite direction of the lesion in the frontal plane (roll) and tilting the subjective vertical line [8]. Therefore, spatial representation errors lead to positional disorders. The SV errors that occur in the first three months after stroke can predict imbalance and dependence of patients within the following six months; hence, they can be considered an important factor in the occurrence of functional disability in the activities of daily living (ADLs) [9].

According to the examination of cortical areas involved in vertical perception in healthy individuals, the basis of visual vertical judgment is a wide and bilateral cortical networking consisting of different areas such as the occipital cortex, lingual gyrus, cuneus, precuneus, cerebellum, and brainstem. The results of neuroimaging performed in patients with brain injuries indicated that several cortical areas could be involved in the vertical perception cortical network [2]. Vertical misjudgments have been reported in patients with damage to the temporal and parietal cortices, posterior insula, inferior frontal gyrus, upper temporal gyrus, and rolandic operculum [10]. The areas mentioned in various studies (on stroke survivors or healthy people) for vertical perception are parts of the cortical vestibular network [1].

After stroke, variations in the resting-state EEG frequency characteristics may represent underlying structural changes. Evidently, brain networks with a large group of neurons or a large spatial amplitude oscillate at lower frequencies [11]. The study of cortical rhythms is especially suitable for the study of the vestibular cortex, which includes a distributed (extensive) network of multisensory brain regions [12]. With the evolution of neuroimaging techniques, communication models within the human brain have been designed functionally and structurally. In this regard, the concept of connectome was introduced by Sporns et al. (2005). Disease connectomics and comparative connectomics have received a great deal of attention for the analysis of common differences and substrates within and among species [1]. The study of human lesions allows for relevant clinical interpretations [13], and connectome localizations can set new therapeutic goals for patients with complex neurological and psychological symptoms [14].

Raiser et al. (2020) identified a very precise organization of cortical vestibular connections [1]. According to the research findings, injuries to the right hemisphere cause more vestibular symptoms and impairment of vertical perception than injuries to the left hemisphere, and these symptoms last longer [1]. However, Yelnik et al. (2002) found no correlation between impaired visual vertical perception and injury location in patients with right and left hemisphere strokes [15].

Some studies do not confirm the correlation between vertical perception and location of injury [15,16], and because previous studies have provided conflicting results; hence, the relationship between injury location and pathological perception of verticality still remains controversial [10]. A recent pilot study addressed some cortical areas in vertical perception [17].

Furthermore, functional neuroanatomy and precise connections between regions identified in vertical perception are still uncertain. This study aimed to evaluate the cortico-cortical network of vertical perception among patients with the right hemisphere stroke and abnormal visual vertical perception in comparison with healthy individuals through brain mapping (EEG neuroimagimg method). The network was analyzed with accuracy and details based on the centrality of individual nodes in the vestibular network.

2. Methods

2.1. Research design and participants

This observational and exploratory cross-sectional study was conducted in the audiology department of Rofeideh Rehabilitation Hospital in Tehran. The patients experienced a confirmed unilateral stroke of the right hemisphere the first time during the past year based on MRI results without regarding the affected arterial territory. The inclusion criteria for stroke survivors were as follows: age below 60 years, stable neurological condition, abnormal visual vertical perception, absence of cerebellar injuries, mini-mental status examination score (MMSE) above 21, left hemiparesis due to lesion in the right hemisphere, and right-handedness (A score above 18/20 in the *Edinburgh Manual Excellence Questionnaire* [18]), to eliminate any lateralized effects due to manual superiority that may interfere with lateralization of vestibular processes [19,20].

The exclusion criteria were as follows: history of brain disease, epilepsy, head trauma, vestibular disorders (peripheral occulomotor disorders or nystagmus), major mental disease, visual acuity below 3/10 after correction, addiction to or use of any medication interfering with neural activities or cerebral blood flows, aphasia, visual field impairment, hemineglect, apraxia, history of alcohol use,

Table 1

Demographic and clinical features of subjects included in the study sample.

group	Age (years)	gender	SVV[a] (degree)	Day after onset	Lesion side	etiology	Additional signs and symptoms
Stroke Survivor	52.3 ± 4.3	Female (52.5 %) Male (47.5 %)	−5.6 ± 1.2	162 ± 13	Right	Ischemic	Left Hemiparesis
Normal	49.8 ± 3.6	Female (54.5 %) Male (45.5 %)	1.3 ± 0.7	none	none	none	none

[a] Subjective Visual Vertical (SVV).

and severe cognitive impairment preventing the patients from perceiving instructions orally or written.

According to these criteria, 40 patients with right hemisphere strokes were selected. The average time from the onset of stroke to participation in the study was 162 ± 13 days.

The patients were compared with 35 healthy participants in terms of age and education. The healthy volunteers were all right-handed. They had normal or corrected vision and reported no history of vestibular, neurological, or mental diseases. They also did not take any medicine on a regular basis.

Table 1 reports the characteristics of participants. According to the Declaration of Helsinki, after the study method was fully explained to the participants, they signed written informed consent forms and ensured that their participation in the research is voluntary and they were able to withdraw from the study in every stage of the data collection process. Following their consent, data were collected in the participant's convenient time and day. The exploratory study was approved by the Ethics Committee (University of Social Welfare and Rehabilitation Sciences, Tehran, Iran; (with number IR. USWR.REC.1398.118).

3. Clinical evaluation

3.1. Subjective visual vertical (SVV)

Visual vertical perception was clinically assessed with SVV evaluation to determine the inclusion criteria. The tools used in this evaluation included SVV goggle and SVV-VII software (Synapsys, Inventis Co, Italy). A value of 0 indicates that the line is aligned with the objective vertical with respect to the convention that a negative rotation corresponds to a counterclockwise deviation (to the left) and a positive rotation corresponds to a clockwise deviation (to the right).

