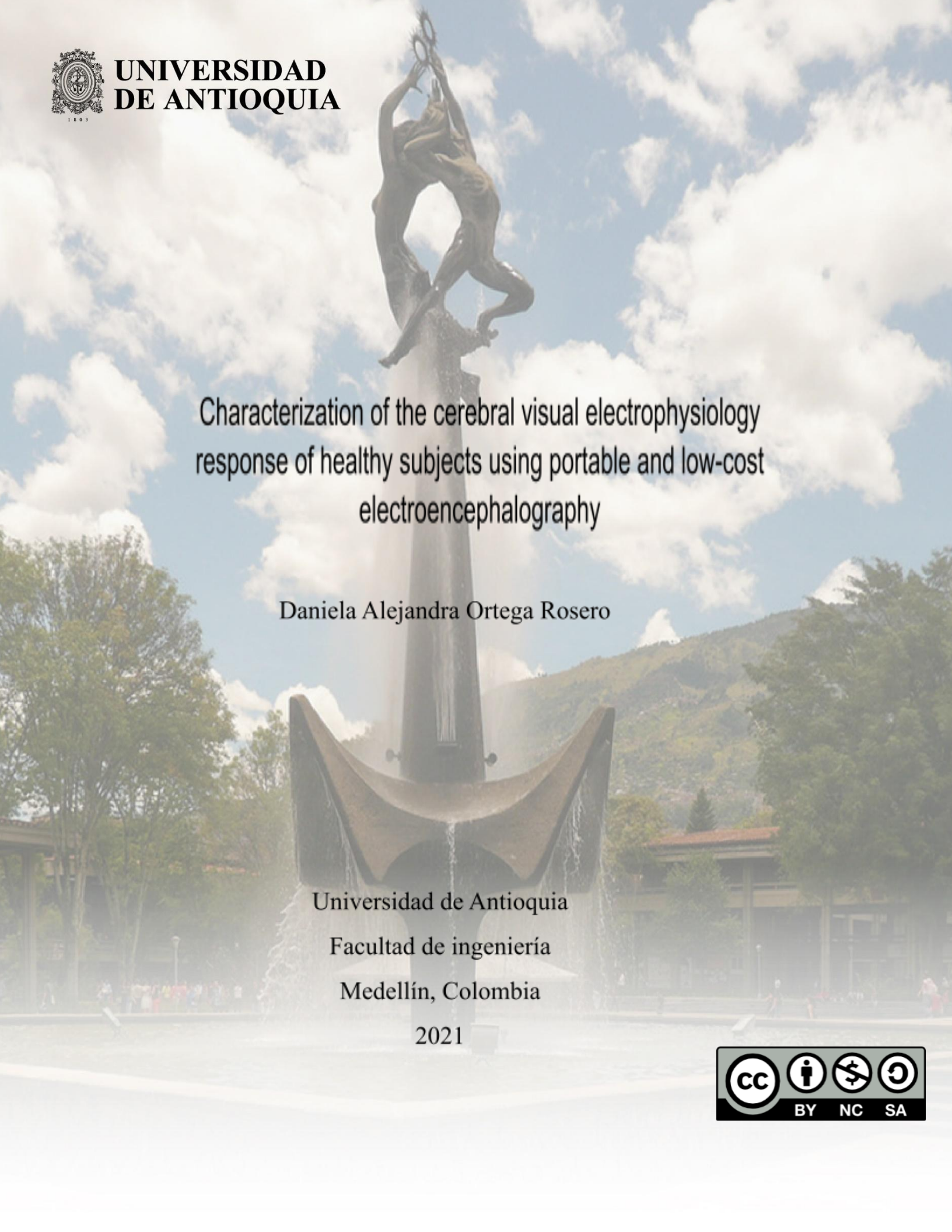


UNIVERSIDAD DE ANTIOQUIA

Characterization of the cerebral visual electrophysiology response of healthy subjects using portable and low-cost electroencephalography

Daniela Alejandra Ortega Rosero

Universidad de Antioquia

Facultad de ingeniería

Medellín, Colombia

2021

Characterization of the cerebral visual electrophysiology response of healthy subjects using portable and low-cost electroencephalography

Daniela Alejandra Ortega Rosero

Tesis o trabajo de investigación presentada(o) como requisito parcial para optar al título de:
Magister en Ingeniería

Asesores (a):

John Fredy Ochoa Gómez - Ph.D. in electronic engineering

Juan Camilo Suárez Escudero - Ph.D. candidate in medical sciences

Línea de Investigación:
Neuroingeniería
Grupo de Investigación:
Grupo de investigación en bioinstrumentación e ingeniería clínica

Universidad de Antioquia
Facultad, Departamento, Escuela, Instituto, etc.
Medellín, Colombia
2021.

Project

Characterization of the cerebral visual electrophysiology response of healthy subjects using portable and low-cost electroencephalography

Daniela Alejandra Ortega Rosero
BSc Bioengineer
Master's project
Research group in bioinstrumentation and clinical engineering (GIBIC)
Universidad de Antioquia

dalejandra.ortega@udea.edu.co - danni9310@gmail.com

Advisor

John Fredy Ochoa Gómez
Ph.D. in electronic engineering

Juan Camilo Suárez Escudero
Ph.D. candidate in medical sciences

June, 2020

Acknowledgements

This work would not have been possible without the support of many people. I am grateful to my supervisors for their accompaniment and their time, to the students who were linked with their semester projects, to the GIBIC group for providing me with the spaces and the tools.

Special thanks to all the participants for their time and patience, without them there would be no results for this project. Finally, thanks to the project evaluators for their time and comments.

Contents

List of tables

List of figures

1. Abstract

The ability to see and process images depends on the function of the eyes and a large extent on the processing of neuronal information, for this reason, it is important to study the neuronal activity obtained as response for visual stimulation. Approximately 60% of stroke survivors have visual impairments implying the need for rehabilitation therapy and about 74% of patients with traumatic brain injury have visual alterations, and 38% of these alterations are visually impaired. However, although neuronal information is important, currently, brain activity is not recorded during therapies, so the neuronal changes due to therapy are unknown, only the clinical changes of the patients are measured, and only on those cases in which response to the therapy exists. A limitation to the study of brains' activity during therapy is the cost and portability of the instrumentation required. The present study aims to characterize the cerebral visual electrophysiology response of healthy subjects with measures such as power spectrum and coherence, acquired through portable and low cost electroencephalography in healthy subjects in order to have biomarker that allow in future studies to follow up the patients' process in neurological visual rehabilitation.

A set of stimuli to perform visual cortex activation covering most of the visual skills was developed. As a result, six stimuli were designed, each of these with editable parameters for other tests. This set presents 3 previously reported stimuli and 3 exploratory stimuli. The stimuli were designed for activating different visual function: acuity, contrast sensitivity, visual field, motion perception, form recognition, and color detection.

These stimuli were presented to 37 healthy control subjects. During the whole experiment, subjects were seated in a comfortable chair in a slightly dimmed room about 1 m in front of the stimulation unit. Different stimuli were showed and analyzed to identify which have the most significant difference in power spectrum and coherence measures.

In the first part an exploratory analysis was performed to identify outliers, initial trends and frequency response for the acuity and contrast stimuli. Also, statistical analyses were conducted, such as repeated measures ANOVA.

Our results indicated that relative delta, theta and alpha power could be an indicator to distinguish between eyes open and eyes closed while specific power bands can give information for stimulation stages. Similarly, coherence analysis allowed us to find sensibility factors for each stage. With these stimuli and baseline in some measures characteristic of each one will be possible to compare these variables in patient with neuro-ophthalmological disorders and in neurological rehabilitation using the proposed stimuli to activate the different visual functions.

The values obtained for power and frequency to respond to different behaviors depending on the type of stimulus, type of configuration and type of vision, this opens the analysis to understand if the trends are maintained in patients with visual impairment.

Keywords: Visual cortex - Visual electrophysiology - Quantitative electroencephalography (qEEG) - Neurological rehabilitation - Vision disorders

2. Introduction

2.1 Motivation

The ability to see and process images depend on the function of the eyes and also to a large extent on the processing of neuronal information, in addition, the area used for visual perception represents an important percentage of the visual cortex [1], more than 50% of human cerebral activity is related to vision [2]. For these reasons, it is important to study the neuronal activity in charge of the phenomenon of vision. Loss of vision may be the consequence of damage of the eye, the optic nerve, the visual pathways, or consequence of brain damage in occipital lobe due to stroke or neuro trauma which affects the visual system [3], [4]. Between 30% and 85% of patients will experience some type of visual dysfunction following a stroke [5][6]. The visual deficits most frequent in patients with stroke are visual field loss, hemianopsia and diplopia [7]. More than half a million patients are treated annually for head injuries, 90.000 of whom require rehabilitation services [8]. In moderate to severe traumatic brain injury (TBI), it is reported that about 74% of patients have visual alterations, and 38% are visually impaired [9], [10]. Stroke is one of the first causes of disability-adjusted life year (DALYs) in the world [11].

Although the problems with vision loss due to damage of the central nervous system (CNS) have been assumed as irreversible, over the past two decades, neuropsychological research has shown that the “blind” regions of the visual field have a hitherto little-recognized ability to process residual vision. In the last years, new efforts have been made to “reactivate” such residual visual potential through vision training methods [3] [12]. The broad aim of rehabilitation is to achieve the best functional outcome for the patient. Within the rehabilitation team, the occupational therapist aims to improve or maintain independent function in all aspects of daily living including physical, cognitive and social behavior [6] [7].

For these reasons, successful management of these lesions depends on accurate diagnostic, prognostic assessment, and a careful rehabilitation process. The use of positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) following stroke or TBI are important as measures of cerebral physiology [14] [15]. These are imaging tools that clinicians still rely on for the very first stage of diagnosis after TBI and stroke. fMRI and PET are useful in the first stage of diagnosis and establishing the extent of damage with the highest spatial resolution. Functional neuroimaging methods have been developed and new structural neuroimaging techniques also have been added to the toolbox of rehabilitation researchers because these techniques offer the ability to assess human white matter pathways *in vivo* and have a highest spatial resolution [16]. These are imaging techniques that clinicians use on for the very first stage of diagnosis after TBI and stroke.

However, for therapy and rehabilitation follow-up, PET is not often used due to its use of radioactive materials is invasive and is extremely expensive. fMRI is a technique that produces images at a higher resolution than PET and does not require radioactive materials, although is also very expensive and not portable. In contrast, non-invasive electroencephalography (EEG) is inexpensive with highest temporal resolution and useful technology to measure of cerebral neurophysiology [8] [17] [18].

In this line, quantitative EEG (qEEG) has proven to be useful in the diagnosis and rehabilitation [19] of cognitive problems of TBI individual [20] and visual evoked potentials (VEPs) have shown information on the functional status of the visual system [21]. Other studies have used these potentials to characterize vision function in children and adults and to have objective measures that support clinical evaluations in healthy subjects and in patients with visual impairment [22] [23] [24] [25] [26] [27]. However, although VEPs are measurements that offer important information of amplitude, latency, spectral characteristics, some of them are sensitive to external factors such as the monitor type [28], signal acquisition system for latency times, etc.

This means that current measures could be not enough to allow know more about the visual system when different areas are activated and it can be more complex to have a baseline for different stimuli. Although some studies have researched the visual cortex there is not a reference of the same measure with different stimuli in healthy subject and patients. For this reason, it is important to analyze new EEG measures that can be sensitive indicators of pathologies [29] and use portable equipment that facilitates the implementation in clinical environments.

The present study aims to characterize EEG signals of the visual system –visual cortex- in healthy subjects, to have new parameters or biomarkers that allow in future studies to follow up patients in therapy. This project was a cross-sectional study with an exploratory and descriptive analysis. The signals in this study were measured with a portable system to facilitate its use in rehabilitation centers.

2.2 Objectives

General objective

Characterize the cerebral visual physiology response of healthy subjects using portable and low-cost electroencephalography (EEG).

Specific objectives

1. To design and build a set of tests to evaluate vision during EEG recordings.
2. To measure neuronal activation using EEG in healthy control individuals during visual stimulation to obtain the baseline of clinical measures and qEEG values.

3. To evaluate the capacity of qEEG measures obtained in healthy subjects, in order to find variables to discriminate experimental states.

3. Neurophysiological foundations

3.1 Medical condition

3.1.1 Stroke

Stroke is one of the main causes of death and functional disability worldwide, this cerebrovascular disease affects more than 800,000 people each year in the United States [30], 110,000 people in the United Kingdom (UK) [4]. Stroke is the main cause of death in Latin America and the third most common cause of death in developed countries [31]. A large portion of the CNS, especially in the cerebral cortex, is dedicated to the vision and therefore strokes have a high likelihood of involving vision in some way [1].

It is estimated that about 87% of strokes are ischemic and the remaining 13% are hemorrhagic [32]. In general, ischemic stroke is due to thrombotic or embolic phenomena. Cardiogenic stroke occurs when a blood vessel that carries oxygen and nutrients to the brain is either blocked by a clot, or as a result of severe heart failure and cerebral hypoperfusion.

Approximately 30% of all stroke patients suffer from post-stroke visual problems. The occurrence of neurologic visual impairment is higher in patients with occipital strokes, the frequency is reported to be up to 60% or 70% [33]. Hemianopia is the most common symptom, but also neglect, diplopia, reduced visual acuity, ptosis, anisocoria, and nystagmus are frequent [34].

3.1.2 Traumatic brain injury (TBI)

TBI is a CNS injury that happens when a mechanical force is applied to the body or cranium that is transmitted to the brain and its structures, as occipital lobe and neurologic visual connections. This occurs, by definition, in milliseconds and initiates subsequent physiological and cellular processes [35]. The incidence of TBI varies between 200 and 300 cases per 100,000 inhabitants. It is more frequent in men than in women, with a higher prevalence in ages 15-24 [36] .

The severity of TBI is classified as mild, moderate or severe depending on its characteristics and consequences [36]:

a. TBI mild: external damage to the brain, confusion, disorientation, or loss of consciousness for less than 30 minutes; a Glasgow Coma Scale score of 13 to 15; and post-traumatic amnesia fewer than 24 hours

b. TBI moderate: loss of consciousness between 30 minutes and 24 hours, between 9 and 12 points on the Glasgow Coma Scale, and post-traumatic amnesia between 1 and 7 days.
c. TBI severe: extensive memory and consciousness loss with much more dramatic results of cognitive loss. Glasgow Coma Scale ≤ than 8 points.

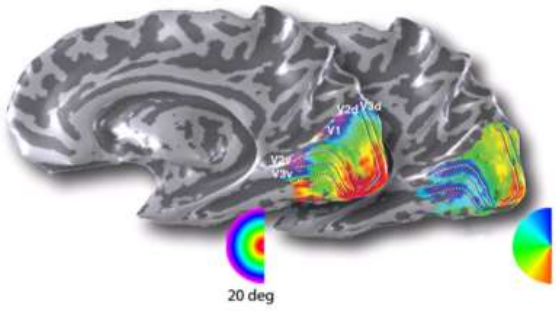
A retrospective study determined the frequency of occurrence of visual field defects in a sample of visually symptomatic, ambulatory patients who have acquired either TBI, neurological visual defects were present in 62 (38.75%) of the patients and the most frequent defects were scattered (58.06%) followed by homonymous (22.58%) [37]. In other studies, known visual consequences of TBI include compromised visual acuity, visual fields, diplopia, and oculomotor function [2][38].

3.2 Visual system map

The search for organizing principles of visual processing in the cortex has proven long and fruitful, demonstrating specific types of organization arising on multiple scales. One of the more important larger scale organizing principles of visual cortical organization is the visual field map (VFM) that has allowed to form one complete representation of contralateral visual space. [39]

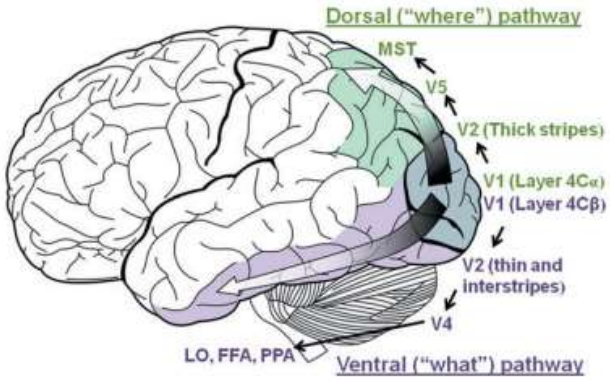
The neurological visual system has been subdivided into many functional areas. These areas have been found with post-mortem material based on the heavy myelination or with fMRI [40]. The study of visual cortex has revealed three human hemifield maps near the calcarine sulcus in the occipital lobe (Figure 1). Primary visual cortex (V1), which receives direct input from the retinogeniculate pathway, occupies calcarine cortex and represents a hemifield of visual space. Two additional maps (V2, V3) occupy a strip of cortex, roughly 1–3 cm wide, which encircles V1 [41]. Additionally human motion-sensitive is located in V5 area [42]. This map allows to focus the visual function in the occipital area, for this reason, the study in visual impairment is made in this zone.

Figure 1. Visual field maps are measured in the right hemisphere of a single subject using expanding ring and rotating wedge stimuli. Mesial view: V1= primary visual cortex; V2 and V3= visual association cortex. Image taken from [41]



Multiple extrastriate visual areas, each one specialized for the detection of particular attributes of visual scenes, are organized into two roughly parallel processing streams (Figure 2). The ventral stream mediates visual recognition of objects (i.e., the “what” pathway) and the dorsal stream is specialized for processing spatial relationships among objects (i.e., the “where” pathway). Lesions of inferior temporal cortex caused severe deficits of visual discrimination or visual agnosia (i.e., disturbance for identifying objects, color, patterns, or shapes) without affecting visuospatial performance (i.e., visually guided reaching or judging the distance between objects). Lesions of posterior parietal cortex had the opposite effects. [43]

Figure 2. Schematic of the dorsal and ventral processing streams. MST, medial superior temporal area; LO, lateral occipital; FFA, fusiform face area; PPA, parahippocampal place area. Lateral view. Image taken from [43]



3.3 Visual functions

There are different visual functions that are evaluated for the ophthalmologists, in clinical applications they try to verify the functions that have an important role in daily life. Usually, the visual functions are grouped into: visual acuity (i.e., ability to see details, regardless of the distance of the object), color vision (i.e, ability to discriminate variations in the wavelength), stereopsis (i.e., binocular vision that allows depth perception), contrast sensitivity (i.e., ability to distinguish a background object, especially in low light situations), and vision of the visual fields (e.g., peripheral and central) [44].

In this study, we specified the visual function in acuity, contrast sensitivity, visual field, motion perception, form recognition and color detection. These functions and the distribution areas will be explaining in this chapter.

3.3.1 Acuity

Visual acuity (VA) is a measure of the ability of the eye to distinguish shapes and the details of objects at a given distance. It is important to assess VA in a consistent way to detect any changes in vision. In acuity studies, each eye is tested at a time [45] [46].

There are many causes of decreased visual acuity in stroke patients, TBI patients and the general population, including refractive error, glaucoma, cataract, and others. But in stroke and TBI it is due to neurological visual injuries – cortex and connections-. Some causes are more readily treatable than others, but if poor visual acuity is not even highlighted in a patient, then easily correctable causes may go untreated and the rehabilitation and subsequent quality of life may be adversely affected [47][6].

Acuity thresholds can be determined either by psychophysical techniques such as Teller acuity cards [46], Snellen chart [48], Bailey-Lovie and ETDRS chart or by electrophysiological procedures [49][50][51][52]. This last measure will be explained in section 4.2.1.1.