Every participant sat on a chair in a dark room, and straps were placed around their torsos and heads to keep the body upright and prevent any unwanted movements. The SVV evaluation was then performed. Glasses were placed on their faces to cover the entire field of vision. Only through a circular output could a person view the scene. In this method, the visual scene is narrowed to a circular surface (25 cm in diameter) to prevent any vertical and horizontal reference interferences. (See Lopez et al., 2009 [21] for similar methods). A 15-cm long beam of light was presented on the screen (Full HD 1080p LED, 43" screen, 1920×1080 resolution, LG, Korea) in line with the level of the person's eye 1.2 m away from the person's face (nasion) (Fig. 1). The beam of light was tilted to the left and right by the tester using arrow keys on a keyboard (tilt resolution = 0.2°), and the participant would notify the tester when the beam was in the vertical position. The participant then closed his/her eyes for a few seconds, and the next test beam was shown for 1500 ms with an intermittent interval of 3000–1500 ms (false random jumps). Ten trials were then presented to the individual in a false random sequence. The means and standard deviations of ten deviations were calculated for the subjective vertical per person. A tilt value above ±2.6° was considered pathological. The final mean deviation was obtained in stroke survivors as well as those in the control group.

3.2. Electroencephalography (EEG)

3.2.1. Data collection

The experiments were conducted when every participant was sitting on a comfortable chair in a quiet room. They were asked to stay still as long as they could, close their eyes, minimize eye movements, calm their minds, and control the movements of their tongues and muscles of the forehead, neck, and jaw to reduce extracranial artifacts. The raw EEG data were collected for approximately 3 min in the rest and relaxed state. Their mastoids and foreheads were gently cleansed with abrasive alcohol to remove any grease and dirt from the skin. The EEG was recorded from 32 cranial locations, according to the International System of 10–20 through electrodes mounted on a Waveguard™ cap (ANT Neuro, Enschede, the Netherlands). The 33rd electrode was placed 10 % anterior to Fz (called GND electrode, AFz position) as a common reference. The EEG cap was placed on the individual's head so that the Cz electrode would be aligned with the prearticular points of the frontal plane and with the nasion and inion points of the sagittal plane. An electro-gel (ELECTRO CAP CENTER, Nieuwkoop, the Netherlands) was used between the skull and the electrodes to keep the electrode impedances below 5 KOhm to prevent any polarization effects.

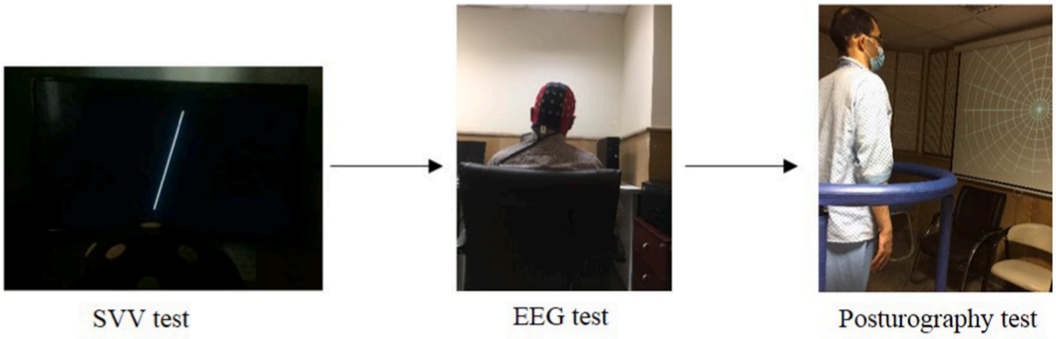

Fig. 1. Schematic picture of evaluation process.

The EEG data were recorded by using asalab ® software and amplifiers (ANT Neuro, Enschede, the Netherlands) at a sampling rate of 256 Hz. Moreover, a 0.1–100-Hz band-pass filter and a 50-Hz notch filter were utilized for surveillance, blinking, and other artifact-related movements. All raw EEG signals were stored for offline analysis.

3.2.2. *Pre-processing*

The preprocessing was performed in MATLAB (version 2014a, Mathworks, Inc., Natick, MA, USA) through the EEGLAB toolbox (version v13.4.4 b), and the recorded raw data were filtered by using a linear finite impulse response (FIR) bandpass filter (1–80 Hz). EEG artifacts were manually removed by visual inspection of the topographies and time courses of the components by a skilled and certified electroencephalographer. In order to avoid EEG and behavioral drowsiness, the expert examiner monitored the subject and the final appearance of EEG drowsiness, if there was any, verbally gave the subject the necessary instructions and warnings. Such EEG drowsiness was also rejected in data processing. Therefore, EEG data with low-amplitude basal rhythms (less than 10 μV) were excluded. Eye and muscle artifacts were also rejected. These activities are usually shown with amplitudes greater than 100 μV. Then the independent component analysis (ICA) was performed to remove other small value artifacts including blink, eye movements, auditory artifacts, persistent scalp muscle activity, electrode noise or other motion-related artifacts. ICA was applied using the RUNICA algorithm implemented in EEGLAB. Each component classified with a probability rating >0.8 for any class of artifacts (line noise, channel noise, muscle activity, eye activity, or heart artifacts) was removed from the data. Finally, residual bad channels were excluded if their standard deviation exceeds a threshold of 25 μV or is smaller than 1 μV. Bad channels with excessive artifacts were then excluded from the mean (With an upper limit 2 channels for each subject). Subsequently, the missing channels removed in the preprocessing were interpolated by using a spherical spline interpolation (EEGLAB function eeg_interp.m) and all channels were re-referenced to the common average. Finally, 60 s of artifact-free EEG in each sample was selected for the subsequent analysis.

3.2.3. *EEG-source localization analysis*

The localization of an EEG data source is a controversial problem. In recent decades, various algorithms have been developed through various methods and hypotheses to estimate the locations of EEG sources [22]. The exact low-resolution brain electromagnetic tomography analysis (eLORETA) is among the most commonly used methods. In this study, eLORETA was employed to estimate cortical activity from surface EEG data. Designed and developed by Pascual–Marqui [23–25], it is available at the LORETA website (http://www.uzh.ch/keyinst/loreta.htm). The accuracy of LORETA was demonstrated by several comparative studies of EEG–PET [26] and EEG–fMRI [27,28]. In addition, LORETA has also been used successfully to locate activities in areas with complex spatial configurations such as insula [29]. In fact, LORETA employs a real head model [30], and the estimated solutions are limited to the cortical gray matter modeled on 6239 voxels and 5-mm spatial resolution [29]. This feature allows for the identification of macro-cortical multiple regions of interest (ROIs), each of which includes different Broadmann areas (BAs). In this study, all voxels

Table 2
The 28 ROIs[a] created in LORETA for Analysis of functional connectivity in terms of "lagged phase synchronization".

Seeds/hob	MNI (X, Y, Z)
OP2 (Parietal Operculum)	L: 39 -30 20
	R: 37–31 19
IPL (Inferior Parietal lobule)	L: 39 -51 60
	R: 35–45 55
SPL (Superior Parietal lobule)	L: 22 -62 54
	R: 16–66 57
Parietal lobe (postcentral)	L: 60 -20 10
	R: 63–16 22
Precuneus	L: 3 -52 39
	R: 9–52 52
Precentral Gyrus	L: 51 -3 42
	R: 30–4 49
Post-central gyrus	L: 10 -40 65
	R: 15–40 65
Middle frontal gyrus	L: −27 21 36
	R: 30 65 13
Superior frontal gyrus	L: −10 15 65
	R: 24 33 45
SMA (supplementary motor area) (prearcuate)	L: 8 -8 65
	R: 4 1 60
CSv (cingulate sulcus visual)	L: 10 -17 41
	R: 12–24 43
Cingulate Gyrus	L: −10 0 40
	R: 5–10 40
STG (superior temporal gyrus)	L: 66 -22 22
	R: 30 23 -26
Insular Cortex (IC)	L: −38 8 8
	R: 49 4 -2

[a] Region of Interests (ROIs).

were selected within a radius of 15 mm to define ROIs from seed points. The intracranial spectral density of the purified EEG was calculated through eLORETA at a resolution of 1 Hz (1–30 Hz). The eLORETA functional images were estimated from spectral density for eight frequency bands: delta (1.5–4 Hz), theta (4–8 Hz), alpha 1 (8–10 Hz), alpha 2 (10–13 Hz), beta 1 (13–18 Hz), beta 2 (19–21 Hz), beta 3 (22–30 Hz), and gamma (>30 Hz).

3.2.4. Functional connectivity analysis

The Brodmann areas (BAs) of whole-brain regions created in eLORETA based on Talairach Daemon (http://www.talairach.org/) were selected to calculate the functional connectivity [31]. After common areas were defined in the vestibular and visual-vertical perception (Table 2) [1,2,4,10,29,32–38] through seed points with a radius of 15 mm [39] in both hemispheres, the lagged phase synchronization (LPS) was used as a measure of nonlinear functional connectivity.

4. Statistical analysis

The statistical analyzes were performed in SPSS 24 and eLORETA [40,41]Significant differences between cortical voxels were identified through statistical nonparametric mapping (SnPM) with randomization in LORETA to determine the cortical potential threshold values for the modified observed t-values of multiple comparisons between all voxels and all frequencies. A total of 5000 permutations were utilized to determine the significance of each randomization test [42]. Independent sample *t*-tests and randomization processes were employed to compare the cortical electrical activity within each frequency band between the groups of stroke survivors and healthy individuals. The statistical tests allowed for the calculation of the threshold values in the expression “log F-ratio” and resulted in a file containing the calculated extremes of probabilities (ExtremePs), the corresponding maximum thresholds, and the

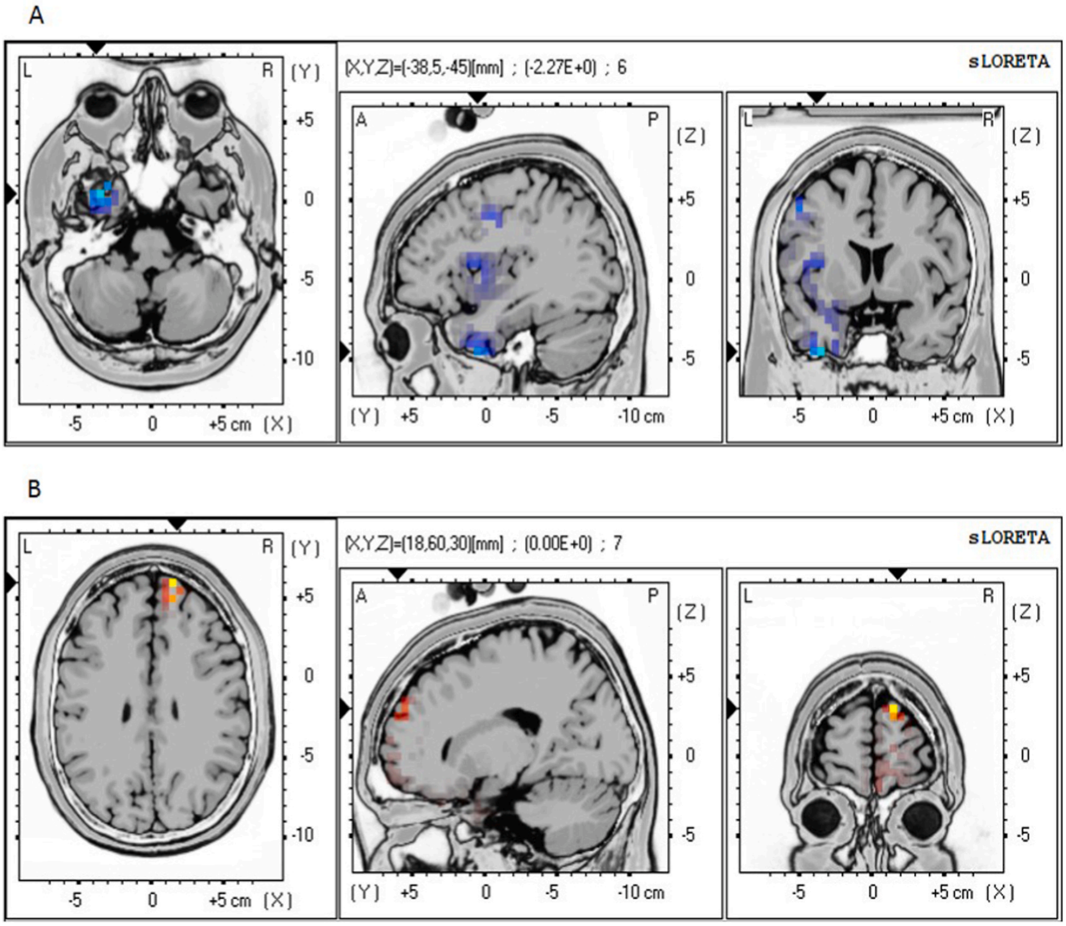

Fig. 2. eLORETA statistical maps of (A) β2 band oscillations and (B) β3 band oscillations. Colored areas represent the spatial extent of voxels with significant differences (red-coded for $p < 0.05$; blue and yellow-coded for $p < 0.01$) in source current density in stroke survivors vs. healthy participants. Significant results are projected onto a brain MRI template. The MRI slices are located at the MNI-space coordinate indicated in the figure that corresponds to the voxel of highest significance. ($P = 0.008400$, Log-F = 2.07) for β2 band oscillations and ($P = 0.006$, Log-F = 1.9) for β3 band oscillations.

thresholds in probability values of $p < 0.01$, $p < 0.05$, and $p < 0.10$. The thresholds with $p < 0.05$ were considered the indicators of statistical significance.