Poor visual acuity is a risk factor for falls and a common impediment to rehabilitation, and after stroke, visual impairment may exacerbate the impact of other impairments on overall disability. Postural stability has been shown to be related to visual conditions, and visual ability has been shown to contribute to both the level of care needed and the patient's level of satisfaction with life following stroke [47].

3.3.2 Contrast sensitivity

Contrast sensitivity is the measure of the ability of an individual to detect a difference in the luminance between two areas. It is important in detecting objects without clear outlines and discriminating objects or details from their background [53] [54].

This ability is diminished following a stroke. Patients complain of not being able to tell the curb from the road or read the newspaper because the print closely resembles the background [6]. Contrast sensitivity can be measured using the Pelli-Robson Chart [55][53] or by electrophysiological procedures [25][24] (it will be explaining in section 4.2.1.2.)

3.3.3 Visual field

The visual field is how wide of an area the eye can see when you focus on a central point. Visual field testing is the way in which ophthalmologists measure how much vision is present in either eye, and how much vision loss may have occurred over time [56]. Some tests for evaluating this function are: high-resolution perimetry, Tubingen Automatic Perimeter, Scanning Laser Ophthalmoscope [57] [58]. The Humphrey Visual Field Analyzer is often the instrument of choice for subjects with peripheral field loss or hemianopia. In the case of central field loss, the Humphrey 10-2 test, which focuses on the central 10º of the visual field, may be used [15].

Visual field loss has many causes but is a well-recognized complication of stroke, with an incidence in acute stroke patients reported as 20%. A large study of people in the community showed homonymous visual field defects in 8.3% of post-stroke patients. A smaller study showed asymptomatic visual field loss in 29% of transient ischemic attack patients and 57% of minor stroke patients, which, though asymptomatic, may carry implications for tasks such as driving [47] [6].

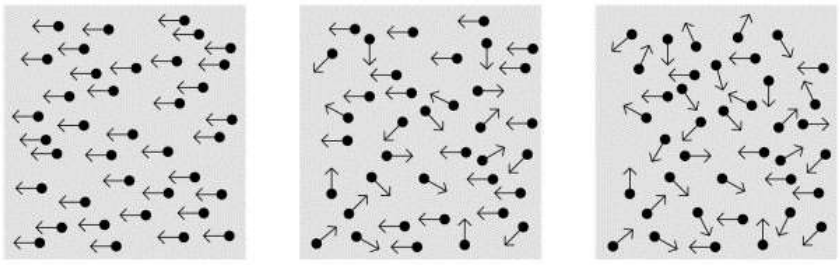
Visual field loss is associated with impairment in daily functioning and a higher risk of incident falling, which obviously has implications for rehabilitation. It is also an important predictor of functional status on discharge from stroke rehabilitation units. Some studies have shown that vision restoration therapy or computer-based training program improves significantly the visual fields [59][57]. A German study of 21 hemianopic patients and 23 controls showed that 4 weeks of compensatory visual field training led to a marked improvement in detection and reaction time of visual stimuli in all their subjects with hemianopia and that this improvement was still maintained at 8 months [47].

3.3.4 Motion perception

Motion information is required for the solution of many complex tasks of the visual system such as depth perception by motion parallax and figure/ground discrimination by relative motion [60]. Brain imaging studies report an increase in activation in and around area V5 when subjects are presented with moving checkerboards, form from-motion displays coherent or incoherent motion displays and even illusory motion [42] [61] [62].

Neurological patients whose cortical damage includes area V5 have deficits in perceiving motion which range from an almost total inability to perceive the movement of objects to deficits in second-order motion only [61].

Figure 3. Random-dot kinematograms (RDKs). A fully coherent RDK (a) and two partially coherent RDKs (b and c) are shown. The direction of each dot's movement, indicated here by an arrow, is separately controlled so that the percentage of dots moving in the same. Image taken from [63]



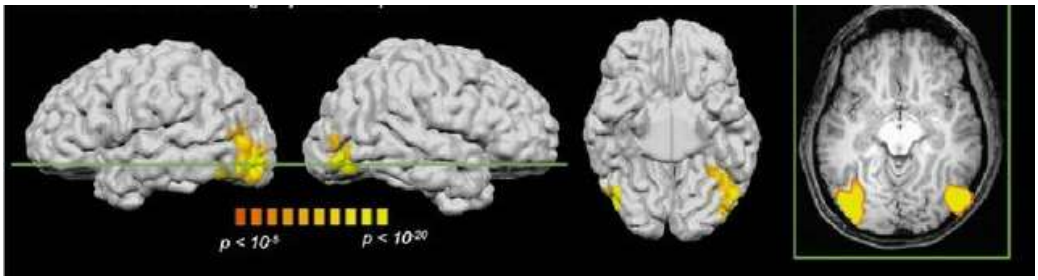
Computer-generated random-dot kinematograms (RDKs) can be used to study these motion-selective brain regions. RDKs are made up of two populations of moving dots;

a “signal” and a “noise” population. Signal dots move in a common direction, whereas noise dots move randomly (Figure 3). Each dot is assigned a particular motion vector. The observer’s task is to indicate the direction of the signal dots. Theoretically, cells in V1 provide information relating to the motion of individual dots, whereas cells within V5/MT are able to integrate information from V1 to resolve the global motion of the stimulus [62][42][64][63].

3.3.5 Form recognition

Another of the extraordinary capabilities of the human visual system is its ability to rapidly group elements in a complex visual scene, a process that can greatly simplify the description of an image. For example, a collection of parallel lines can be described as a single texture pattern without specifying the location, length, and orientation of each element within the pattern. Such grouping processes are reflected in the activities of neurons at various stages of the visual system. Recent neuroimaging studies (Figure 4) have shown that the lateral occipital complex is a higher visual area critical for object shape perception [65]

Figure 4. The expected location of LOC based on group data from seven neurologically intact participants. Image taken from [66]



The overall shape of an object is an important cue for object recognition, as many objects are perfectly recognizable from the shape cues alone, e.g., in the case of silhouettes and line drawings. In general, shape integration in humans seems to be fast and largely invariant to such low-level physical properties of stimuli as contrast or gross size [67].

Patients with visual agnosia have difficulties recognizing objects because of impairments in basic perceptual processing or higher-level recognition processes, due to involvement of the extra striate cortex such as V2, V3, V4 or V5-MT. Such patients can still recognize objects by using other senses such as touch, hearing, or smell, so the loss of function is strictly visual. The word *agnosia* can be translated from Greek as meaning “to lack knowledge of,” so visual agnosia implies a loss of visual knowledge [68] [69].

Visual agnosia is diagnosed by assessing the patient's ability to name, describe uses for, and pantomime the use of visually presented objects. Extensive occipital damage due to anoxic insult or severe infarction is the usual cause of this rare syndrome [70].

In addition to this, previous studies have shown that this grouping process modulates neural activity in the primary visual cortex (V1) that is signaling the local elements. However, the nature of this modulation is controversial. Some studies find that shape perception reduces neural activity in V1, while others report increased V1 activity during shape perception [71].

3.3.6 Color detection

Color vision, the ability to discriminate variations in the wavelength of light independent of intensity, involves multiple stages of processing. Each region of the retina has cone photoreceptors containing photopigments of different spectral sensitivities [72].

Color is primarily processed in the blobs of V1, in the thin strips of V2, in the human V4 complex, and in regions anterior to it. Although the information on both features is present in V1, V2, and V4, it appears to be largely segregated at the cellular level. There is seemingly no evidence for chromatically selective neurons in V5/MT+, although the area does have reciprocal connections with V4 and some of its neurons can respond to moving isoluminant edges [73]

Achromatopsia is a syndrome in which after cortical damage to a specific part of the human brain namely the color center in the fusiform gyrus, the patient is unable to see the world in color but only ‘dirty’ shades of grey [74][75]. The physiological evidence for this segregation is confirmed in a causal way by patient studies, showing that lesions in the vicinity of V4 impair color perception.

Achromatopsia can result from cortical damage and are most associated with stroke located in the territory of the posterior cerebral artery (PCA). Such cases have the potential to provide useful information regarding the loci of the generation of the percept of the color [76]. It is a form of visual agnosia.

To evaluate color detection, in one study, three types of visual stimuli were presented to the subjects during an experimental session. The first stimulus was a chromatic Mondrian pattern which comprised eight differently colored elements. The colored Mondrian pattern was alternated at a rate of 1 Hz with a blank background of the same mean luminance and mean hue. The second stimulus was an achromatic Mondrian, identical to the chromatic version except that each of the elements was of a different grey level. The third stimulus, the resting condition, consisted of a blank screen. [77]

3.4 Therapy and neuroplasticity

Vision loss is one of the most debilitating sensory deficits for humans given that we rely heavily on our sense of sight when gathering information from the external environment. This becomes more evident when the percentage of cerebral cortex allocated to our visual system is considered, which imposes a high risk for visual loss whenever brain damage occurs. There is a 20% to 30% chance of losing some amount of visual capacity leading to visual field disorder (VFD) after a stroke or TBI [3] [33] [78].

Rehabilitation training programs are based on the theory that neuroplasticity reorganizes the damaged cerebral cortex, and it focuses on recovery of the damaged cognitive function and the minimization of the effects of the damage [79]. Neuroplasticity is an intrinsic property of the CNS that is also present during adult life and allows remodeling of specific brain networks in an attempt to optimize cortical function in response to learning and injury [80]. When this plasticity genuinely aids clinical recovery or maintains clinical function in the presence of persistent structural damage, it is known as compensatory plasticity [81].

Contrast sensitivity, visual acuity, and visual field are the most common outcome measures to evaluate functional changes due to a therapy [33], [55] [47]. Some techniques as vision restoration therapy (VRT) have reported subjective improvements in activities of daily life (ADL). For example, the patients felt more comfortable walking on the street because they felt safer after VRT than before. Also, they were able to read the newspaper again. Interestingly, some patients with no evidence of improved visual field size (according to diagnostic testing), still reported subjective improvements in ADL. These results suggest that besides training induced visual field changes other factors may play an important role in subjective ADL improvements after VRT [82]

Neurovisual rehabilitation is still offered less frequently than motor and speech therapy. However, there is an increasing awareness of the need for it. Neurovisual rehabilitation focuses on three major strategies: restitution, compensation, and/or substitution.

Restitution focuses on the utilization of areas described as ‘areas of residual vision’. This implies that there are sectors of the visual field that do not function normally, but where some of the visual brain capacities have survived ischemic injury. Most treatments of neurovisual disorders try to use intact functions (e.g., compensation), use or try to develop optic and prosthetic devices, or aim at improving the adaptation of the environment to the patient's impairment (e.g., substitution). Nevertheless, there are approaches for direct retraining of an impaired function (i.e., restitution)—that is, perimetric visual field training or training of convergent fusion [83].

4. Visual electrophysiology

4.1 Electroencephalography (EEG)

EEG signals have a high temporal resolution and are easily recorded in a non-invasive manner through electrodes placed over the scalp, being these the reasons why EEG is the most widespread recording modality. EEG measures electric brain activity caused by the flow of electric currents during synaptic excitations of the dendrites in the neurons. [84] [85]. This technique is portable, economical and with high temporal resolution and offering the possibility to monitor the fast dynamic changes in brain activity [86].

The recorded EEG signal is a monitoring method to record brain electrical activity over time. This method captures frequency components that can be measured and analyzed [84] [87]. Analysis of the EEG electrical activity can be performed using Fourier techniques and the frequency components have been described mainly in the bands delta (δ), theta (θ), alpha (α), beta (β), and gamma (γ) from low to high frequency, respectively. Table 1 shows the commonly defined waves or rhythms, their frequency, and their properties.

Table 1. Properties for each frequency band [84] [87].

Rhythms name	Frequency band (Hz)	Properties
Delta	<4	The amplitude of delta signals detected in babies decreases as they age. Delta rhythms are usually only observed in adults in deep sleep state and are unusual in adults in awake state. A large amount of delta activity in awake adults is abnormal and is related to neurological diseases.
Theta	4-7	In a normal awake adult, only a small amount of theta frequencies can be recorded. A larger amount of theta frequencies can be seen in young children, older children, and adults in drowsy, meditative or sleep states. Like delta waves, a large amount of theta activity in awake adults is related to neurological disease. Theta band has been associated with meditative concentration and a wide range of cognitive processes such as mental calculation, maze task demands, or conscious awareness.
		Their amplitude increases when the eyes close and the body relaxes and they attenuate when the eyes open and mental effort is made. These rhythms primarily reflect visual processing in the occipital brain region and may also be related

Alpha	8-12	to the memory brain function. There is also evidence that alpha activity may be associated with the mental effort. Attention tasks cause a suppression of alpha activity, particularly from the frontal areas. Consequently, these rhythms might be useful signals to measure mental effort.
Beta	12-30	Beta rhythms are recorded in the frontal and central regions of the brain and are associated with motor activities and cognitive effort. Beta rhythms are desynchronized during real movement or motor imagery. Beta waves are characterized by their symmetrical distribution when there is no motor activity. However, in the case of active movement, beta waves attenuate, and their symmetrical distribution changes.
Gamma	>30	The presence of gamma waves in the brain activity of a healthy adult is related to certain motor functions or perceptions. This gamma band coherence is replaced by a beta band coherence during weak contractions, suggesting a correlation between gamma or beta cortical oscillatory activity and force. Also, several studies have provided evidence for the role of gamma activity in the perception of both visual and auditory stimuli. Gamma rhythms are less commonly used in EEG-based BCI systems because artifacts such as electromyography (EMG) or electrooculography (EOG) are likely to affect them.

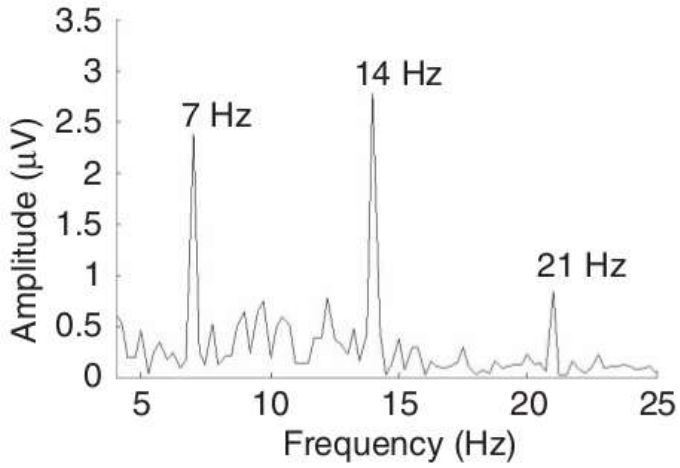
4.2 Quantitative electroencephalography (qEEG)

qEEG, as the name implies, is a means of electrically processing the EEG signal to quantify the relative contributions of each frequency or other characteristics in the signal. qEEG represents a family of related technologies and techniques, however, the common foundation upon which they all are built is spectral analysis. Spectral analysis is a process by which a given segment of the complex EEG signal is separated into its component frequencies. Spectral analysis of the EEG signal reveals the amount of alpha, beta, delta, and theta activity contained in the signal [8]. This allows for comparison over time of changes in the composition of the EEG signal. A new area of research focusing on the changes in qEEG measures as a result of rehabilitation attempts has begun to appear, with interesting results [20]. Leon-Carrion et al. [88] reported on the relationship between recovery at 6 months and delta–alpha ratios in eyes closed data. A higher delta–alpha initial value was associated with poorer recovery.

4.2.1 Steady-state visual evoked potentials (SSVEPs)

Some studies have used steady-state VEPs (SSVEP) to analyze neuro-ophthalmologic diseases [21][89][90][91]. The SSVEP is a robust method to study visual perception, spatial and selective attention, cognitive fatigue, and working memory [92]. Repetitive (or flickering) visual stimuli are presented at a high rate (usually from 6 to 20 Hz) [93], eliciting a continuous and steady sequence of oscillatory potential changes arising mainly in the visual cortex. This stimulation is rapid enough to prevent the evoked neural activity to returning to baseline. The SSVEPs reflect high propagation properties (i.e. a combination of locally and widely temporally distributed sources), are less sensitive to different kinds of artifacts, require much less time to acquire data and have a larger signal-to-noise ratio (SNR) than transient VEPs [21] [94] [95]. An example of the SSVEPs seen using the Fast Fourier Transform is shown in Figure 5.

Figure 5. The SSVEP elicited by the 7-Hz stimulation shows characteristic frequency components with peaks at the fundamental and harmonic frequencies at the O2 electrode. Image adapted [95].



SSVEPs have allowed measuring acuity [96] and contrast sensitivity [51] and it is important to find an objective measure.

4.2.1.1 Acuity measure

The assessment of vision is an essential part of any ophthalmological or optometric examination with visual acuity being the most commonly measured visual function. Contrast sensitivity is another important visual function that has been studied extensively in terms of its development in infants. A subjective assessment is usually done for verbal and cooperative individuals by using visual acuity and contrast sensitivity charts [25].

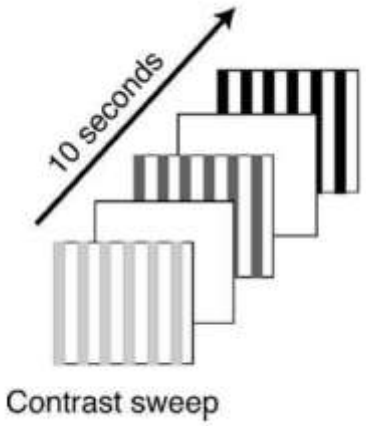
Different techniques have been used to find acuity, Vernier acuity is a measure of the eyes' ability to perceive that misalignment exists between the elements of the stimulus,

when compared with a stimulus without such misalignment. By sweeping spatial frequency from low to high in about 10 s, an estimation of visual acuity is obtained by determining the highest spatial frequency to which the visual system responds [25] [52].

4.2.1.2 Contrast measure

Measurements of spatial frequency threshold (grating acuity) and contrast sensitivity using the sVEP have been obtained previously in full-term, healthy infants and adults. [24]. Figure 6 is a schematic of the typical stimuli for contrast measure. In this case, the contrast sweep stimulus was a 1 cycles per degree of visual angle (c/deg) black vertical cosine-wave grating presented on a 109 cd/m2 space-average luminance white background screen in a pattern on/off mode at a rate of 3.76 Hz. Six presentations (on-off) was used, in each presentation a different percentage of contrast was set and it took 4 seconds.

Figure 6. Stimuli for contrast sensitivity. Image adapted [24]



Using the same processing than in Vernier acuity it possible to get the contrast value. The threshold is determined by extrapolation of a regression line from the signal peak to zero microvolt amplitude against percentage contrast for contrast threshold measurement [97].

4.2.2 Power spectrum estimation

Welch's method (also called the periodogram method) for estimating power spectra is carried out by dividing the time signal into successive blocks, forming the periodogram for each block, and averaging.

Denote the m the windowed, zero-padded frame from the signal x by

$$x_m(n) = w(n)x(n + mR), \qquad n = 0,1, \dots, M-1, m = 0,1, \dots, K-1$$

Where R is defined as the window hop size, and let K denote the number of available frames. Then the periodogram of the m the block is given by

$$P_{x_m}, \mathrm{M}(w_k) = \frac{1}{M}\left|\sum_{n=0}^{N-1} x_m(n)e^{-j2\pi nk/N}\right|^2$$

Where N represents the number of computations. The Welch estimate of the power spectral density is given by

$$S_x^W(w_k) = \frac{1}{K}\sum_{m=0}^{K-1} P_{x_m}, \mathrm{M}(w_k)$$

In other words, it's just an average of periodograms across time. When $w(n)$ is the rectangular window, the periodograms are formed from non-overlapping successive blocks of data [98].