The LPS was adopted to measure the functional connectivity. For this purpose, the *t*-statistic test was conducted with variance smoothing parameters equal to 0 and 5000 randomizations. ExtremePs, maximum thresholds, and thresholds of probability values of $p < 0.01$, $p < 0.05$, and $p < 0.10$ were all collected in a file.

5. Results

5.1. Demographic variables

This study was conducted on 40 stroke survivors aged 34–59 years (52.3 ± 4.3 years, 52.5 % women) in the stroke group, and 35 healthy subjects aged 37–58 years (49.8 ± 3.6 years, 54.5 % women) in the control group. The results of vertical perception were reported −5.6 ± 1.2° and 1.3 ± 0.7° in the experimental and control groups, respectively (Table 1).

5.2. Source localization

According to the power spectral density results, the stroke patients had lower electrical cortical activities than the healthy individuals within the beta-2 frequency band in the left hemisphere. The beta-2 frequency band power showed a significant decrease ($p < 0.01$) in the frontal, temporal, and parietal lobes in addition to the insula (Fig. 2 (A, B) and Table 3).

The stroke patients experienced significant increases in the beta-3 band power in their right hemispheres ($p < 0.01$) in the medial frontal gyrus, superior frontal gyrus, and anterior cingulate (Fig. 2 (A, B) and Table 3).

5.3. Functional connectivity

The experimental and control groups were compared in terms of the lagged phase synchrony differences in the common areas between the vestibular network and the visual vertical perception within all band frequencies. According to the statistical analysis results, stroke survivors showed decreases in the phase synchronization within the delta band and increases within the alpha-1, beta-2, and beta-3 bands compared with the control group in the vestibular network involved in the visual vertical perception ($p < 0.01$) (Fig. 3 (A-D)).

6. Discussion

Previous studies have shown that patients experience impaired balance after stroke. The abnormal vertical perception is a factor affecting the balance function of stroke survivors. However, there is still insufficient information regarding to what extent the active

Table 3

Regional location and significant comparisons of the voxel values between stroke survivors and healthy controls.

Band oscillation	Area	Lobe	R/L	BA[a]	Voxel	X	Y	Z
β2	Middle Temporal Gyrus (TGm)	Temporal lobe	L	38	−2.30053	−35	5	−45
				21		−40	10	−40
	Superior Temporal Gyrus (TGs)	Temporal lobe	L	38	−2.27539	−30	10	−45
				22		−45	0	−5
	Inferior Temporal Gyrus (TGi)	Temporal lobe	L	20	−2.27009	−35	0	−45
	Sub-Gyral	Temporal lobe	L	13	−2.11923	−40	0	−10
				21		−40	−5	−10
	Fusiform Gyrus	Temporal lobe	L	20	−2.00768	−40	−10	−30
	Middle Frontal Gyrus (FGm)	Frontal lobe	L	6/8/9	−2.28271	−50	5	40
				46		−55	25	25
	Precentral Gyrus	Frontal lobe	L	6/4/9	−2.26674	−50	5	45
				44		−40	10	10
	Inferior Frontal Gyrus (FGi)	Frontal lobe	L	45/44/6/9/47	−2.24495	−50	15	15
	Subcallosal Gyrus	Frontal lobe	L	34	−2.14474	−25	5	−15
	Uncus	Limbic lobe	L	20/38/28/36	−2.232	−30	5	−40
	Parahippocampal Gyrus	Limbic lobe	L	34	−2.15808	−30	5	−20
				28		−15	−5	−15
	Insula		L	13	−2.22023	−40	5	10
	Extra-Nuclear		L	13	−2.10147	−40	5	−10
	Postcentral Gyrus	Parietal lobe	L	2/3/1	−2.14078	−60	−20	35
				43			−15	20
	Inferior Parietal Lobule (PLi)	Parietal lobe	L	40	−2.10599	−55	−25	30
β3	Superior Frontal Gyrus (FGs)	Frontal lobe	R	9/10	1.99917	15	50	25
	Medial Frontal Gyrus	Frontal lobe	R	10	1.96826	10	45	15
	Anterior cingulate	Limbic lobe	R	32	1.92137	10	45	10

[a] Brodmann area.

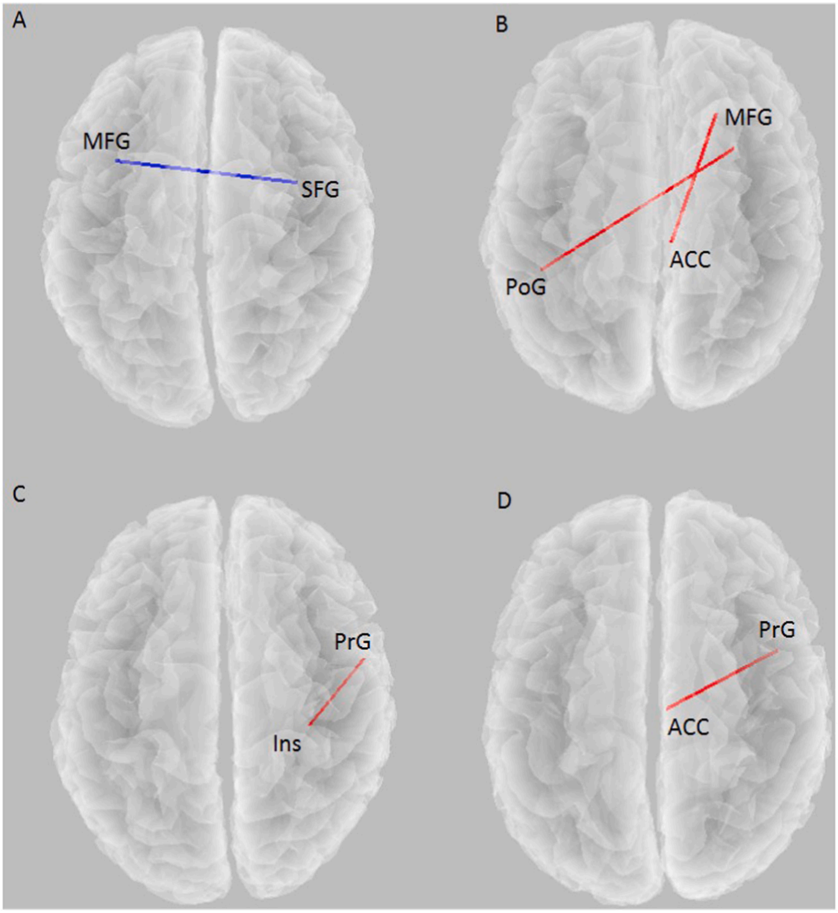

Fig. 3. eLORETA diagram illustrating cortical regions in vestibular network with significantly decreased δ (A) and increased α1(B), β2 (C) and β3 (D) frequency bands lagged phase synchronization (functional connectivity) in stroke survivors vs. healthy participants. The red and blue colors of the arrows indicate a significant increase and decrease in functional connectivity between brain areas in the two groups respectively. MFG: Medial Frontal Gyrus, SFG: Superior Frontal Gyrus, PoG: Postcentral Gyrus, ACC: Anterior Cingulate Gyrus, PrG: Precentral Gyrus, Ins: Insula.

cortical areas are involved in vertical perception among stroke survivors. Variations in cortical activities after stroke have been well established.

In this study, stroke survivors were compared with healthy individuals in terms of EEG activities in the vestibular cortex. The results indicated variations in oscillation power and functional connectivity within specific frequency bands during the resting state. First, there was a decrease within the beta-2 frequency band activity in the areas of the left hemisphere as well as an increase within the beta-3 frequency band activity in the areas of the right hemisphere. Second, there was a decrease in the functional connectivity of the delta frequency band in the medial frontal gyrus (MFG) region and an increase in the functional connectivity within the alpha-1, beta-2, and beta-3 frequency bands in the areas of the vestibular cortex.

6.1. *Variations in functions of vestibular cortex areas*

The results of this study showed increases in the activities of the beta-3 (upper beta) band (22–30 Hz) in areas of the frontal lobe (superior and medial frontal gyrus) and the anterior cingulate cortex of the right hemisphere (damaged hemisphere). There were also decreases in the activities of the beta-2 band (19–21 Hz) in areas of the temporal lobe (middle, superior, and inferior temporal gyrus), frontal lobe (middle and inferior frontal gyrus and precentral), inferior parietal lobe, postcentral gyrus, and insula region in the left hemisphere (healthy hemisphere). All of these areas are in the vestibular cortex [43].

Lower beta band activities (beta-2) are related to the multisensory integration. According to the results of this study, the activity of this frequency band decreased in areas of the left hemisphere. These areas include precentral gyrus, post-central gyrus, and insula, middle, and inferior temporal gyri. The precentral gyrus (PrG) (Broadman Region 6) is the part of the pre-motor cortex in the brain involved in the planning of movements as well as in the organization of certain postural movements [44,45]. It plays a key role in transmitting vestibular signals in the brain of primates [12] and acts as part of a direct locomotor pathway [46]. The posterior parietal region (post-central gyrus) is part of the sensory-motor network that processes the multisensory inputs used in motor responses. It can also possibly contribute to the processing of gravitational perception information regarding the upright orientation [47]. The insula is considered a multisensory processing area of the brain. The posterior part of the insula is a multimodal region receiving inputs from the scattered sensory systems. The vestibular system is a prominent part of such convergent inputs [48,49]. The middle and inferior temporal gyri are involved in looking at complex and often emotional stimuli as well as the subjective rotation and differentiation of places in space [49]. In addition, the beta-2 activities are involved in motor system functions, inhibition, alertness, and maintenance of current sensorimotor and cognitive status [50,51]. Therefore, the decreased or suspended beta activities indicate the readiness to start moving. This sign is manifested by the left hemisphere.

Contrary to the results of this study, Assenza et al. (2013) and Wang et al. (2012) reported bilateral increases in the power of the delta and theta frequency bands [52,53]. Far from the inherent differences in their analysis methods, this current study was conducted on the people with only right hemisphere strokes and abnormal vertical perception. This can be the reason for further differences between this study and the previous ones.

As mentioned earlier, the activity of the upper beta band (beta 3) is involved in local sensory integration. The results of this study indicated an increase in the beta-3 activity within the areas of superior frontal gyrus, medial frontal gyrus, and anterior cingulate cortex (ACC) of the right hemisphere. Superior and medial frontal gyri are involved in the cognitive control of visuomotor timing and movement preparation [49]. In particular, this study showed the central role of the anterior cingulate cortex. The anterior cingulate cortex is involved in monitoring the action and tracking the error signal [54]. Regarding balance control, Adkin et al. defined the "error signal" as the difference between the expected state and the actual state of balance during transient balance perturbations [55]. Several studies reported increases in frontocentral and/or ACC activities during a balance test for the balance instability detection [56,57]. The studies of fMRI indicated increases in ACC activities during the successful recognition of instability [58].

In line with the study conducted by Hülsdünker et al. (2015), the results of this study emphasized the major role of frontal and parietal beta fluctuations in maintaining balance [54]. Since the beta band represents the oscillation that is not yet fully understood [59], it is difficult to explain its role in vestibular processing without further data. It is probably related to the coupling of sensory vestibular input with ocular motors and motor outputs [29]. Beta band fluctuations used to be linked to sensorimotor functions, and they were thought to represent the "idling rhythm" in the motor system [60]. However, a recent hypothesis links beta band activities to maintaining the current motor state [59]. The motor reactions of pusher patients are caused by a severe conflict between the visual vertical perception and the body [47]. Considering the results of this study and those of the previous studies, it can be hypothesized that increased beta activities in the right (damaged) hemisphere lead to an idling system, which can be considered a possible cause of the left lateropulsion observed in stroke survivors who participated in the study.

6.2. *Changing functional connectivity between active cortical areas in vertical perception*

It has been suggested that nesting between fast and slow fluctuations may facilitate cross-modal interactions between sensory channels related to information processing on different time scales [61].