Some studies investigated the power spectrum in rehabilitation therapy. Stathopoulou and Lubar [99] reported that the most systemic change on the EEG data (eyes closed, eyes open conditions) in the TBI patients following 22 sessions of a cognitive rehabilitation program was a decrease in alpha, contrary to the expectation of decreased delta, theta, and alpha (microvolts and relative power) and increases in beta. Vespa et al. [100] examined the daily percent alpha variability (PAV) variable on continuous EEG monitoring with moderate to severe TBI 0–10 days after injury. The lower the alpha variability, the poorer was the clinical outcome.

4.2.3 Coherence

The coherence function provides the linear correlation between two signals, x and y, as a function of the frequency. Coherence, also termed as magnitude squared coherence or coherence spectrum, between two signals is their cross-spectral density function. It is expressed as follows:

$$k_{xy}^2(f) = \frac{|\langle S_{xy}(f)\rangle|^2}{|\langle S_{xx}(f)\rangle||\langle S_{yy}(f)\rangle|}$$

Where f is the frequency and $\langle . \rangle$ indicates the average of M segments or times of equal magnitude of the EEG signals The spectrum is estimated using the Welch method, averaging the period plot over all segments [101].

The estimated coherence ranges between 0 and 1. For a given frequency f_o, $k_{xy}(f_0) = 0$ indicates that the activities of the signals in this frequency are linearly independent, whereas a value of $k_{xy}(f_0) = 1$ gives the maximum linear correlation for this frequency.

Some studies have shown how connectivity measures can be useful as biomarkers in stroke and TBI. Guo, Xiaoli et. al [102], reported a research in resting-state networks of mild occipital stroke patients with hemianopia using partial directed coherence in multi-channel EEGs. They found the patients presented enhanced connectivity due to newly formed connections which suggested that the enhancement of connectivity as a neural mechanism of recovery of stroke-induced hemianopia and demonstrated the potential usefulness of effective networks in the characterization of stroke patients.

In another study, authors found electroencephalography measures of motor cortical connectivity are strongly related to motor deficits and their improvement with therapy after stroke and so may be useful biomarkers of cortical function and plasticity. They mentioned that such measures might provide a biological approach to distinguishing patient subgroups after stroke [103]

In the case of TBI, Lewine, Jeffrey et. al [104], found, in patients with mild traumatic brain injury (mTBI), differences in global relative theta power (increased for mTBI patients), global relative alpha power (decreased for mTBI patients), and global beta-band interhemispheric coherence (decreased for mTBI patients). Additionally, they reported the combination of a multivariate approach with machine learning methods yielded a composite metric that provided an overall predictive accuracy of 75% for correct classification of individual subjects as coming from control versus mTBI groups. This study indicates that in the identification, classification, and tracking of individual subjects with mTBI, quantitative EEG methods may be useful.

5 Analysis methods

5.2 Reduction of dimensionality

In data analysis, it is common to find many variables that describe each sample, however, the volume of information limits processing. In these cases, the reduction of dimensionality is important. One of the techniques that allows this is known as factor analysis (FA). This technique is a method for analyzing a whole matrix of all the correlations among a number of different variables to reveal the latent sources of variance that could account for the correlations among many seemingly diverse tests or other variables. It is usually helpful to reduce the variables to a smaller set of factors, aiming mainly to understand the underlying structure of the data matrix. Usually, the first factor extracted explains most of the variance [105].

In factor analysis principal component (PCA) measure is the most common method used. PCA starts extracting the maximum variance and puts them into the first factor. After that, it removes that variance explained by the first factors and then starts extracting maximum variance for the second factor. This process goes to the last factor.

In addition, rotation method, also can be configured. Eigenvalues do not affect the rotation method, but the rotation method affects the Eigenvalues or percentage of variance extracted. There are a number of rotation methods available: (1) No rotation method, (2) Varimax rotation method, (3) Quartimax rotation method, (4) Direct oblimin rotation method, and (5) Promax rotation method. The most common method is Varimax.

5.3 Repeated measure design

Repeated measurements often exist in clinical trials, when the response of patients to a treatment is regularly measured to monitor it, also when the design is characterized by the inclusion of several observations per experimental unit (e.g., subjects), each obtained under a different experimental condition (e.g., treatment).

Repeated measurements in each experimental unit provide information on the time trend of the response variable under different treatment conditions. Trends in time can reveal how quickly units respond to treatment or how long treatment effects manifest themselves in the units of the study. It is also possible to assess differences between treatment trends [106].

The increase in accuracy in this kind of analysis is due to the fact that measurements in the same unit tend to be less variable than measurements in different units;

therefore, the effect of repeated measurements is similar to the effect of using blocks [106].

In the analyses of repeated measurements, it is necessary to evaluate the sphericity assumption to validate the conclusions. Sphericity is calculated with the differences between each pair of levels of the repeated measures factor and with the variance of these difference scores. Sphericity requires that the variances for each set of difference scores be equal. Mauchly's sphericity test or Mauchly's W is a statistical test used to validate a repeated measures analysis of variance. If P-value for Mauchly's test is greater than or equal to 0.05, the assumption of sphericity is not rejected at the 5.0% significance level [107].

6 Set of test

Objective: To design and build a set of tests to evaluate vision during EEG recordings.

Different visual functions are affected after a stroke or TBI, these functions involve decreased visual acuity, impairment in identifying contrast changes, loss of visual field or motion recognition, difficulty in recognizing shapes or in detecting color. This means that in order to obtain a characterization of the cerebral electrophysiology in healthy subjects that allows later evaluation of the evolution of the patients it is necessary to design different stimuli focused on the visual functions that can be affected by damages at cerebral level. This section aims to show the methodology and results obtained for this stage.

6.2 Methodology

For the first objective different studies were analyzed to find stimuli that generate visual cortex activation according to different visual abilities. The studies vary for EEG or fMRI measurements. For each visual skill different options were evaluated.

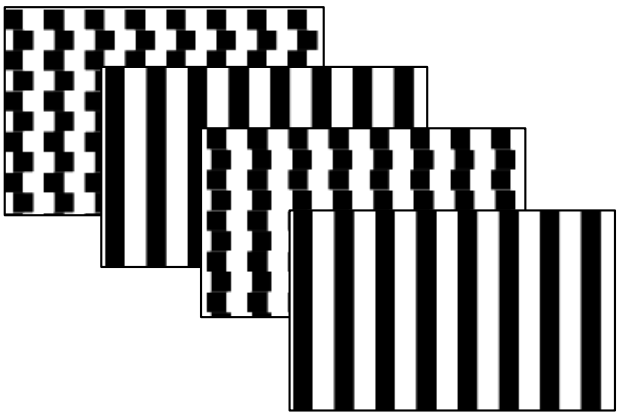
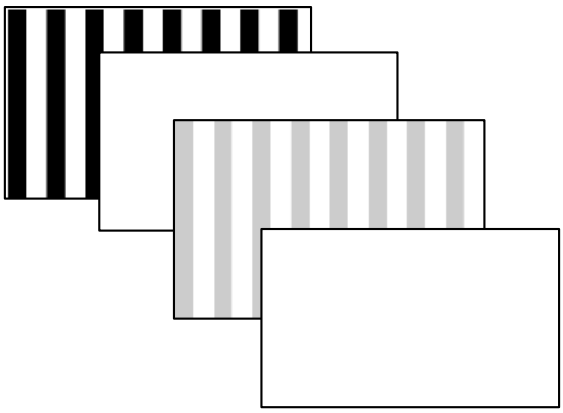
Once the stimuli were defined, depending on the characteristics of each one, software that better adapted to be designed was used. Python, psychoPy3 and openDesigner were the software on which they were mounted to evaluate functionality. Each stimulus meets conditions of time, frequency, light intensity, among others.

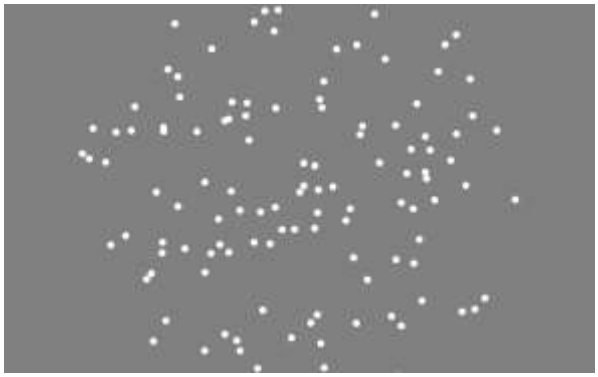
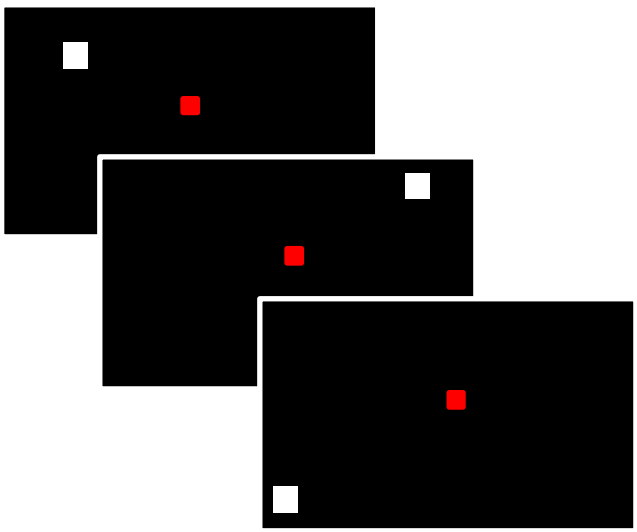
6.3 Results and discussion

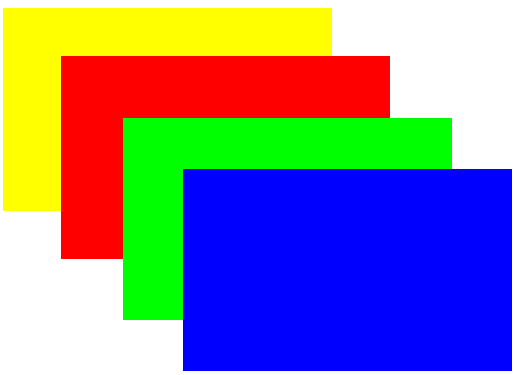
In order to evaluate the visual function, the test set was designed to stimulate vision for different skills. The set contains stimuli to measure: Vernier acuity, contrast sensitivity, motion perception, visual field, form recognition, and color detection. This selection answers the different skills that are affected when there is a stroke or TBI. Open-source scripts are available on GitHub: https://github.com/danni9310/Thesis_stimuli.

Table 2 explains the characteristics of each test. From resting-state with eyes closed, to visual field stimulus, the participants do not talk, only passively watch. In some cases, participants have to report with their finger the direction of the points for motion stimulus, or whether they can see the square in the monitor for visual field stimulus. For form recognition and color detection, the participants need to report the forms and colors they see.

Table 2. Stimuli description

Stimulus	Diagram	Description
Resting-state eyes closed	-	30 seconds with close eyes (time tested to be stable)
Resting-state eyes open	-	30 seconds for binocular and monocular vision with eyes open. (time defined to keep comparison with eyes closed)
Vernier acuity		All stimuli alternated between two states at a rate of 3.75 Hz. For the swept paradigm, the size of the displacements of Vernier offset ranged from 2 to 30 cycles per degree (cpd) in a period of 28 s [49][108][109]. Stimulus in openDesigner. Total time of stimulation for each eye: 28s Participant's action: passively fixate on the center of the screen.
Contrast sensitivity		Contrast sweep 3.75 Hz onset-offset vertical cosine-wave grating with 2 cpd onset-offset vertical grating space-average luminance white background screen was swept from 0.5% to 100% contrast in linear steps [24]. Stimulus in openDesigner. Total time of stimulation for each eye: 28s

		Participant's action: passively fixate on the center of the screen.
Motion perception		Dynamic random-dot kinematograms (RDKs) consisted of a large number of moving dots randomly positioned within a restricted area. Each dot is assigned a particular motion vector. With these stimuli, a variable percentage of dots can be moved in a single coherent (signal) direction whilst remaining dots are moved in random directions (noise) [63][62]. This stimulus was designed in psychoPy3 using 120 dots 0.1 in speed (displacement per frame) and 22 px for dot size. Total time of stimulation for each eye: 62s Participant's action: report with their finger the direction of the points.
Visual field		In visual field stimulus, the patient focuses on a central fixation point in the screen during the entire period of examination, light stimulus was repetitively presented in different parts of the space screen [59]. Only for this stimulus, subject have attended stimulus from 50 cm distance. Stimulus in openDesigner. The positions were selected to cover all the visual field

		and for square size we use the minimum visual acuity for the first test (2 cpd). White square size: 60x60 px Total time of stimulation for each eye: 114s Participant's action: report with their finger if they could see the white square.
Form recognition		Form recognition was measured while volunteers were watching universal icons for some objects. Three objects were static and 3 more was showed in different sizes. Eleven different forms were used: heart, phone, apple, ball, plane, light bulb, clock, scissors, umbrella, house and tooth. Stimulus designed in python. We selected image with lines and curves and we tested if the images were easy to recognize. Total time of stimulation for each eye: 50s Participant's action: report the forms they see.
Color detection		Color detection stimulus was designed in three parts. First, basic color (red, blue, green and yellow) was performed in the screen for 5 seconds, after the same color flicker between two different colors in order to change the contrast and finally, stroop effect was tested to maintain the

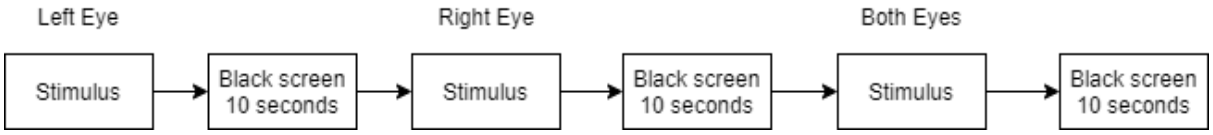
		concentration in the image. In this experiment different words with different colors are showed and the participants are required to say the color of the word, not what the word says. For example, for the word, **AZUL**, participants should say "green". Stimulus designed in python. Total time of stimulation for each eye: 95s Participant's action: report the colors they see.

According to the results, a set of stimuli was designed to activate the visual cortex, some stimuli were configured according to reports in the literature and others are part of an exploratory analysis. This set activates the visual skills from basic processing to complex analysis and allows that neurons in occipital and temporal-occipital cortex areas V1, V2, V3, V4 y V5 are stimulating to get an EEG measure. EEG recordings during resting state were very important because they represent the baseline for comparing signals when there is stimulation.

Stimuli for acuity and contrast measures have been reported in previous research studies [23][25][110][111][97][108][109][112][113]. In some of them, there are experiments to examine whether a higher density of recording electrodes improves the estimation of individual low-level visual thresholds with swept-parameter visual evoked potential (sVEP) [23], others validate intersession and intrasession variabilities of sVEP measurements [110] and some studies use this measure for the detection of amblyopia in adults and children [109][112].

For motion perception [64][63][114][62] and visual field [59] there are some papers with test used in clinical part or in rehabilitation process. However, there is not a world standard for forms recognition and color detection stimuli, so in these cases, the stimuli were designed taking into account general clinical information. It was important to use basic forms and main colors. This part is an exploratory section.

Figure 7. Flow complete for each stimuli



All the stimulus scripts were designed following the structure of the diagram in Figure 7. Each stimulus has different editable parameters for other types of experiments, table 3 shows the summary. Stimulation time and time between tests is common to all stimuli. For all the tests in this work the rest time between tests was 10 seconds and the stimulation time varied for each stimulus.

Table 3. Editable parameters for each stimulus

Stimulus	Editable parameters
Resting-state eyes closed	Time
Resting-state eyes open	Time
Vernier acuity	Stimulus time Resting time between tests Stimulation frequency Cycles per degree in each image
Contrast sensitivity	Stimulus time Resting time between tests Stimulation frequency Contrast and cycles per degree in each image
Motion perception	Stimulus time Resting time between tests Dots number Dots speed Dots size
Visual field	Stimulus time Resting time between tests Box size Background color Box Items
Form recognition	Stimulus time Resting time between tests Background color Images shown Number of images
Color detection	Stimulus time Resting time between tests Time of each color on the screen Background color Color and size of letters Color and text order

In Vernier acuity and contrast sensitivity stimulus there is a stimulation in a specific frequency (3.75 Hz) [109], it means that in the electrophysiological signal this frequency need to be as easily identifiable. If in the experiment, the stimulation frequency change, a peak should appear at the set frequency and at the following harmonics.

6.4 Conclusion

The subdivision of the visual cortex can help to define the type of stimuli that we can use to activate the visual system. In this case stimuli with editable parameters for acuity measures, contrast sensitivity, visual field, motion perception, form recognition, and color detection are necessary for activating V1, V1, V3, V4 and V5 with dorsal and ventral streams. Scripts are free and were developed in open source tool, whereby they can be used in other visual experiments.

7 Study in healthy control individuals

Objective: To measure neuronal activation using EEG in healthy control individuals during visual stimulation to obtain the baseline of clinical measures and qEEG values.

With the stimuli designed in the previous objective, the measurements had to be made on healthy subjects and exploratory analysis carried out to understand the general behavior of the data. Power and coherence were the measures chosen to be analyzed.

7.2 Methodology

7.1.1 Subjects

This study was conducted in 37 healthy control subjects. Participants were recruited at the University of Antioquia and all measurements were made in laboratory facilities located in the university campus. Patient demographics is included as supplementary material (Appendix 1).

The inclusion criteria and exclusion criteria for the healthy subjects in this research were:

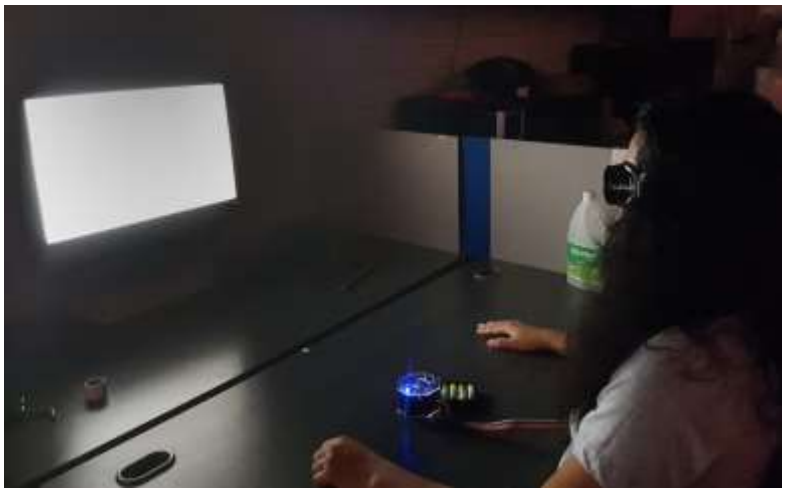
- Both genders
- Adults (>18 years and <60 years)
- Healthy subjects: no ophthalmologic or neurological disease (acute or chronic). Without epilepsy.

7.1.2 Experimental setup

During the whole experiment, subjects were seated in a comfortable chair in a slightly dimmed room about 1 m in front of the stimulation unit. All subjects completed the test at the same time. Figure 8 shows the condition for the room and the basic position for the subjects.

Each subject was in the experiment for 40 minutes. The stimuli were shown for binocular and monocular vision. During the experiment, participants wore specific glasses that allowed us to cover one eye for monocular vision. In each subject 8 tests were made. Stimuli were designed in python, openDesigner and psychopy and performed in a screen SyncMaster 2243 LNX with a vertical refresh rate of 75 Hz and horizontal refresh rate of 81 kHz. Scripts are open and can be used in other projects (https://github.com/danni9310/Thesis_stimuli).

Figure 8. Conditions for the room

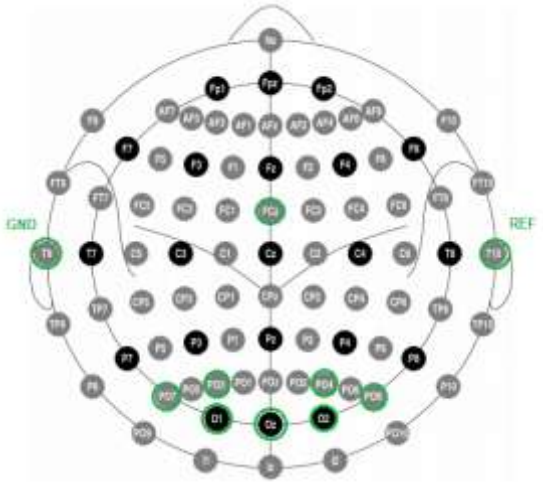


7.1.3 EEG acquisition

An open-source BCI headset and data acquisition board OpenBCI were used to acquire EEG signals from the surface of the scalp. The sampling rate was 250 Hz. According to the International 10–10 system, sensors were placed on the scalp at locations FCz, Oz, O1, O2, PO7, PO8, PO3, PO4 (Figure 9). Additionally, two sensors were used on right and left earlobes for reference and ground signals respectively.

The OpenBCI Cyton Board is an Arduino-compatible, 8-channel neural interface with a 32-bit processor. At its core, the OpenBCI Cyton Board implements the PIC32MX250F128B microcontroller, giving it lots of local memory and fast processing speeds. The board comes pre-flashed with the chipKIT™ bootloader, and the latest OpenBCI firmware [115].

Figure 9. Electrode Placement. Image adapted [116]



7.1.4 EEG processing and data analysis

The EEG recordings acquired from OpenBCI were processed with Python and statistical analysis was performed by STATGRAPHICS and R. The signals were band-pass linear filtered at 3-30 Hz and divided in monocular and binocular vision (right and left). Depending of the features (power spectrum or coherence), a specific script was developed in Python. An exploratory analysis of the data was carried out to identify outliers.

Features were extracted using the electrodes selected using aspatial filter based on Independent Component Analysis (ICA), in order to use a maximally independent, multichannel EEG decomposition. This filter is important because it is obtained taking into account the neurophysiological behavior for visual stimuli. The configurations used were: Oz-FCz (Oz), O1+O2-FCz (O1O2), PO3+PO4+PO7+PO8-FCz (PO), PO3+PO7-FCz (POL), PO4+PO8-FCz (POR)

1. Frequency spectrum were calculated for each bipolar channel by Welch's power spectral density estimate method. This processing was made with a Hamming window. Relative power spectral in each frequency band was calculated for summation of the values for each band, delta (0-4 Hz), theta (4-8 Hz), alpha (8-13 Hz) and beta (13-30 Hz).

   Function signal.welch was used from scipy library, the parameters set were (data_filter is the main signal):

```
fs = 250
nblock = fs*10
overlap = nblock/2;
win = signal.hamming(int(nblock),True);
f, Pxx = signal.welch(data_filter, fs, window=win, noverlap=overlap, nfft=nblock, return_onesided=True)
```

2. Coherence was obtained for each frequency band taking into account the different combination between spatial filters. Function signal.coherence was used from scipy library, the parameters set were:

```
fs = 250
nblock = fs*10
overlap = nblock/2;
f1, Cxy1 = signal.coherence(data1, data2, fs, nperseg=nblock, noverlap=overlap)
```

   Coherence values were obtained for each pair of channels and in each frequency. It means we got: Alpha O1O2-PO, Alpha O1O2-POL, Alpha O1O2-POR, Alpha Oz-O1O2, Alpha Oz-PO, Alpha Oz-POL, Alpha Oz-POR, Alpha POL-POR, Alpha PO-POL, Alpha PO-POR, and the combination for each frequency.

7.1.5 Ethics statement

The study was presented to the Research Ethics Committee at the University of Antioquia and was approved in December 2018. Subjects did not receive any financial reward for participating in this study. Written informed consent was obtained from all participants after explanation of the nature and possible consequences of this study.

In Resolution 8430 of October 4, 1993 (Articles 9 and 11), the definition of risk and the categories that apply to investigations are proposed. The present project was classified as research with minimal risk since it will be a cross-sectional study based on the characterization of signals acquired by non-invasive instruments.

There was not intentional intervention or modification of the behavior or social, medical or work variables of the people (healthy subjects and patients) participating in the study. Medications were not applied and invasive sensors will not be used at the level of the orbital cavity or the eyeball. No new electroencephalography devices will be tested on patients. The sensors used in the project (electrodes of EEG), are evaluated devices and with commercial use in humans so that new devices or in prototype phase will not be used.

7.1 Results and discussion

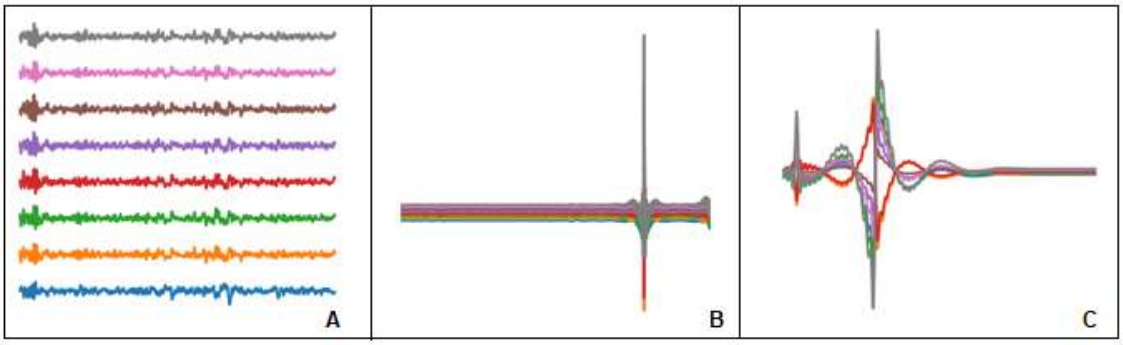
Using the set designed, to groups of control subjects was recording. The first measures were made between March and June 2019 and 37 subjects were in the test. Table 4 shows the average age, range age and the number of women and men in each group. Complete information can be found in the supplementary material.

Table 4. Subjects caracterization

Average age	Range age	Women	Men
26.5	19 – 53	15	22

An exploratory visual analysis on the EEG recording allowed us to clean the database and determine the final signals for analysis by each type of stimulus. Some signals had outlier data or problems with the acquisition equipment. The sample signals are shown in Figure 10. Normal signals (Figure 10A) were approved, signals with only one outlier were filtered with Hampel filter (Figure 10B) and signals with many outlier data (Figure 10C) were discarded. Drastic errors in the acquisition of the signals were produced by saturation in the sending of data from the openBCI. Eye blinks was removed with band-pass linear filtered at 3-30 Hz and in the visual inspection the outliers was classified according to Figure 10. All signals were visualized with the same methods and in the same scale.

Figure 10. Sample signals A) Normal signals B) Signals with only atypical data C) Signals with many atypical data



After visual inspection, 31 participants were included, resulting in 580 test sets, this dataset has records for each stimulus and type of vision (binocular - B, monocular left - L and monocular right - R). The datasets are available in a repository on GitHub (https://github.com/danni9310/Thesis_group_mix/tree/master/DataProcessingMix).

7.2.1 Power spectrum estimation

Relative power in each frequency band for channels Oz-FCz (Oz), O1+O2-FCz (O1O2), PO3+PO4+PO7+PO8-FCz (PO), PO3+PO7-FCz (POL), PO4+PO8-FCz (POR), was got and analyzed.

An exploratory analysis of the variables was carried out to identify trends and characterize each stimulus according to the results for the power spectrum. This chapter shows an overview of the data, the statistical tests are presented in the following section. Each type of stimulus is analyzed in the same way: graph of confidence bands for mean value of all channel in each frequency band and test of repeated measures in the next chapter. These analyses consider resting states (i.e., eyes open, eyes closed), visual stimulation, and type of vision (i.e., binocular – both eyes, monocular right eye, and monocular left eye).

7.2.1.1 Vernier acuity

Figure 11 shows the confidence interval for each frequency band taking into account the states and the electrode configuration. In the figure it is possible to observe that for the theta and alpha bands there is a difference between the three states: eyes closed, eyes open, and stimulation (binocular, monocular left and monocular right). For theta band, it shows low values when participants' eyes are closed and these values increase when eyes are open and when there is stimulation. The trend is upwards in this band for all configurations. Moreover, in the alpha band, the trend is downwards. Delta band only shows a representative increase between open and eyes closed and beta band does not show a clear trend. It is also observed that the power

values when participants are watching the stimulus are similar in binocular and monocular vision for all bands.

Figure 11. Confidence bands for Vernier acuity stimulus for relative power in each frequency band. Oz-FCz (Oz), O1+O2-FCz (O1O2), PO3+PO4+PO7+PO8-FCz (PO), PO3+PO7-FCz (POL), PO4+PO8-FCz (POR).

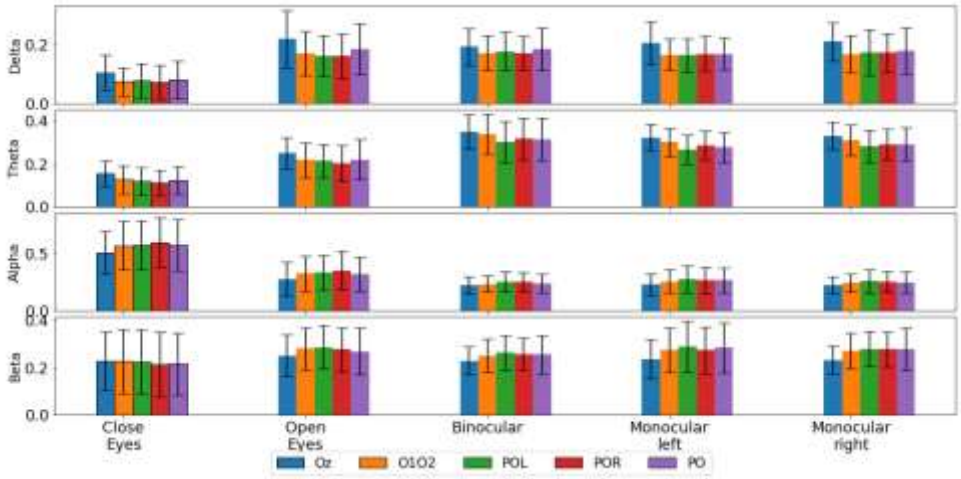
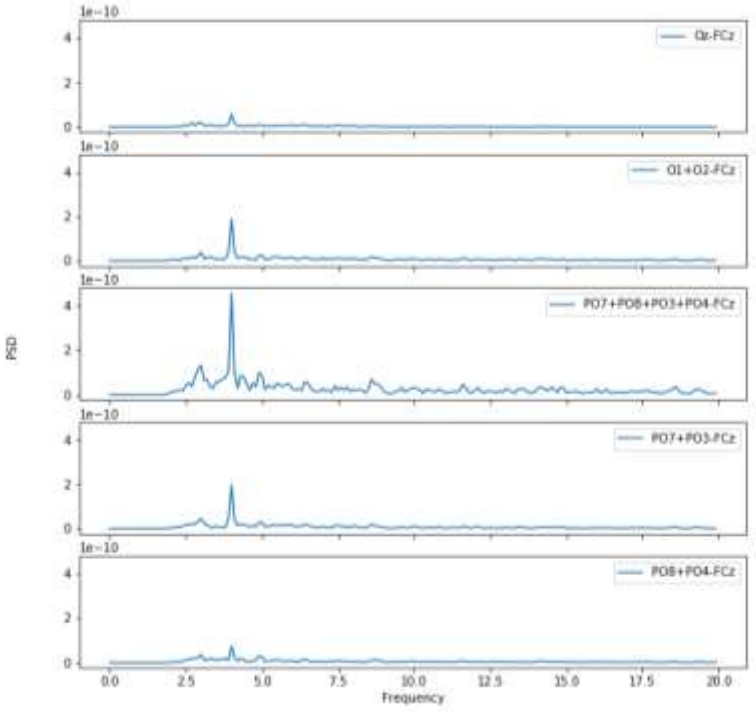


Figure 12 represents a typical power spectrum for different spatial filter, peak in 3.5 Hz is visible and corresponds to stimulation frequency.

Figure 12. Power spectrum for S7 in Vernier acuity with binocular vision in different configuration.



Percentage of subjects where the peak frequency is observable was analyzed (table 5), to define if the peak was representative the maximum values was compare with the maximum values in lateral frequencies. If the central value was 1.5 time the lateral

peaks, it was saved as a representative peak. For O1+O2-FCz configuration the peak was observable in the 79% of the test in monocular – right eye, 86% in monocular – left eye test and in the 89% of binocular test. In other cases, in binocular vision configurations Oz-FCZ and PO8+PO4-FCz show a relevant percentage of test although it was not the same for monocular vision. This result shows that the type of stimulus presented on the screen generate a specific response in power spectrum in the EEG signals.

Table 5. Percentage of subjects where the peak frequency is observable in Vernier acuity stimulus.

Spatial filter	Monocular Right eye	Monocular Left eye	Binocular
O1+O2-FCz	79	86	89
Oz-FCz	69	68	89
PO7+PO3-FCz	52	50	70
PO7+PO8+PO3+PO4-FCz	62	57	67
PO8+PO4-FCz	48	64	81

7.2.1.2 Contrast sensitivity

Confidence band analysis in contrast sensitivity stimulus shows the same tendency than in Vernier acuity stimulus (Figure 13). The trend is upwards in theta band for all configurations, downwards in alpha band and small changes in delta band for eyes closed and eyes open. Also, the power values when participants are watching the stimulus are similar in binocular and monocular vision for all bands.

Figure 13. Confidence bands for contrast sensitivity stimulus for relative power in each frequency band. Oz-FCz (Oz), O1+O2-FCz (O1O2), PO3+PO4+PO7+PO8-FCz (PO), PO3+PO7-FCz (POL), PO4+PO8-FCz (POR).

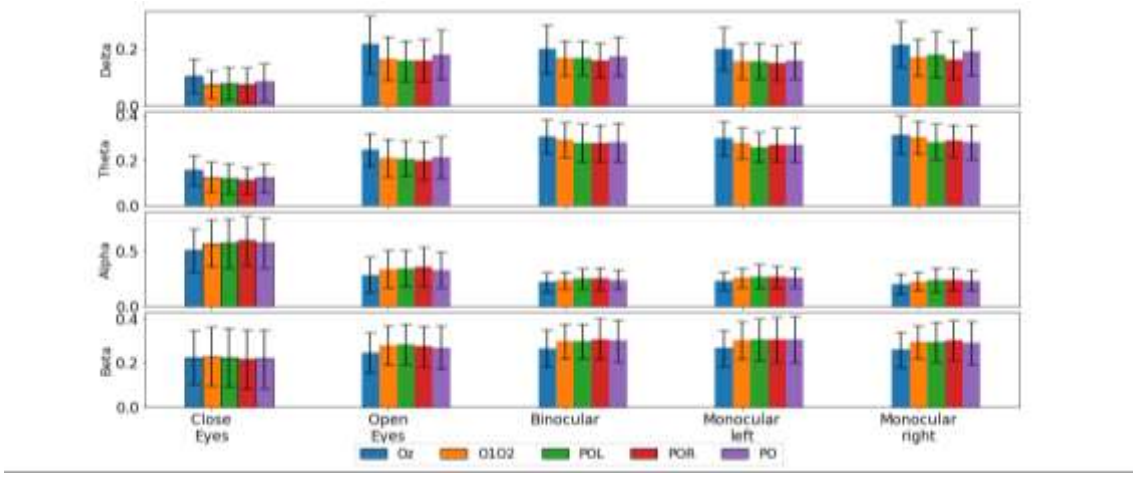


Figure 14 represents a typical power spectrum for different spatial filter, peak in 3.5 Hz is visible and corresponds to stimulation frequency.

Figure 14. Power spectrum for S27 in contrast sensitivity with binocular vision in different configuration.

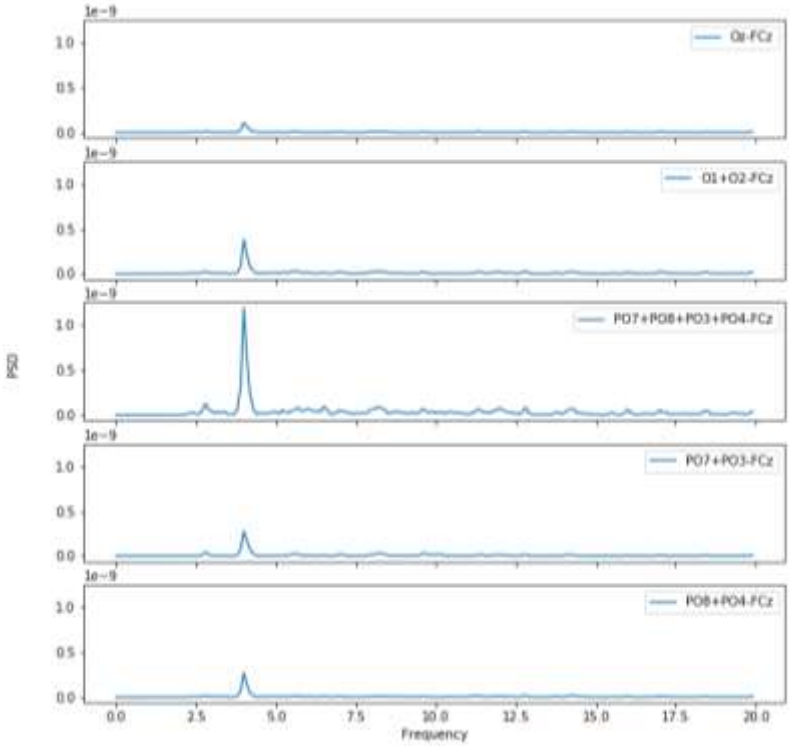


Table 6 shows the percentage of subjects where the peak frequency is observable. In this case the percentage are higher than in acuity stimulus because the change of images generates perceivable changes in brightness. In this stimulus, O1+O2-FCz special filter shows the highest percentages, in 97% of the monocular vision – right eyes recording, the peak was measured, in 79% in monocular – left eye and in 83% of the binocular recording.