Increased Alpha Band Synchrony: Connecting vestibular processing to alpha band fluctuations can provide new insights into the vestibular system and the human vestibular cortex [12]. This finding is consistent with the hypothesis and suggestion that the 8–13-Hz rhythm is a major neural index for sensory motor integration and "human connection with the environment" [62] and is selectively suppressed by a variety of motor and multisensory sensory tasks [63]. Alpha suppression is a distinct pattern reflecting multisensory vestibular cortical activity in bilateral temporoparietal cranial regions [64]. These different functions are all related to primary vestibular functions such as self-motion and postural control [65]. Accordingly, alpha suppression reflects the cortical processing of vestibular signals in the vestibular cortex and is a sign of correlation in cortical vestibular processing [66]. In addition, recent theories have suggested that alpha band fluctuations may also be related to the separation of brain regions from unrelated tasks [59,67].

The increased synchrony of alpha band fluctuations observed in the results of this study is related to the inhibitory neural activity [68]. The modulation of alpha band oscillations during self-motion may indicate an inhibitory interaction between the visual and vestibular systems during visual-vestibular conflicts. These fluctuations show some degrees of discrepancy between actual vestibular activity and what is expected during the continuous self-motion. They can be employed to distinguish between the types of sensory ambiguities encountered in body postures. The alpha activity reflects the degrees of differences between actual and expected vestibular activities [69].

The difference between visual and vestibulo-somastatic signals can be considered an increase in the inhibitory mechanisms observed in the upright position, in which there is a continuous sensory conflict between experienced and expected gravitational perception activities. At the same time, the alpha amplitude is assumed to be a reflection of mechanisms to increase the signal-to-noise ratio. The higher the task demand, the more the inhibition. Consequently, the alpha power increases. However, roll vection requires the removal of gravitational perception information (due to the vestibular cortex activity) in an upright observer [69].

This hypothesis is consistent with the results of microgravity experiments conducted by Cheron (2006), who reported that the intensity of alpha band fluctuations in the parito-occipital regions increased when the effect of gravity was not felt [70].

The present study also observed an increase in the functional correlations of alpha band oscillations between the right middle frontal gyrus and the left postcentral gyrus. In other words, the inhibition and reduction of activities in areas related to the left vestibular cortex play a key role in vertical perception and transmit conflicting information.

Reduction of Delta Band Fluctuations: The delta band is the leading frequency during a deep sleep. This frequency range is related to the learning, motivational, and reward systems of the brain [59,71]. In healthy individuals, the delta response is also mainly correlated with signal tracking and decision-making, whereas the reduced synchronization indicates impairment in these cognitive functions [72]. In addition to cognitive functions, the delta frequency band is involved in motion, attention processing, and cognitive control parameters [50]. Also, in the study of Ertl et al. (2021), the results of the localization of the source of low-frequency oscillations in the delta band indicate that the low frequencies reflect the interaction between the parts of the vestibular "core" network (PIVC, CSv) and frontal structures (MFG, MOG) [73]. Hence, delta synchronization has a great effect on attention modulation and motivation. However, the decrease in synchrony between the superior frontal gyrus of the right hemisphere and the middle frontal gyrus of the left hemisphere probably indicates a decrease in attention functions within cognitive processes such as vertical perception.

Increased Synchronization of Beta Band Fluctuations: At the resting state between movement areas in the affected hemisphere in the high beta frequency band, synchronization is an indicator of the baseline movement status, variation in the movement status, and prediction of the effectiveness of the treatment process [51]. This study also reported an increase in synchrony between the precentral gyrus and the anterior cingulate cortex as well as the insula in the right hemisphere (damaged hemisphere), a finding which may indicate variations in the information control processing areas in the affected hemisphere.

This is the first study to analyze the activities and functional correlations between different areas of the vestibular cortex involved in the visual vertical perception among patients with stroke. There were several research limitations. First, the EEG system is unable to measure activities in subcortical structures such as the brainstem and cerebellum, which plays a central role in the balance control. Second, individual differences in stroke or background characteristics may affect the results of this cross-sectional study. Thus, further longitudinal studies are required to validate the findings of this study. Third, due to consideration of a damaged specific area in stroke patients and homogenizing it among the patients participating in the study would lead to a reduction in the available samples, so this variable was not considered in this study and according to the studies previously, right hemisphere damage was used in general. If possible, it is suggested that this variable be homogenized among the participants.

It is also suggested that the activity and functional connectivity of different oscillation bands be examined among the patients suffering suffered a right hemisphere stroke but having normal vertical perception. A more accurate description of the cortical areas involved in vertical perception after brain injury might be obtained by comparing the results of these two groups.

7. Conclusion

The results of this observational cross-sectional study indicated variations in the functions and functional connectivity of cortical areas involved in the visual vertical perception. These areas are mainly located in the vestibular cortex. According to the research findings, it can be concluded that these cortical variations are involved in the development of balance problems in stroke patients. Furthermore, EEG-based measurements (frequency band power and cortical functional connectivity) can manifest change and balance impairment after stroke.

Neurorehabilitation methods are employed to reduce harmful processes and support beneficial processes in post-stroke neuroplasticity. Continuous brain monitoring helps track the brain function derangement in a possible reversible state. Rapid tracking of brain function derangement enables therapists to consider which rehabilitation program will have the greatest impact on changes in the cerebral cortex. Due to the high prevalence of stroke, even relatively small improvements in clinical outcomes will be beneficial to patients.

Author contribution statement

Meymaneh Jafari: Conceived and designed the experiments; Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Moslem Shaabani: Performed the experiments.

Seyed Ruhollah Hosseini; Enayatollah Bakhshi: Analyzed and interpreted the data.

Hassan Ashayeri: Conceived and designed the experiments.

Hojjat Allah Haghgoo: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Data availability statement

Data will be made available on request.

Funding statement

This manuscript was extracted from the PhD dissertation of Meymaneh Jafari from the Department of Audiology at University of Social Welfare and Rehabilitation Sciences in Iran. However, this research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Hojjat Allah Haghgoo reports administrative support and equipment, drugs, or supplies were provided by University of Social Welfare and Rehabilitation Science.

Acknowledgements

We would like to appreciate the assistance of authorities at the University of Social Welfare and Rehabilitation Sciences and all participants in this study.

References

[1] T. Raiser, et al., The human corticocortical vestibular network, Neuroimage 223 (2020), 117362.
[2] A. Saj, L. Borel, J. Honoré, Functional neuroanatomy of vertical visual perception in humans, Front. Neurol. 10 (2019) 142.
[3] M. Rousseaux, et al., An anatomical and psychophysical comparison of subjective verticals in patients with right brain damage, Cortex 69 (2015) 60–67.
[4] P. zu Eulenburg, et al., Meta-analytical definition and functional connectivity of the human vestibular cortex, Neuroimage 60 (1) (2012) 162–169.
[5] A. Khan, et al., Changes in electroencephalography complexity and functional magnetic resonance imaging connectivity following robotic hand training in chronic stroke, Top. Stroke Rehabil. 28 (4) (2021) 276–288.
[6] F. Biscetti, et al., RANK/RANKL/OPG pathway: genetic association with history of ischemic stroke in Italian population, Eur. Rev. Med. Pharmacol. Sci. 2016 (20) (2016) 4574–4580.
[7] M. Mihara, et al., Cortical control of postural balance in patients with hemiplegic stroke, Neuroreport 23 (5) (2012) 314–319.
[8] D. Pérennou, et al., Lateropulsion, pushing and verticality perception in hemisphere stroke: a causal relationship? Brain 131 (9) (2008) 2401–2413.
[9] M. Rousseaux, et al., Neuroanatomy of space, body, and posture perception in patients with right hemisphere stroke 81 (15) (2013) 1291–1297.
[10] B. Baier, et al., Neural correlates of disturbed perception of verticality 78 (10) (2012) 728–735.
[11] D.B. Snyder, et al., Electroencephalography resting-state networks in people with Stroke, Brain and behavior (2021), e02097.
[12] W. Guldin, O. Grüsser, Is there a vestibular cortex? Trends Neurosci. 21 (6) (1998) 254–259.
[13] S. Glasauer, M. Dieterich, T. Brandt, Neuronal network-based mathematical modeling of perceived verticality in acute unilateral vestibular lesions: from nerve to thalamus and cortex, J. Neurol. 265 (1) (2018) 101–112.
[14] M.D. Fox, Mapping symptoms to brain networks with the human connectome, N. Engl. J. Med. 379 (23) (2018) 2237–2245.
[15] A.P. Yelnik, et al., Perception of verticality after recent cerebral hemispheric stroke, Stroke 33 (9) (2002) 2247–2253.
[16] G. Kerkhoff, C. Zoelch, Disorders of visuospatial orientation in the frontal plane in patients with visual neglect following right or left parietal lesions, Exp. Brain Res. 122 (1) (1998) 108–120.
[17] C. Lemaire, et al., Functional connectivity within the network of verticality, Annals Phys. Rehab. Med. 64 (6) (2021), 101463.
[18] R.C. Oldfield, The assessment and analysis of handedness: the Edinburgh inventory, Neuropsychologia 9 (1) (1971) 97–113.
[19] C. Lopez, O. Blanke, F. Mast, The human vestibular cortex revealed by coordinate-based activation likelihood estimation meta-analysis, Neuroscience 212 (2012) 159–179.
[20] M. Dieterich, et al., Dominance for vestibular cortical function in the non-dominant hemisphere, Cerebr. Cortex 13 (9) (2003) 994–1007.
[21] C. Lopez, et al., Gravity and observer's body orientation influence the visual perception of human body postures, J. Vis. 9 (5) (2009), 1-1.
[22] R. Grech, et al., Review on solving the inverse problem in EEG source analysis, J. NeuroEng. Rehabil. 5 (1) (2008) 1–33.
[23] R.D. Pascual-Marqui, Standardized low-resolution brain electromagnetic tomography (sLORETA): technical details, Methods Find Exp. Clin. Pharmacol. 24 (Suppl D) (2002) 5–12.
[24] R.D. Pascual-Marqui, Discrete, 3D Distributed, Linear Imaging Methods of Electric Neuronal Activity. Part 1: Exact, Zero Error Localization, 2007 arXiv preprint arXiv:0710.3341.
[25] R.D. Pascual-Marqui, et al., Assessing interactions in the brain with exact low-resolution electromagnetic tomography, Phil. Trans. Math. Phys. Eng. Sci. 369 (1952) (2011) 3768–3784.
[26] D.A. Pizzagalli, T.R. Oakes, R.J. Davidson, Coupling of theta activity and glucose metabolism in the human rostral anterior cingulate cortex: an EEG/PET study of normal and depressed subjects, Psychophysiology 40 (6) (2003) 939–949.
[27] C. Mulert, et al., Integration of fMRI and simultaneous EEG: towards a comprehensive understanding of localization and time-course of brain activity in target detection, Neuroimage 22 (1) (2004) 83–94.
[28] D. Vitacco, et al., Correspondence of event-related potential tomography and functional magnetic resonance imaging during language processing, Hum. Brain Mapp. 17 (1) (2002) 4–12.
[29] M. Ertl, et al., The cortical spatiotemporal correlate of otolith stimulation: vestibular evoked potentials by body translations, Neuroimage 155 (2017) 50–59.
[30] M. Fuchs, et al., A standardized boundary element method volume conductor model, Clin. Neurophysiol. 113 (5) (2002) 702–712.
[31] F. Taremian, et al., Disrupted resting-state functional connectivity of frontal network in opium use disorder, Appl. Neuropsychol.: Adultspan (2021) 1–9.
[32] S. Eguchi, G. Hirose, M. Miaki, Vestibular symptoms in acute hemispheric strokes, J. Neurol. 266 (8) (2019) 1852–1858.
[33] S.B. Eickhoff, et al., Identifying human parieto-insular vestibular cortex using fMRI and cytoarchitectonic mapping, Hum. Brain Mapp. 27 (7) (2006) 611–621.
[34] C. Helmchen, et al., Effects of galvanic vestibular stimulation on resting state brain activity in patients with bilateral vestibulopathy, Hum. Brain Mapp. 41 (9) (2020) 2527–2547.
[35] T. Mitsutake, et al., Greater functional activation during galvanic vestibular stimulation is associated with improved postural stability: a GVS-fMRI study, SMR (Somatosens. Mot. Res.) 37 (4) (2020) 257–261.
[36] L.-W. Ko, et al., Noisy galvanic vestibular stimulation (stochastic resonance) changes electroencephalography activities and postural control in patients with bilateral vestibular hypofunction, Brain Sci. 10 (10) (2020) 740.
[37] P. zu Eulenburg, et al., The Human Vestibular Cortex, ScienceOpen Posters, 2020.
[38] S. Becker-Bense, et al., Direct comparison of activation maps during galvanic vestibular stimulation: a hybrid H2 [15 O] PET—BOLD MRI activation study, PLoS One 15 (5) (2020), e0233262.
[39] S. Olbrich, et al., Altered EEG lagged coherence during rest in obsessive–compulsive disorder, Clin. Neurophysiol. 124 (12) (2013) 2421–2430.
[40] Y. Aoki, et al., Detection of EEG-resting state independent networks by eLORETA-ICA method, Front. Hum. Neurosci. 9 (2015) 31.
[41] M.A. Jatoi, et al., EEG based brain source localization comparison of sLORETA and eLORETA, Australas. Phys. Eng. Sci. Med. 37 (2014) 713–721.
[42] L. Canuet, et al., Resting-state EEG source localization and functional connectivity in schizophrenia-like psychosis of epilepsy, PLoS One 6 (11) (2011), e27863.
[43] T. Brandt, T. Brandt, Vestibular Cortex: its Locations, Functions, and Disorders, Vertigo: Its multisensory syndromes, 2003, pp. 219–231.
[44] K.M. McNerney, et al., Use of 64-channel electroencephalography to study neural otolith-evoked responses, J. Am. Acad. Audiol. 22 (3) (2011) 143–155.
[45] N.P. Todd, et al., Vestibular evoked potentials (VsEPs) of cortical origin produced by impulsive acceleration applied at the nasion, Exp. Brain Res. 232 (12) (2014) 3771–3784.
[46] F. Herold, et al., Cortical activation during balancing on a balance board, Hum. Mov. Sci. 51 (2017) 51–58.
[47] T.E.G. Santos-Pontelli, et al., Neuroimaging in stroke and non-stroke pusher patients, Arquivos de Neuro-Psiquiatria 69 (2011) 914–919.