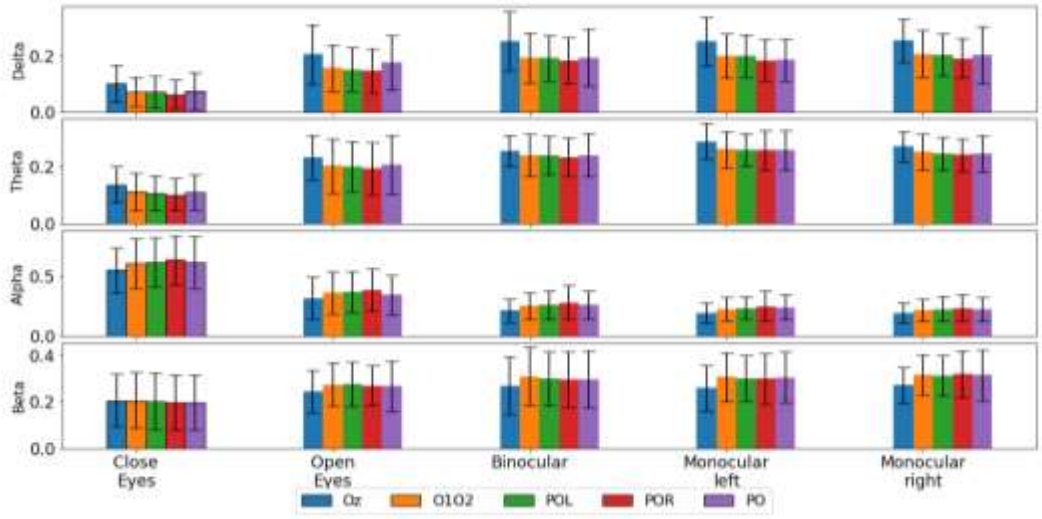
Table 6. Percentage of subjects where the peak frequency is observable in contrast sensitivity stimulus.

Spatial filter	Monocular Right eye	Monocular Left eye	Binocular
O1+O2-FCz	97	79	83
Oz-FCz	69	62	80
PO7+PO3-FCz	72	72	70
PO7+PO8+PO3+PO4-FCz	72	52	73
PO8+PO4-FCz	79	69	80

7.2.1.3 Motion perception

In this case, the behavior of the data is similar to the stimuli presented above (Figure 15), the trends are the same with small alteration in theta band where the difference between eyes open and stimulation stage (binocular and monocular) is not so marked.

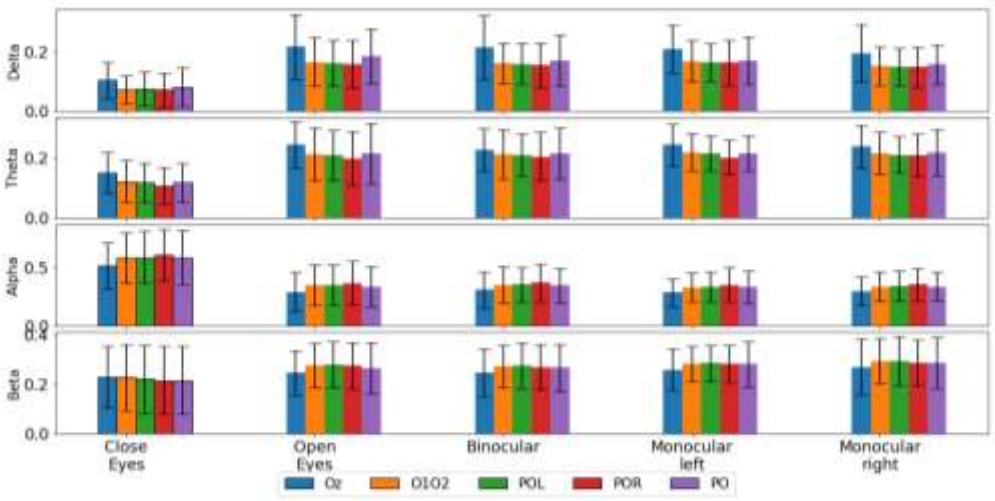
Figure 15. Confidence bands for motion perception stimulus for relative power in each frequency band. Oz-FCz (Oz), O1+O2-FCz (O1O2), PO3+PO4+PO7+PO8-FCz (PO), PO3+PO7-FCz (POL), PO4+PO8-FCz (POR).



7.2.1.4 Visual field

For this stimulus, figure 16 shows the interval confidence for relative power. In this case, there are no clear trends, only it is possible to find a small change between eyes closed and eyes open for delta, theta, and alpha band but it is not easy to identify differences with stimulation test. Beta band does not show a significant change.

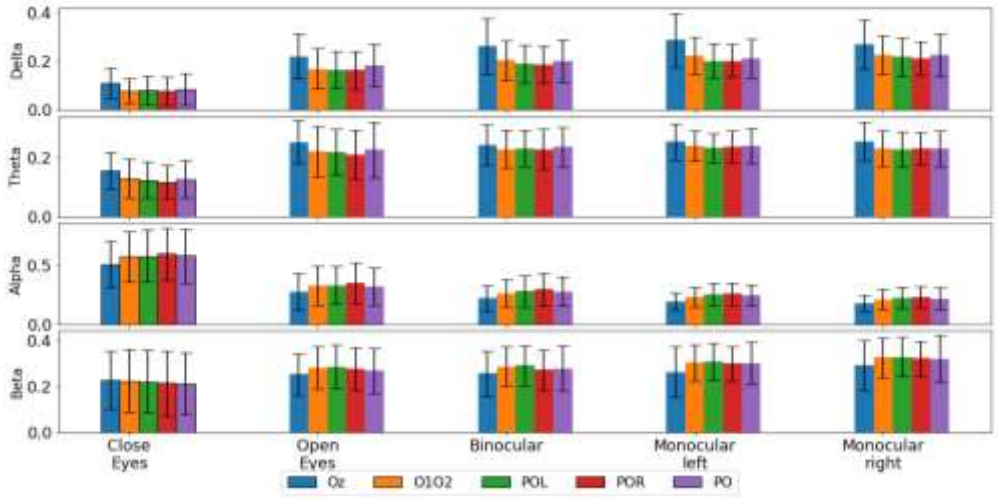
Figure 16. Confidence bands for visual field stimulus for relative power in each frequency band. Oz-FCz (Oz), O1+O2-FCz (O1O2), PO3+PO4+PO7+PO8-FCz (PO), PO3+PO7-FCz (POL), PO4+PO8-FCz (POR).



7.2.1.5 Form recognition

As with the visual field stimulus, the relative power data does not show a clear trend (Figure 17), only a small difference between eyes closed and eyes open can be seen for theta and alpha bands.

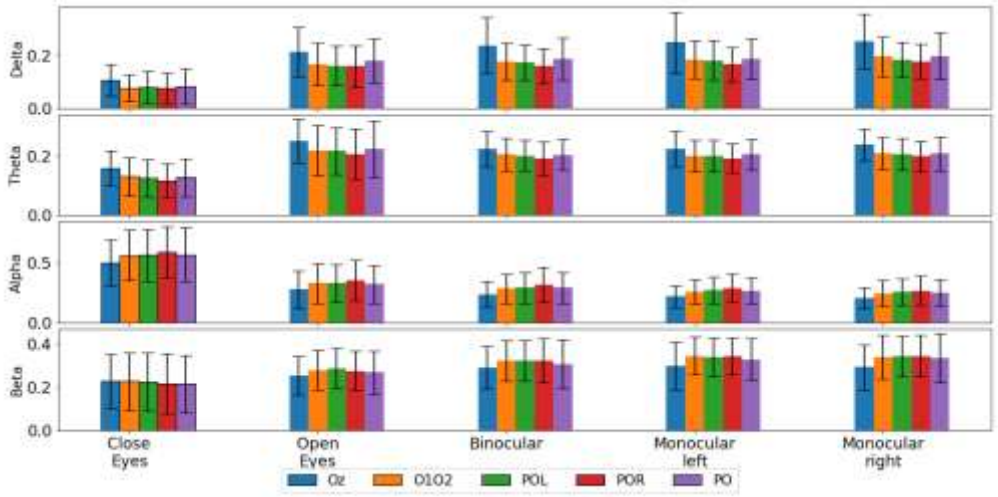
Figure 17. Confidence bands for form recognition stimulus for relative power in each frequency band. Oz-FCz (Oz), O1+O2-FCz (O1O2), PO3+PO4+PO7+PO8-FCz (PO), PO3+PO7-FCz (POL), PO4+PO8-FCz (POR).



7.2.1.6 Color detection

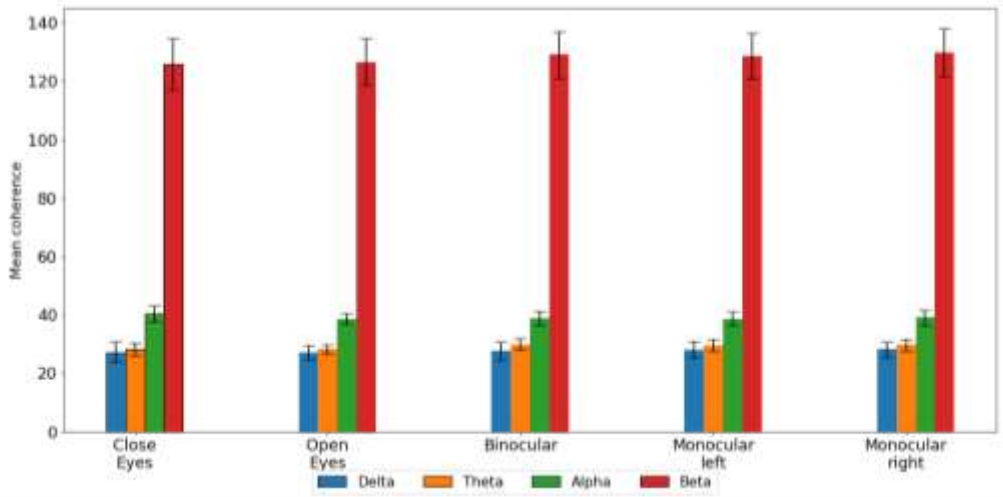
Figure 18 shows the results for the confidence bands in color detection stimulus. In this case, it is only possible to see a difference between eyes closed and eyes open for delta, theta and alpha band. Differences between the stimulation stage and eyes open are not obtained.

Figure 18. Confidence bands for color detection stimulus for relative power in each frequency band. Oz-FCz (Oz), O1+O2-FCz (O1O2), PO3+PO4+PO7+PO8-FCz (PO), PO3+PO7-FCz (POL), PO4+PO8-FCz (POR).



7.2.2 Coherence

Figure 19. Confidence bands for coherence in each frequency band for Vernier acuity stimulus



Coherence was obtained in each frequency band for all possible combinations with the channels Oz-FCz (Oz), O1+O2-FCz (O1O2), PO3+PO4+PO7+PO8-FCz (PO), PO3+PO7-FCz (POL), PO4+PO8-FCz (POR). The mean in each bands were calculated and figure 19 shows the results for each state. Here we observe that regardless of whether the state is rest or stimulation, the behavior of coherence is similar for all cases. Low coherence in delta band and increases for theta, alpha and delta, being significantly high in delta. This trend is observed for all stimuli with no drastic observable and conclusive differences

7.3 Conclusion

The exploratory analysis of the power spectrum allows us to conclude that there are differences between the stimulation and eyes open stages with respect to the values obtained for the closed eye state and that in specific stimuli like Vernier acuity and contrast sensitivity, the configuration O1+O2-FCz shows clearer the typical spectrum for this stimulation. On the other hand, the consistency measure does not visually show significant changes between different states and stimuli. This analysis is complemented in the following section by statistical tests.

8 Statistical analysis

Objective: To evaluate the capacity of qEEG measures obtained in healthy subjects, in order to find variables to discriminate experimental states.

Finally, the measures obtained in the previous objective are evaluated using statistical methods to evaluate the capacity of the qEEG measures obtained to classify the test vision in healthy subjects and select the variables with best behavior. This section describe the methodology and results obtained.

8.1 Methodology

The signals obtained were analyzed by means of a repeated measurement ANOVA. In the case of power, each spatial filter was analyzed, while in the case of coherence, a factorial analysis was initially carried out and subsequently the combinations of filters that provided the most information to each factor were studied. The statistical analysis was carried out in Statgraphics XVII-X64.

All analyses compared whether there was a significant difference between keeping the eyes closed and open, between keeping the eyes closed and observing a stimulus, and between keeping the eyes open without stimulation and observing a specific stimulus. The P-value in Mauchly's sphericity is always reported, for values >0.05 the conclusion regarding differences between states is valid.

The labels used in this section are: Oz-FCz (Oz), O1+O2-FCz (O1O2), PO3+PO4+PO7+PO8-FCz (PO), PO3+PO7-FCz (POL) and PO4+PO8-FCz (POR)

8.2 Result and discussion

8.2.1 Power spectrum estimation

A repeated measures analysis was made in order to evaluate the qEEG values behavior between states. The analysis takes into account the states (eyes open rest, eyes closed rest and stimulation) and the type of vision (binocular - both, monocular right eye and monocular left eye).

8.2.1.1 Vernier acuity

Repeated measures analysis (Table 7) shows that it is possible to separate all the states in the test in the theta band in all electrode configurations. In yellow rows, there are significant differences between eyes closed and eyes open in the three types of vision (binocular- both, monocular left eye – left and monocular right eye - right), also between eyes closed vs stimulation and eyes open vs stimulation.

Table 7. Repeated measures analysis in Vernier acuity stimulus for each electrode configuration taking into account each state and type of vision.

Frequency band	Eyes closed vs eyes open			Eyes closed vs stimulation			Eyes open vs stimulation			P-value		
	Both	Left	Right	Both	Left	Right	Both	Left	Right	Both	Left	Right
Delta Oz	*	*	*	*	*	*						
Theta Oz	*	*	*	*	*	*	*	*	*			
Alpha Oz	*	*	*	*	*	*		*	*			
Beta Oz		*	*		*							
Delta O1O2	*	*	*	*	*	*		*				
Theta O1O2	*	*	*	*	*	*	*	*	*			
Alpha O1O2	*	*	*	*	*	*	*	*	*			
Beta O1O2	*	*	*		*	*						
Delta POL	*	*	*	*	*	*		*				
Theta POL	*	*	*	*	*	*	*	*	*			
Alpha POL	*	*	*	*	*	*	*		*			
Beta POL	*	*	*		*	*						
Delta POR	*	*	*	*	*	*		*				
Theta POR	*	*	*	*	*	*	*	*	*			
Alpha POR	*	*	*	*	*	*	*	*	*			
Beta POR	*	*	*	*	*	*						
Delta PO	*	*	*	*	*	*						
Theta PO	*	*	*	*	*	*	*	*	*			
Alpha PO	*	*	*	*	*	*	*	*	*			
Beta PO	*	*	*	*	*	*						

** represent that there is significant difference between the states, green color means P-value in Mauchly's sphericity is > 0.05 and rows with yellow color are the bands and electrodes with significant difference in all condition for Vernier acuity stimulus.*

Figure 20. Means and 95.0 percent LSD intervals for relative power in theta in configuration Oz-FCz with Vernier acuity stimulation and binocular vision.

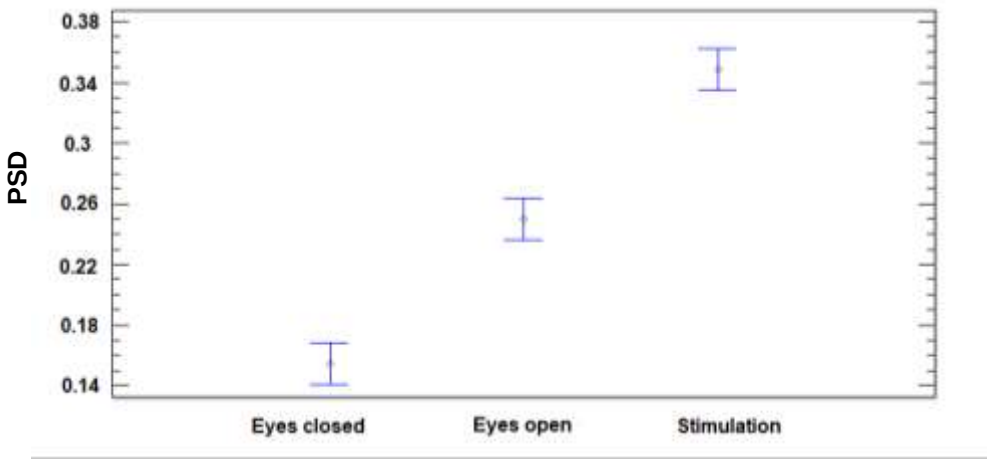


Figure 20 shows one example of Least Significant Difference (LSD) values for relative power in theta band for configuration Oz-FCz in binocular vision. Here, it is possible to observe that all the states are clearly separated. The tendency is equal in all theta configuration and in all types of vision where the values for the theta band are lower when the participants have their eyes closed and increase when the eyes are open, for the stimulation states the values are significantly higher.

8.2.1.2 Contrast sensitivity

The result for the analysis of repeated measurements (Table 8) is also equal to that obtained in the Vernier acuity stimulus. Theta band in all electrode configurations allows to separate the conditions in the experiment and satisfy the sphericity criteria. There are other bands that show significante difference in the same way (alpha Oz, alpha POR and alpha PO) but data in at least one case (both, left or right) violates the assumption of sphericity.

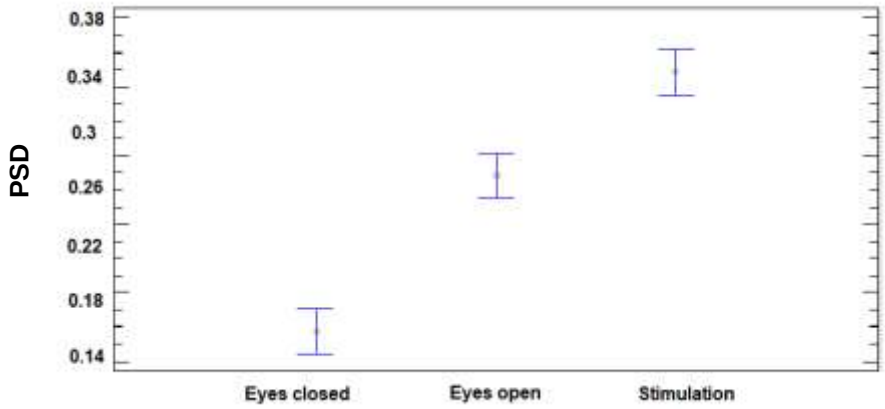
Table 8. Repeated measures analysis in contrast sensitivity stimulus for each electrode configuration taking into account each state and type of vision.

Frequency band	Eyes closed vs eyes open			Eyes closed vs stimulation			Eyes open vs stimulation			P-value		
	Both	Left	Right	Both	Left	Right	Both	Left	Right	Both	Left	Right
Delta Oz	*	*	*	*	*	*						
Theta Oz	*	*	*	*	*	*	*	*	*			
Alpha Oz	*	*	*	*	*	*	*	*	*			
Beta Oz		*		*	*							
Delta O1O2	*	*	*	*	*	*						
Theta O1O2	*	*	*	*	*	*	*	*	*			
Alpha O1O2	*	*	*	*	*	*	*	*	*			
Beta O1O2	*	*	*	*	*	*						
Delta POL	*	*	*	*	*	*						
Theta POL	*	*	*	*	*	*	*	*	*			
Alpha POL	*	*	*	*	*	*	*	*				
Beta POL	*	*	*	*	*	*						
Delta POR	*	*	*	*	*	*						
Theta POR	*	*	*	*	*	*	*	*	*			
Alpha POR	*	*	*	*	*	*	*	*	*			
Beta POR	*	*	*	*	*	*						
Delta PO	*	*	*	*	*	*						
Theta PO	*	*	*	*	*	*	*	*	*			
Alpha PO	*	*	*	*	*	*	*	*	*			
Beta PO	*	*	*	*	*	*						

** represent that there is significant difference between the states, green color means P-value in Mauchly's sphericity is > 0.05 and rows with yellow color are the bands and electrodes with significant difference in all condition for contrast sensitivity stimulus.*

Figure 21 shows one example of Least Significant Difference (LSD) values for relative power in theta band for configuration Oz-FCz in binocular vision. Here, it is possible to observe that all the states are clearly separated. The tendency is equal in all theta configuration and in all types of vision and share the same analysis that in Vernier acuity stimulation.