[48] K. Hagiwara, et al., Cortical modulation of nociception by galvanic vestibular stimulation: a potential clinical tool? Brain Stimul. 13 (1) (2020) 60–68.
[49] V. Kirsch, et al., Beyond binary parcellation of the vestibular cortex–A dataset, Data Brief 23 (2019), 103666.
[50] J.M. Cassidy, et al., Low-frequency oscillations are a biomarker of injury and recovery after stroke, Stroke 51 (5) (2020) 1442–1450.
[51] J. Wu, et al., Connectivity measures are robust biomarkers of cortical function and plasticity after stroke, Brain 138 (8) (2015) 2359–2369.
[52] G. Assenza, et al., A contralesional EEG power increase mediated by interhemispheric disconnection provides negative prognosis in acute stroke, Restor. Neurol. Neurosci. 31 (2) (2013) 177–188.
[53] L. Wang, et al., Cortical networks of hemianopia stroke patients: a graph theoretical analysis of EEG signals at resting state, in: 2012 Annual International Conference of the IEEE Engineering in Medicine and Biology Society, IEEE, 2012.
[54] T. Hülsdünker, et al., Cortical processes associated with continuous balance control as revealed by EEG spectral power, Neurosci. Lett. 592 (2015) 1–5.
[55] A.L. Adkin, et al., Cortical responses associated with predictable and unpredictable compensatory balance reactions, Exp. Brain Res. 172 (1) (2006) 85–93.
[56] J.A. Anguera, R.D. Seidler, W.J. Gehring, Changes in performance monitoring during sensorimotor adaptation, J. Neurophysiol. 102 (3) (2009) 1868–1879.
[57] J.T. Gwin, et al., Electrocortical activity is coupled to gait cycle phase during treadmill walking, Neuroimage 54 (2) (2011) 1289–1296.
[58] S. Slobounov, T. Wu, M. Hallett, Neural basis subserving the detection of postural instability: an fMRI study, Mot. Control 10 (1) (2006) 69–89.
[59] A.K. Engel, P. Fries, Beta-band oscillations—signalling the status quo? Curr. Opin. Neurobiol. 20 (2) (2010) 156–165.
[60] G. Pfurtscheller, A. Stancak Jr., C. Neuper, Post-movement beta synchronization. A correlate of an idling motor area? Electroencephalogr. Clin. Neurophysiol. 98 (4) (1996) 281–293.
[61] C.E. Schroeder, et al., Neuronal oscillations and visual amplification of speech, Trends Cognit. Sci. 12 (3) (2008) 106–113.
[62] R. Hari, Action–perception connection and the cortical mu rhythm, Prog. Brain Res. 159 (2006) 253–260.
[63] C. Babiloni, et al., Golf putt outcomes are predicted by sensorimotor cerebral EEG rhythms, J. Physiol. 586 (1) (2008) 131–139.
[64] S. Gale, et al., Oscillatory neural responses evoked by natural vestibular stimuli in humans, J. Neurophysiol. 115 (3) (2016) 1228–1242.
[65] D.E. Angelaki, E.M. Klier, L.H. Snyder, A vestibular sensation: probabilistic approaches to spatial perception, Neuron 64 (4) (2009) 448–461.
[66] S.E. Chaudhuri, F. Karmali, D.M. Merfeld, Whole body motion-detection tasks can yield much lower thresholds than direction-recognition tasks: implications for the role of vibration, J. Neurophysiol. 110 (12) (2013) 2764–2772.
[67] S. Palva, J.M. Palva, New vistas for α-frequency band oscillations, Trends Neurosci. 30 (4) (2007) 150–158.
[68] W. Klimesch, Alpha-band oscillations, attention, and controlled access to stored information, Trends Cognit. Sci. 16 (12) (2012) 606–617.
[69] S. Harquel, et al., Modulation of alpha waves in sensorimotor cortical networks during self-motion perception evoked by different visual-vestibular conflicts, J. Neurophysiol. 123 (1) (2020) 346–355.
[70] G. Chéron, et al., Effect of gravity on human spontaneous 10-Hz electroencephalographic oscillations during the arrest reaction, Brain Res. 1121 (1) (2006) 104–116.
[71] G.G. Knyazev, Motivation, emotion, and their inhibitory control mirrored in brain oscillations, Neurosci. Biobehav. Rev. 31 (3) (2007) 377–395.
[72] C. Kamarajan, et al., The role of brain oscillations as functional correlates of cognitive systems: a study of frontal inhibitory control in alcoholism, Int. J. Psychophysiol. 51 (2) (2004) 155–180.
[73] M. Ertl, et al., The role of delta and theta oscillations during ego-motion in healthy adult volunteers, Exp. Brain Res. 239 (2021) 1073–1083.