Figure 21. Least Significant Difference (LSD) values for relative power in theta band for configuration Oz-FCz in binocular vision



8.2.1.3 Motion perception

Repeated measures analysis (Table 9) shows that it is possible to separate all the conditions in the test in the alpha band in all electrode configurations and in delta band for Oz, O1O2 and POL. In yellow rows, there are significant differences between eyes closed and eyes open in the three types of vision (binocular- both, monocular left eye – left and monocular right eye - right), also between eyes closed vs stimulation and eyes open vs stimulation.

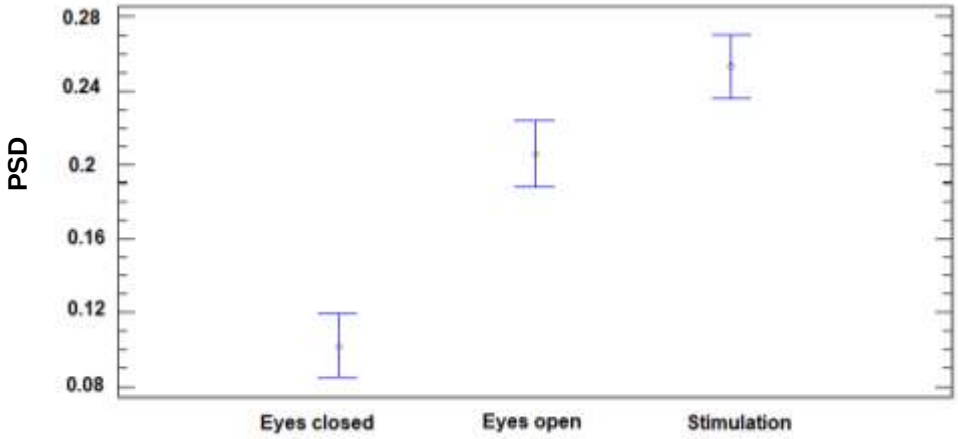
Table 9. Repeated measures analysis in motion perception stimulus for each electrode configuration taking into account each state and type of vision.

Frequency band	Eyes closed vs eyes open			Eyes closed vs stimulation			Eyes open vs stimulation			P-value		
	Both	Left	Right	Both	Left	Right	Both	Left	Right	Both	Left	Right
Delta Oz	*	*	*	*	*	*	*	*	*			
Theta Oz	*	*	*	*	*	*		*	*			
Alpha Oz	*	*	*	*	*	*	*	*	*			
Beta Oz				*	*	*						
Delta O1O2	*	*	*	*	*	*	*	*	*			
Theta O1O2	*	*	*	*	*	*		*	*			
Alpha O1O2	*	*	*	*	*	*	*	*	*			
Beta O1O2	*	*	*	*	*	*			*			
Delta POL	*	*	*	*	*	*	*	*	*			
Theta POL	*	*	*	*	*	*	*	*	*			
Alpha POL	*	*	*	*	*	*	*	*	*			
Beta POL	*	*	*	*	*	*			*			
Delta POR	*	*	*	*	*	*	*	*				
Theta POR	*	*	*	*	*	*	*	*	*			
Alpha POR	*	*	*	*	*	*	*	*	*			
Beta POR	*	*	*	*	*	*						
Delta PO	*	*	*	*	*	*						
Theta PO	*	*	*	*	*	*		*				
Alpha PO	*	*	*	*	*	*	*	*	*			
Beta PO	*	*	*	*	*	*			*			

** represent that there is significant difference between the states, green color means P-value in Mauchly's sphericity is > 0.05 and rows with yellow color are the bands and electrodes with significant difference in all condition for motion perception stimulus.*

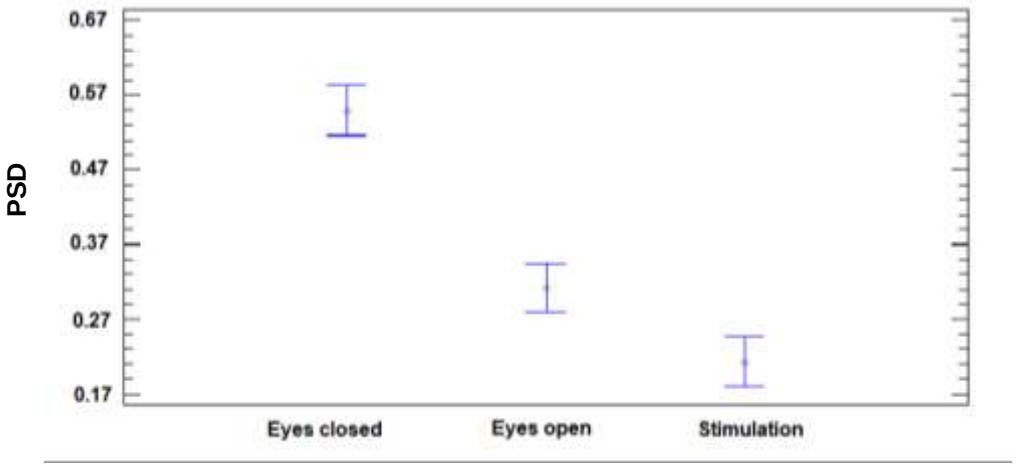
Figure 22 shows one example of Least Significant Difference (LSD) values for relative power in delta band for configuration Oz-FCz in binocular vision. Here, it is possible to observe that all the states are clearly separated. The tendency is equal in all yellow delta configuration (Table 9).

Figure 22. Least Significant Difference (LSD) values for relative power in delta band for configuration Oz-FCz in binocular vision



Least Significant Difference (LSD) values for relative power in alpha band for configuration Oz-FCz in binocular vision is opposite to delta band (Figure 23). The tendency is equal in all yellow alpha configuration (Table 9).

Figure 23. Least Significant Difference (LSD) values for relative power in alpha band for configuration Oz-FCz in binocular vision



In this case the trends are different according to the bands to be analyzed. For the delta band the values increase when passing from closed eyes, to open eyes and to stimulation state, while for the alpha band the behavior is decreasing, lower values for stimulation states and higher values for closed eyes rest.

8.2.1.4 Visual field

For the analysis of repeated measurements, no band shows a significant difference between the participant with the eyes open and the participant watching at the stimulus (Table 10). It is only possible to separate eyes open from eyes closed and eyes closed from the stimulation stage.

Table 10. Repeated measures analysis in visual field stimulus for each electrode configuration taking into account each state and type of vision.

Frequency band	Closed eyes vs open eyes			Closed eyes vs stimulation			Open eyes vs stimulation			P-value		
	Both	Left	Right	Both	Left	Right	Both	Left	Right	Both	Left	Right
Delta Oz	*	*	*	*	*	*						
Theta Oz	*	*	*	*	*	*						
Alpha Oz	*	*	*	*	*	*						
Beta Oz				*	*	*						
Delta O1O2	*	*	*	*	*	*						
Theta O1O2	*	*	*	*	*	*						
Alpha O1O2	*	*	*	*	*	*						
Beta O1O2	*	*	*	*	*	*						
Delta POL	*	*	*	*	*	*						
Theta POL	*	*	*	*	*	*						
Alpha POL	*	*	*	*	*	*						
Beta POL	*	*	*	*	*	*						
Delta POR	*	*	*	*	*	*						
Theta POR	*	*	*	*	*	*						
Alpha POR	*	*	*	*	*	*						
Beta POR	*	*	*	*	*	*						
Delta PO	*	*	*	*	*	*						
Theta PO	*	*	*	*	*	*						
Alpha PO	*	*	*	*	*	*						
Beta PO	*	*	*	*	*	*						

** represent that there is significant difference between the states, green color means P-value in Mauchly's sphericity is > 0.05 and rows with yellow color are the bands and electrodes with significant difference in all condition for visual field stimulus.*

8.2.1.5 Form recognition

Repeated measures analysis (Table 11) in this stimulus does not show components with a difference in all conditions. Although delta Oz offers a significant difference, data violates the assumption of sphericity. In this case, the selected rows meet spherical criteria for all cases but in at least one type of vision, it is not possible to separate the stage of eyes open versus stimulation.

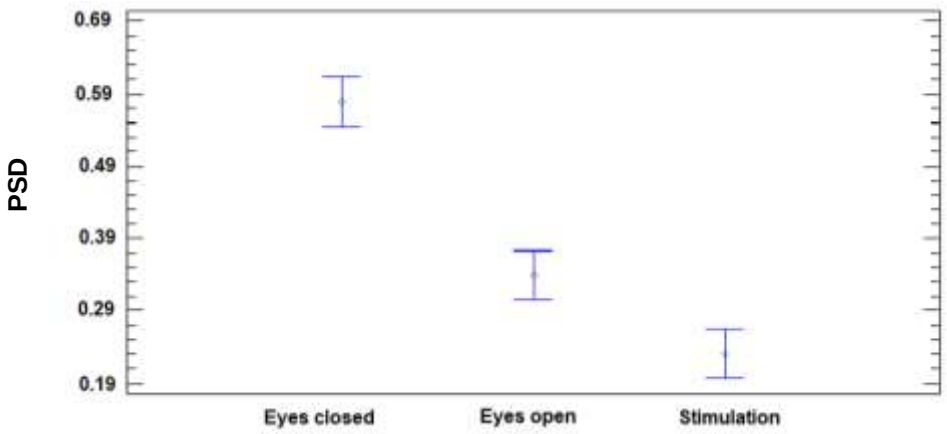
Figure 24 shows one example of Least Significant Difference (LSD) values for relative power in alpha band for configuration O1+O2-FCz in monocular vision (left). Here, it is possible to observe that all the states are clearly separated. The tendency is equal in all yellow alpha configuration for right and left eye (Table 11).

Table 11. Repeated measures analysis in form recognition stimulus for each electrode configuration taking into account each state and type of vision.

Frequency band	Eyes closed vs eyes open			Eyes closed vs stimulation			Eyes open vs stimulation			P-value		
	Both	Left	Right	Both	Left	Right	Both	Left	Right	Both	Left	Right
Delta Oz	*	*	*	*	*	*		*	*			
Theta Oz	*	*	*	*	*	*						
Alpha Oz	*	*	*	*	*	*		*	*			
Beta Oz		*			*	*						
Delta O1O2	*	*	*	*	*	*		*	*			
Theta O1O2	*	*	*	*	*	*						
Alpha O1O2	*	*	*	*	*	*		*	*			
Beta O1O2	*	*	*	*	*	*			*			
Delta POL	*	*	*	*	*	*		*	*			
Theta POL	*	*	*	*	*	*		*				
Alpha POL	*	*	*	*	*	*		*	*			
Beta POL	*	*	*	*	*	*			*			
Delta POR	*	*	*	*	*	*		*	*			
Theta POR	*	*	*	*	*	*						
Alpha POR	*	*	*	*	*	*		*	*			
Beta POR		*	*		*	*			*			
Delta PO	*	*	*	*	*	*			*			
Theta PO	*	*	*	*	*	*		*				
Alpha PO	*	*	*	*	*	*		*	*			
Beta PO	*	*	*	*	*	*			*			

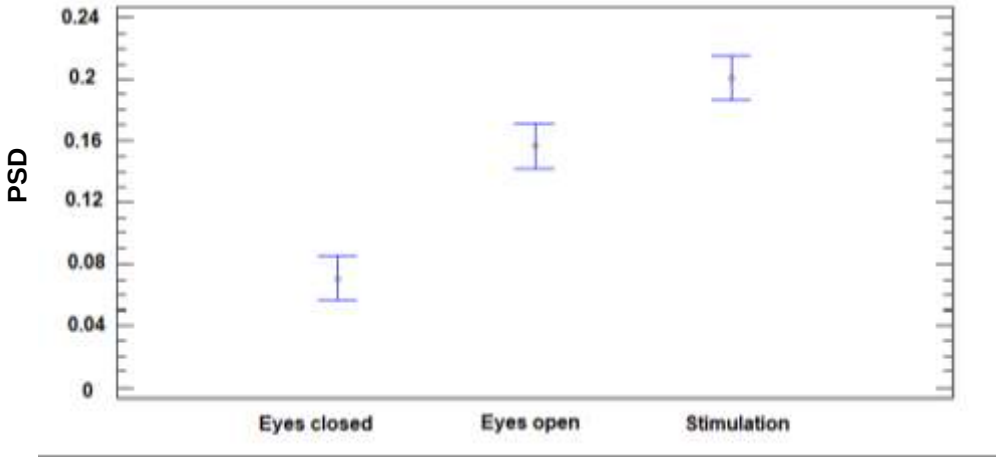
** represent that there is significant difference between the states, green color means P-value in Mauchly's sphericity is > 0.05 rows with yellow color are the bands and electrodes with significant difference in all condition for form recognition stimulus.*

Figure 24. Least Significant Difference (LSD) values for relative power in alpha band for configuration O1+O2-FCz in monocular vision (left)



Least Significant Difference (LSD) values for relative power in delta band for configuration PO3+PO7-FCz (POL) in monocular vision (left) is opposite to delta band (Figure 25). The tendency is equal in all yellow delta configuration for right and left eye (Table 11).

Figure 25. Least Significant Difference (LSD) values for relative power in delta band for configuration PO3+PO7-FCz (POL) in monocular vision (left)



As well as the trend of movement perception, for alpha band there is a decreasing behavior, while for delta the trend is increasing.

8.2.1.6 Color detection

According to repeated measures analysis (Table 12), clear markings are not achieved as with other stimuli, for beta band there is a difference between the 3 states (eyes closed, eyes open and stimulation), however, in at least one of the type of vision, data violates the assumption of sphericity. Beta band is selected in this stimulus for the following analyses although it is important taking into account that the conclusion cannot be applicable.

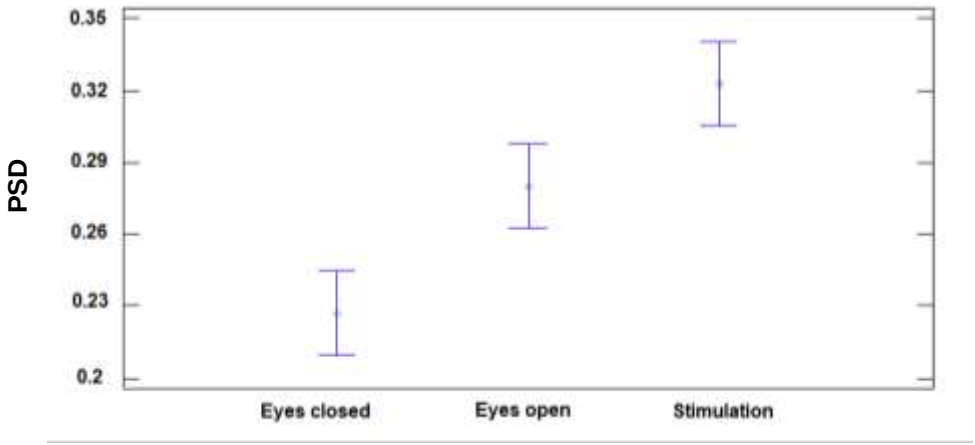
Table 12. Repeated measures analysis in color detection stimulus for each electrode configuration taking into account each state and type of vision.

Frequency band	Eyes closed vs eyes open			Eyes closed vs stimulation			Eyes open vs stimulation			P-value		
	Both	Left	Right	Both	Left	Right	Both	Left	Right	Both	Left	Right
Delta Oz	*	*	*	*	*	*		*	*			
Theta Oz	*	*	*	*	*	*						
Alpha Oz	*	*	*	*	*	*		*	*			
Beta Oz				*	*	*	*	*	*			
Delta O1O2	*	*	*	*	*	*			*			
Theta O1O2	*	*	*	*	*	*						
Alpha O1O2	*	*	*	*	*	*		*	*			
Beta O1O2	*	*	*	*	*	*	*	*	*			
Delta POL	*	*	*	*	*	*		*	*			
Theta POL	*	*	*	*	*	*						
Alpha POL	*	*	*	*	*	*		*	*			
Beta POL	*	*	*	*	*	*	*	*	*			
Delta POR	*	*	*	*	*	*						
Theta POR	*	*	*	*	*	*						
Alpha POR	*	*	*	*	*	*		*	*			
Beta POR	*	*	*	*	*	*	*	*	*			
Delta PO	*	*	*	*	*	*						
Theta PO	*	*	*	*	*	*						
Alpha PO	*	*	*	*	*	*		*	*			
Beta PO	*	*	*	*	*	*	*	*	*			

** represent that there is significant difference between the states, green color means P-value in Mauchly's sphericity is > 0.05 rows with yellow color are the bands and electrodes with significant difference in all condition for color detection stimulus.*

Figure 26 shows one example of Least Significant Difference (LSD) values for relative power in beta band for configuration O1+O2-FCz in binocular vision. The tendency is equal in all beta configuration for all type of vision (Table 12) where the stimulation values are higher than those obtained for resting state with eyes open or eyes closed.

Figure 26. Least Significant Difference (LSD) values for relative power in beta band for configuration O1+O2-FCz in binocular vision



8.2.2 Coherence

Coherence was obtained in each frequency band for all possible combinations with the channels Oz-FCz (Oz), O1+O2-FCz (O1O2), PO3+PO4+PO7+PO8-FCz (PO), PO3+PO7-FCz (POL), PO4+PO8-FCz (POR). 40 variables were got, 10 relations for 4 frequency bands. Factor analysis was used to reduce the dimension in each test, 8 factors that keep more than 83% of the variability were calculated. Finally, repeated measures ANOVA analyses was made with each factor in other to identify which factors show a significant difference.

8.2.2.1 Vernier acuity

Coherence analysis in Vernier acuity shows (Table 13) that factor 2 allows differentiating eyes open from eyes closed and eyes open from the state of stimulation and p-value is greater than 0.05. In this factor, the variables with influence greater than 65% were Delta Oz-O1O2, Theta Oz-O1O2, Delta Oz-PO, Theta Oz-PO, Delta Oz-POL, Theta Oz-POL, Delta Oz-POR, Theta Oz-POR. With theta and beta being the most relevant bands as well as the relation between Oz with the other configurations.

Table 13. Repeated measures analysis in for Vernier acuity stimulus for each coherence factor taking into account each state and type of vision.

Factor	Eyes closed vs eyes open			Eyes closed vs stimulation			Eyes open vs stimulation			P-value		
	Both	Left	Right	Both	Left	Right	Both	Left	Right	Both	Left	Right
1				*	*	*	*		*			
2	*	*	*				*	*	*			
3	*		*	*	*	*						
4		*			*							
5						*			*			
6						*	*		*			
7	*			*	*	*	*		*			
8	*	*	*	*	*	*						

** represent that there is significant difference between the states, green color means P-value in Mauchly's sphericity is > 0.05 rows with yellow color are the factor with significant difference in all condition for Vernier acuity stimulus.*

Figure 27 shows one example of Least Significant Difference (LSD) values for coherence in delta band for signals Oz with O1O2 in binocular vision. In this case, values in the stimulation state are higher than those obtained for resting state with eyes open, however they are similar to those obtained for resting state with eyes closed.

Figure 27. Least Significant Difference (LSD) values for coherence in delta band for signals Oz with O1O2 in binocular vision

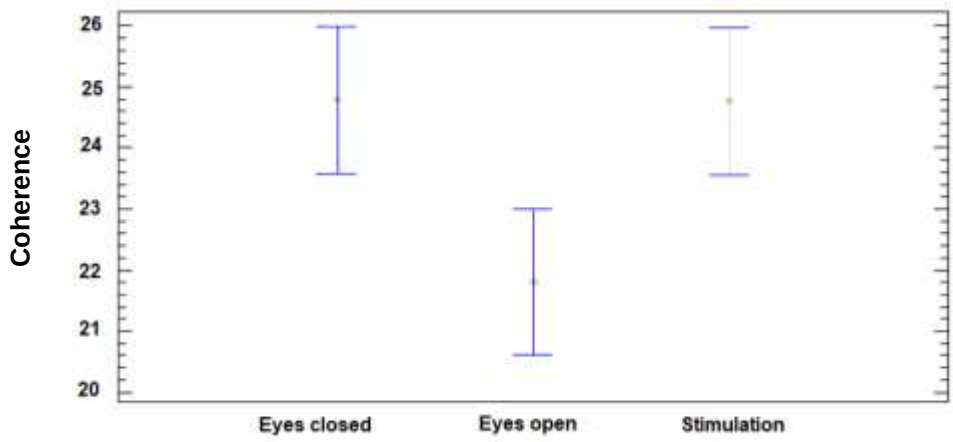
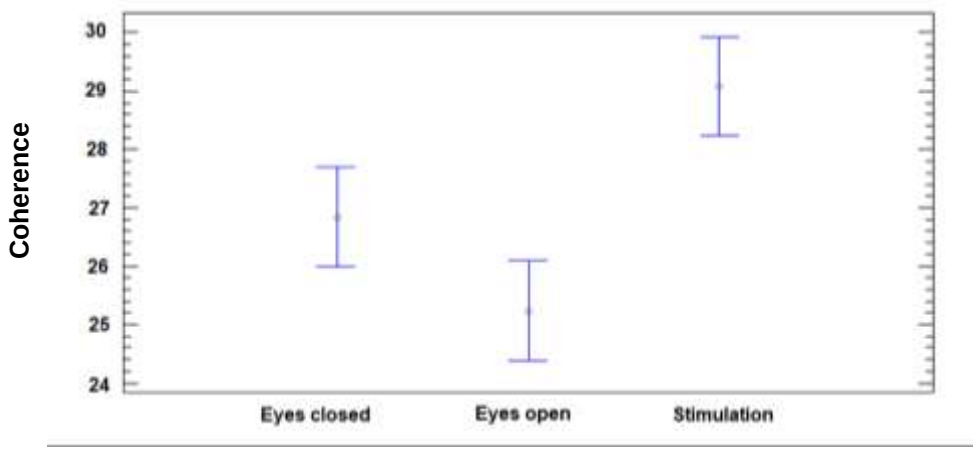


Figure 28 shows one example of Least Significant Difference (LSD) values for coherence in theta band for signals Oz with O1O2 in binocular vision. The trend shows that the values for the state of stimulation are still higher than the resting state with eyes open and for this case also higher than the resting state with eyes closed.

Figure 28. Least Significant Difference (LSD) values for coherence in theta band for signals Oz with O1O2 in binocular vision



8.2.2.2 Contrast sensitivity

In contrast sensitivity stimulus, 3 factors (Table 14) were found with the capacity to separate closes eyes from stimulation and eyes open from stimulation. In this case, the analysis was made in factor 6 and facto 5 because share the results for some combination and bands. The variables with influence greater than 65% were Beta Oz-O1O2, Beta Oz-PO, Beta Oz-POL, Beta Oz-POR. It shows that beta band in the relation of Oz with the other configuration is relevant to separate states.

Table 14. Repeated measures analysis in contrast sensitivity stimulus for each coherence factor taking into account each state and type of vision.

Factor	Eyes closed vs eyes open			Eyes closed vs stimulation			Eyes open vs stimulation			P-value		
	Both	Left	Right	Both	Left	Right	Both	Left	Right	Both	Left	Right
1	*	*		*	*	*	*	*	*			
2	*	*	*		*	*	*	*	*			
3	*	*		*	*		*	*				
4		*		*	*		*					
5	*	*		*	*	*			*			
6		*		*	*	*	*	*	*			
7				*	*	*	*	*	*			
8	*			*			*					

** represent that there is significant difference between the states, green color means P-value in Mauchly's sphericity is > 0.05 rows with yellow color are the factor with significant difference in all condition for contrast sensitivity stimulus.*

Figure 29 shows one example of Least Significant Difference (LSD) values for coherence in beta band for signals Oz with O1O2 in binocular vision and figure 30 shows values for coherence in beta band for signals Oz with PO in binocular vision. The trend for the coherence values in both cases is maintained, being significantly higher for the stimulation with respect to the resting states.

Figure 29. Least Significant Difference (LSD) values for coherence in beta band for signals Oz with O1O2 in binocular vision.

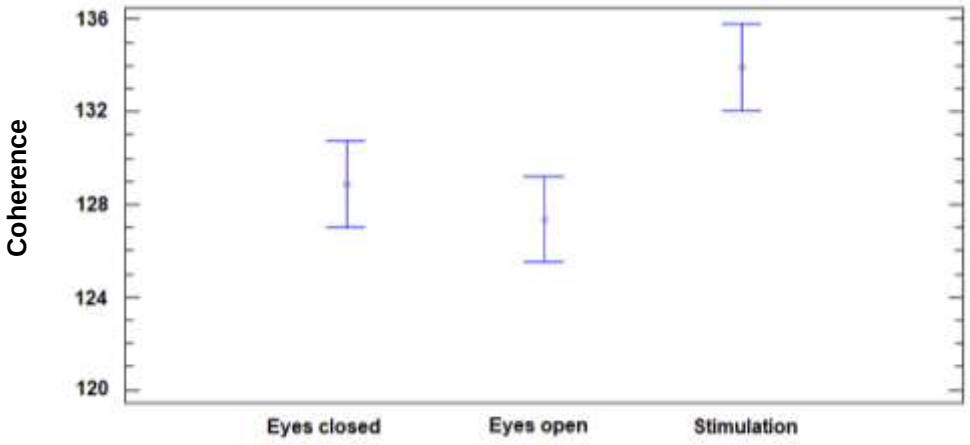
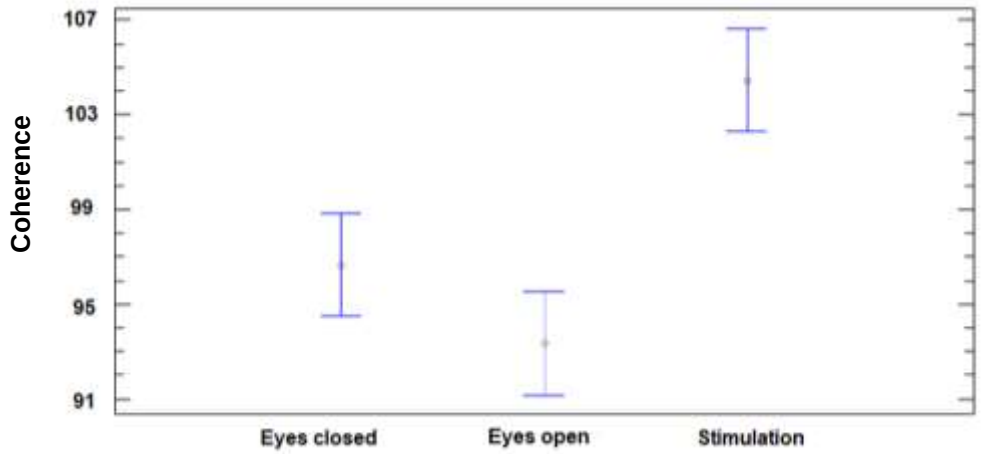


Figure 30. Least Significant Difference (LSD) values for coherence in beta band for signals Oz with PO in binocular vision



8.2.2.3 Motion perception

In this stimulus, factor 4 (Table 15) shows the capacity to differentiate the states of closes eyes from stimulation and eyes open from stimulation. However, unlike the previous stimuli, the factor obtained does not have the same influence variables for the three types of vision.

Table 15. Repeated measures analysis in motion perception stimulus for each coherence factor taking into account each state and type of vision.

Factor	Eyes closed vs eyes open			Eyes closed vs stimulation			Eyes open vs stimulation			P-value		
	Both	Left	Right	Both	Left	Right	Both	Left	Right	Both	Left	Right
1	*	*	*	*	*	*	*		*			
2					*	*			*			
3		*	*		*	*		*	*			
4	*			*	*	*	*	*	*			
5				*					*			
6	*		*						*			
7				*		*	*					
8	*		*	*	*	*			*			

** represent that there is significant difference between the states, green color means P-value in Mauchly's sphericity is > 0.05 rows with yellow color are the factor with significant difference in all condition for motion perception stimulus.*

In this case, factor 4 is constructed with different variables. Table 16 shows the variables with greater than 65% of influence in the factor. Alpha band and beta band are representative in this factor although there is not a clear trend in the relation for electrodes.

Table 16. Variables selected for each type of vision for motion perception stimulus (B - binocular, L - monocular left, R - monocular R)

Motio perception (RDKs)		
Factor 4 (B)	Factor 4 (L)	Factor 4 (R)
Alpha Oz-PO	Beta Oz-O1O2	Alpha O1O2-POR
Alpha Oz-POL	Beta Oz-PO	Alpha PO-POL
AlphaO1O2-PO	Beta Oz-POL	Alpha PO-POR
Alpha PO-POR	Beta Oz-POR	Alpha POL-POR

Figure 31 shows one example of Least Significant Difference (LSD) values for coherence in alpha band for signals Oz with PO in binocular vision. In this case the trend is downwards, a similar behavior for the form recognition stimulus.

Figure 31. Least Significant Difference (LSD) values for coherence in alpha band for signals Oz with PO in binocular vision

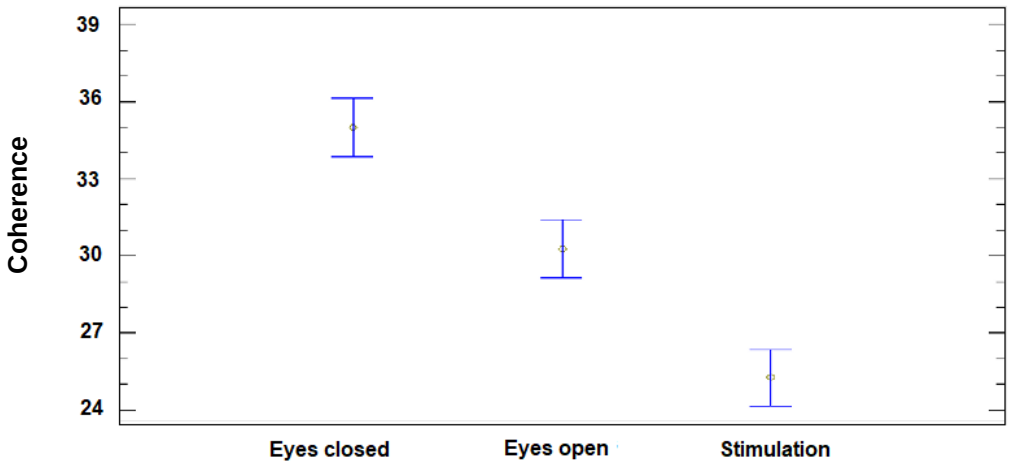


Figure 32 shows one example of Least Significant Difference (LSD) values for coherence in beta band for signals Oz with O1O2 in monocular vision (L). Although the trend is similar to that observed in the previous graph, in this case the coherence values do not allow a difference between the two resting states. This tendency is similar to Figure 33.

Figure 32. Least Significant Difference (LSD) values for coherence in beta band for signals Oz with O1O2 in monocular vision (L)

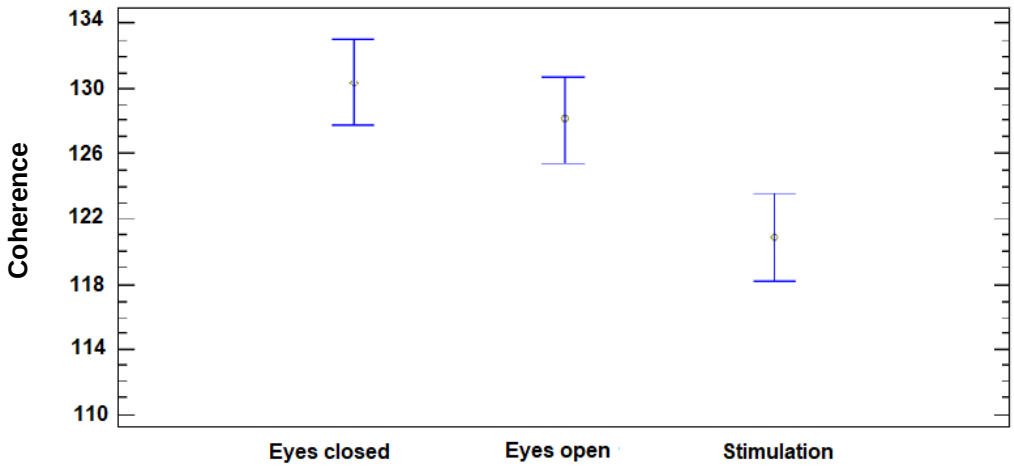
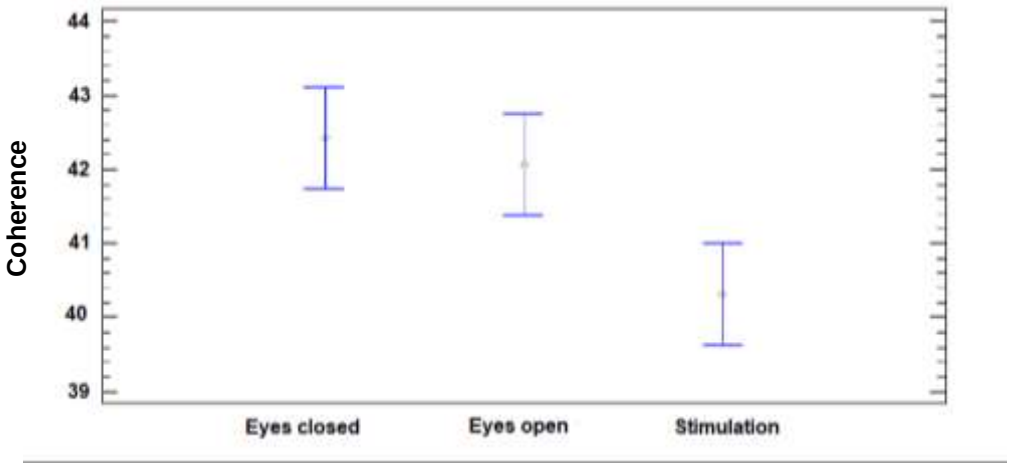


Figure 33. Least Significant Difference (LSD) values for coherence in alpha band for signals O1O2 with POR in monocular vision (R).



8.2.2.4 Visual field

Although in the power analysis it was not possible to separate the eyes open and stimulus states, the coherence analysis shows two factors that can discriminate these states (Table 17). Factor 1 was selected to find the bands and relations because this factor stores more information about variability. This factor was different variables for binocular vision and monocular.

Table 17. Repeated measures analysis in visual field stimulus for each coherence factor taking into account each state and type of vision.

Factor	Eyes closed vs eyes open			Eyes closed vs stimulation			Eyes open vs stimulation			P-value		
	Both	Left	Right	Both	Left	Right	Both	Left	Right	Both	Left	Right
1	*		*	*		*	*	*	*			
2	*	*		*	*	*		*	*			
3		*		*	*			*	*			
4	*	*	*		*	*		*	*			
5	*	*			*		*	*				
6	*	*	*		*		*	*	*			
7	*	*	*	*					*			
8	*		*	*	*			*	*			

** represent that there is significant difference between the states, green color means P-value in Mauchly's sphericity is > 0.05 rows with yellow color are the factor with significant difference in all condition for visual field stimulus.*

Table 18 shows the variables selected with greater than 65% of influence in the factor. Coherence in bands delta, theta and beta are important in factor 1. Relations Oz regarding other electrodes for binocular vision and relation O1O2 and PO with POR and POL for monocular vision are relevant.

Table 18. Variables selected for each type of vision for visual field stimulus (B - binocular, L - monocular left, R - monocular R)

Visual field	
Factor 1 (B)	Factor 1 (L- R)
Delta Oz-O1O2	Beta O1O2-POL
Theta Oz-O1O2	Beta O1O2-POR
Delta Oz-PO	Beta PO-POL
Theta Oz-PO	Beta PO-POR
Delta Oz-POL	Beta POL-POR
Theta Oz-POL	
Delta Oz-POR	
Theta Oz-POR	

Figure 34 shows one example of Least Significant Difference (LSD) values for coherence in delta band for signals Oz with POR in binocular vision.

Figure 34. Least Significant Difference (LSD) values for coherence in delta band for signals Oz with POR in binocular vision

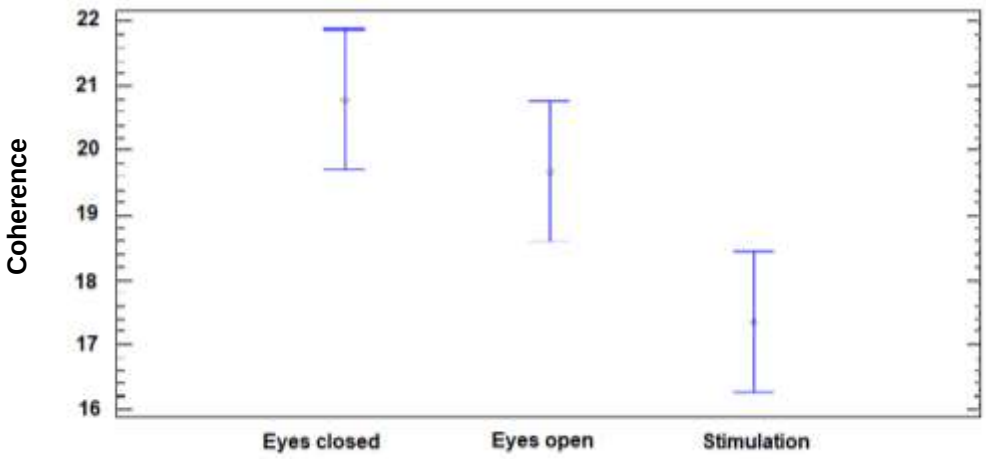


Figure 35 shows one example of Least Significant Difference (LSD) values for coherence in theta band for signals Oz with PO in binocular vision.

Figure 35. Least Significant Difference (LSD) values for coherence in theta band for signals Oz with PO in binocular vision

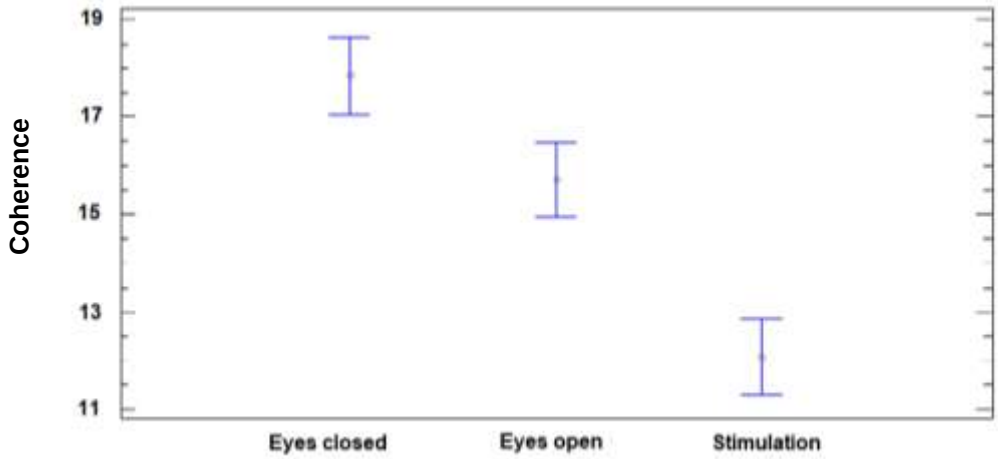


Figure 36 shows one example of Least Significant Difference (LSD) values for coherence in alpha band for signals POL with POR in monocular vision (L).

Figure 36. Least Significant Difference (LSD) values for coherence in alpha band for signals POL with POR in monocular vision (L)

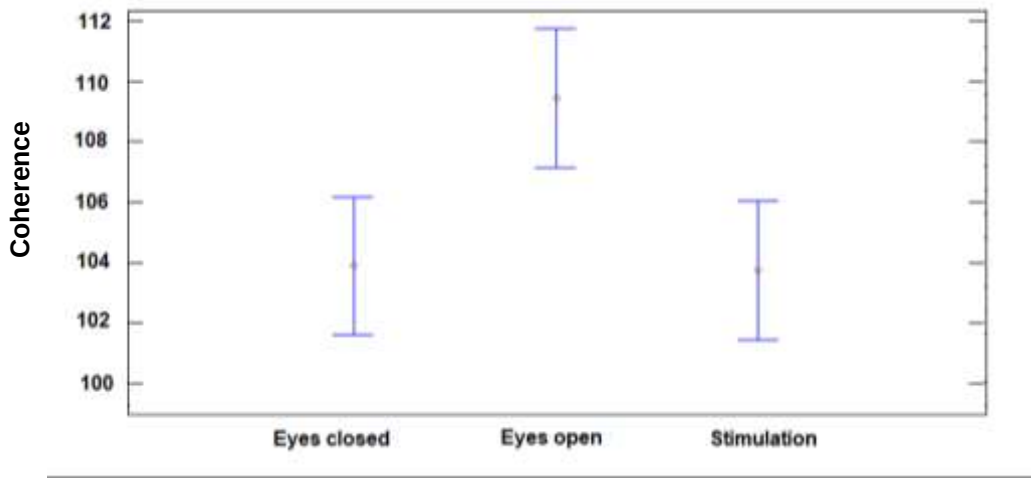
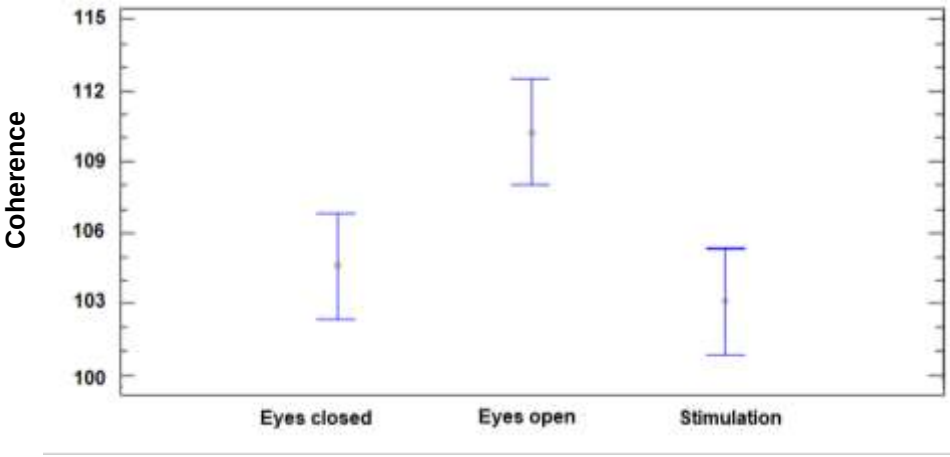


Figure 37 shows one example of Least Significant Difference (LSD) values for coherence in beta band for signals POL with POR in monocular vision (R).

Figure 37. Least Significant Difference (LSD) values for coherence in beta band for signals POL with POR in monocular vision (R)



The trends for figures 34 and 35 are similar in binocular vision, however values for coherence in theta band for signals Oz with PO (figure 35) shows a better ability to differentiate the 3 states.

For the case of monocular vision (Figure 36 and 37), the trend is similar for the right and left eye, however the bands analyzed are not the same.

8.2.2.5 Form recognition

Coherence analysis for this stimulus was not possible to find a factor with the capacity to show a significant difference between eyes open and stimulation (Table 19). Although in power analysis is was possible, coherence does not show this difference. Probably, factor 1 o factor 8 can help to enhance the analysis between eyes closed and eyes open, and eyes closed and stimulation.

Table 19. Repeated measures analysis in form recognition stimulus for each coherence factor taking into account each state and type of vision.

Factor	Eyes closed vs eyes open			Eyes closed vs stimulation			Eyes open vs stimulation			P-value		
	Both	Left	Right	Both	Left	Right	Both	Left	Right	Both	Left	Right
1	*	*	*	*	*	*						
2			*	*	*	*			*			
3	*			*	*			*				
4		*	*		*	*		*				
5	*	*		*	*							
6	*		*	*	*	*						
7		*		*	*							
8	*	*	*	*	*	*						

** represent that there is significant difference between the states, green color means P-value in Mauchly's sphericity is > 0.05 rows with yellow color are the factor with significant difference in all condition for form recognition stimulus.*

8.2.2.6 Color detection

Table 20 shows the result for the coherence factors, in this case, factor 1 and factor 2 can separate the states, however, factor 1 has a better behavior because can differentiate the 3 states, although it is important taking into account that the assumption of sphericity is rejected at the 5.0% significance level. In factor 1, the variables with influence greater than 65% were: Delta Oz-O1O2, Theta Oz-O1O2, Delta Oz-PO, Theta Oz-PO, Delta Oz-POL, Theta Oz-POL, Delta Oz-POR, Theta Oz-POR.

Bands delta and theta provide, in the relation Oz with other electrodes, important information in each state for color detection stimulus.

Table 20. Repeated measures analysis in color detection stimulus for each coherence factor taking into account each state and type of vision.

Factor	Eyes closed vs eyes open			Eyes closed vs stimulation			Eyes open vs stimulation			P-value		
	Both	Left	Right	Both	Left	Right	Both	Left	Right	Both	Left	Right
1	*	*	*	*	*	*	*	*	*			
2					*	*			*			
3				*	*	*	*	*	*			
4		*	*	*	*	*		*				
5		*		*	*	*	*		*			
6	*	*		*	*	*		*	*			
7		*	*	*		*			*			
8	*	*		*	*				*			

** represent that there is significant difference between the states, green color means P-value in Mauchly's sphericity is > 0.05 rows with yellow color are the factor with significant difference in all condition for color detection stimulus.*

Figure 38 shows one example of Least Significant Difference (LSD) values for coherence in delta band for signals Oz with PO in binocular vision.

Figure 38. Least Significant Difference (LSD) values for coherence in delta band for signals Oz with PO in binocular vision

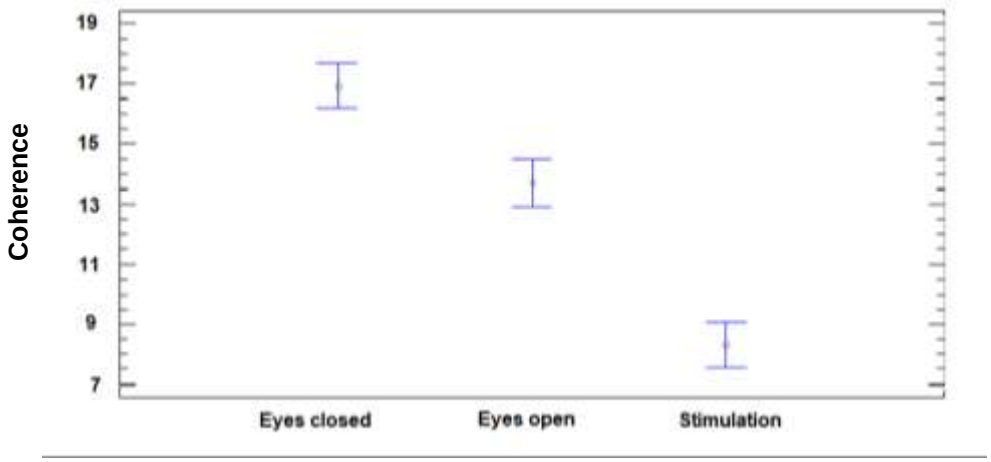
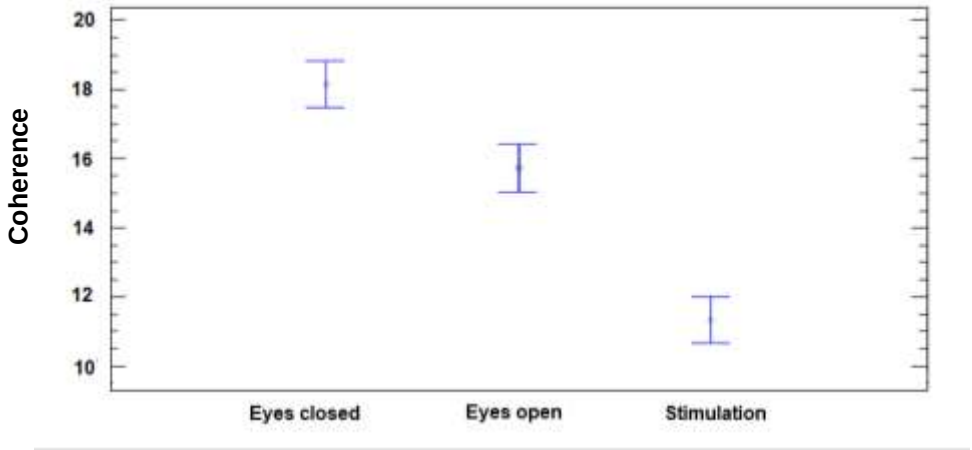


Figure 39 shows one example of Least Significant Difference (LSD) values for coherence in theta band for signals Oz with PO in binocular vision. In this figure and in the previous one it can be seen that the trend of coherence in the theta and delta band is decreasing, with lower values in the stimulation states.

Figure 39. Least Significant Difference (LSD) values for coherence in theta band for signals Oz with PO in binocular vision



The result obtained for relative power in healthy subject shows that delta, theta and alpha bands allows differentiation when participants have their eyes closed from when they have their eyes open [117][118], in contrast, beta band does not allow to differentiate between of the conditions in some case. However, in these bands, it is not clear the difference between when the participants have the eyes open and the stimulation moment.

Table 21. Variable selected for relative power

Vernier acuity	Contrast sensitivity	Motio perception (RDKs)	Visual field	Form recognition	Color detection
Theta Oz	Theta Oz	Delta Oz	-	Alpha O1O2	Beta Oz
Theta O1O2	Theta O1O2	Alpha Oz		Delta POL	Beta O1O2
Theta POL	Theta POL	Delta O1O2		Alpha POR	Beta POL
Theta POR	Theta POR	Alpha O1O2			Beta POR
Theta PO	Theta PO	Delta POL			Beta PO
		Alpha POL			
		Alpha POR			
		Alpha PO			

Table 21 summarizes the variables selected for relative power that best characterize each state. These variables allow us to know when the participants have their eyes closed, when they have their eyes open and when there is stimulation according to relative power. These variables are important because represent the main values for each stimulus.

Theta band in all electrode configuration is representative for Vernier acuity and contrast sensitivity, both stimuli have a specific frequency stimulation and it is reflected in the power spectrum and theta band processing rhythms are involved in our continuous perception of dynamic visual events and these stimuli are highly dynamic [119]. Delta and alpha band in some spatial configuration represents motion perception [120] and form recognitions stimuli.

On the other hand, beta is the band to separate the states in color detection [121]. Some studies [121] have suggested that the subjects' EEG responses in a resting state differed when shown different colored paper, beta wave intensity in the occipital areas can be inhibited, so this band can save stimuli information.

For visual field stimulus, it was not possible to get representative variables, one of the possible reason is that the square size for the stimulus used in the visual field test, did not elicit any frequency response. Although each square had a stimulation frequency, it was not visible in the signals recorded.

In this point, relative power spectrum shows to be a suitable feature to find difference between eyes open and eyes closed in different bands while for each stimulus, specific variables should be used to separate eyes open from stimulation. In order to find more features with sensibility to understand eyes open and stimulation, a coherence analysis was conducted.

Table 22. Factors selected for coherence values and most influential variables

Vernier acuity	Contrast sensitivity	Motion perception (RDKs)			Visual field		Form recognition	Color detection
Factor 2	Factor 7	Factor 4 (B)	Factor 4 (L)	Factor 4 (R)	Factor 1 (B)	Factor 1 (L- R)	-	Factor 1
Delta Oz-O1O2	Beta Oz-O1O2	Alpha Oz-PO	Beta Oz-O1O2	Alpha O1O2-POR	Delta Oz-O1O2	Beta O1O2-POL		Delta Oz-O1O2
Theta Oz-O1O2	Beta Oz-PO	Alpha Oz-POL	Beta Oz-PO	Alpha PO-POL	Theta Oz-O1O2	Beta O1O2-POR		Theta Oz-O1O2
Delta Oz-PO	Beta Oz-POL	AlphaO1O2-PO	Beta Oz-POL	Alpha PO-POR	Delta Oz-PO	Beta PO-POL		Delta Oz-PO
Theta Oz-PO	Beta Oz-POR	Alpha PO-POR	Beta Oz-POR	Alpha POL-POR	Theta Oz-PO	Beta PO-POR		Theta Oz-PO
Delta Oz-POL					Delta Oz-POL	Beta POL-POR		Delta Oz-POL
Theta Oz-POL					Theta Oz-POL			Theta Oz-POL
Delta Oz-POR					Delta Oz-POR			Delta Oz-POR
Theta Oz-POR					Theta Oz-POR			Theta Oz-POR

For coherence analysis, 48 factors were processed. In each stimulus, the factor was selected according to the capacity to differentiate the 3 states. The previous result in power spectrum analysis shows that this analysis can identify while participants have the eyes open and close, whereby in coherence analysis, the factors were prioritized regarding the separation of eyes open from stimulation.

The same analysis was carried out for all stimuli (Appendix C). The factors that showed difference between eyes open and stimulation were prioritized. Table 22 shows the final factors for each stimulus and variables with an influence greater than 65% in each factor. Coherence in delta and theta band is relevant in Vernier acuity, visual field and color detection, beta band has a major influence in contrast sensitivity, motion perception for monocular left vision (L) and visual field monocular. Alpha is present only in motion perception for binocular vision and monocular right vision (R).

In form recognition was not possible to find a factor with coherence measures (table 22) with the capacity to show a significant difference between eyes open and stimulation. However, for this stimulus, relative power spectrum in alpha O1O2, delta POL and alpha POR allow us to separate when subjects have the eyes open or when they are watching the stimulus.

In visual field stimuli coherence showed two factor that can be characteristic to identify between open eyes and stimulation state. For this case power spectrum was not achievable to find a relevant frequency band.

Each stimulus for each condition presents different trends according to the band to be analyzed and the type of vision. This means that the patterns are not constant for all tests. In both power and coherence analysis the differences are more pronounced in stimuli without stimulation frequency, which refers to deeper processing stimuli.

Similarly, with the results presented it is possible to analyze that the behavior for a specific stimulus can generate different variables of interest according to the type of vision, however analysis with isolated variables (without factor analysis), does not show capacity to differentiate between binocular and monocular vision.

8.3 Conclusion

Our results indicated that relative delta, theta and alpha powers could be an indicator to distinguish between eyes open and eyes closed while specific power bands can give information for stimulation stages. Similarly, coherence analysis allowed us to find sensibility factors for each stage. With these stimuli and baseline in some measures characteristic of each one will be possible to compare these variables in patient with neuro-ophthalmological disorders and in neurological rehabilitation using the proposed stimuli to activate the different visual functions.

The values obtained for power and frequency to respond to different behaviors depending on the type of stimulus, type of configuration and type of vision, this opens the analysis to understand if the trends are maintained in patients with visual impairment.

9 General discussion

The first part of the study allowed the development of a set of stimuli to perform visual cortex activation covering most of the visual skills, as a result 6 stimuli were designed with editable parameters for other tests. This set presents 3 previously reported stimuli and 3 exploratory stimuli.

With the designed stimuli, some parameters were set to perform test of healthy subjects. In the second, we recorded resting states and stimulation states for monocular and binocular vision. The signals obtained were filtered and the measures of power and coherence were calculated. The initial exploratory analysis showed that it was possible to replicate results with respect to resting state with eyes open or eyes closed [117][118] and that for stimuli such as contrast and acuity, the result in the power spectrum showed the characteristic peaks for these tests [24][95].

In the third part the power and coherence measurements were analyzed using the repeated measurements method in order to complement the analyses of the previous step and with emphasis on the ability of the measurements to characterize each test state. This analysis is important for understanding whether each test state (open eyes rest, closed eyes rest or stimulation) exhibits differential behavior in the electrophysiological measurements. The results showed that power measurements in some frequency bands allow for differences in all 3 states and that coherence measurements can help to corroborate the separation between open-eye resting state measurements and stimulation.

The differences found between resting states in power spectrum have been reported in other studies [117][118] and the frequency changes in the signals for Vernier acuity and contrast sensitivity [24][95] are important to separate these stimuli states from resting states. Power analysis in specific bands have been useful in motion and color perception studies [119][120][121].

This study presents a baseline of the behavior of some variables that can be compared in patients to evaluate changes in trends that generate value for the follow-up of visual rehabilitation therapies. We achieve to characterize the cerebral visual physiology response of healthy subjects using portable and low-cost EEG taking into account the visual function and the type of stimuli that can help us to cover occipital cortex functionality .

10 Future studies

Due to the current pandemic we were only able to record healthy groups only, and unfortunately patients group was postponed. The results of this research set the grounds for further studies, and establish the most meaningful methods/analyses that can be implemented when it is time to perform follow ups in patients during rehabilitation. Additionally, due to the same situation it was not possible to perform several follow up recordings in healthy subjects in order to study intra-subject variability in the test.

Future work could analyze other signal characterization, in order to identify factors, variables, or electrodes that maximize the difference between the three stages.

The database acquired is an important input to be able to carry out different analyses on the data to find more information regarding the visual system at a physiological level. Future studies can carry out a comparative analysis between the stimuli to identify if there is a difference between each one, they can extract from the signals other characteristics to identify their capacity of discrimination between patients and healthy subjects. Similarly, it is possible to perform a more in-depth analysis only on the resting signals, and comparative studies between monocular and binocular vision can also be carried out. The records obtained for acuity and contrast measurements can be analyzed by means of regressions to obtain the exact value for each subject of these visual abilities.

Finally, in this study the analyses were made from conventional statistical methods due to the limitation in the database, however future studies may increase the sample and work with classification techniques such as support vector machines or k-means.

11 Bibliography

[1] J. H. Pula and C. A. Yuen, “Eyes and stroke: The visual aspects of cerebrovascular disease,” *Stroke Vasc. Neurol.*, vol. 2, no. 4, pp. 210–220, 2017.

[2] M. Berthold-Lindstedt, J. Ygge, and K. Borg, “Visual dysfunction is underestimated in patients with acquired brain injury,” *J. Rehabil. Med.*, vol. 49, no. 4, pp. 327–332, 2017.

[3] I. Pasley, S. Jobke, A. Julia Gudlin, and B. A. Sabel, “Application of Neural Plasticity for Vision Restoration after Brain Damage,” in *Neuroengineering*, 2008, p. 23.

[4] F. I. R. Owe *et al.*, “Visual impairment following stroke : do stroke patients require vision assessment ?,” no. November 2008, pp. 188–193, 2009.

[5] Stroke Association, “State of the nation,” no. January, 2017.

[6] E. Leung and W. M. Jay, “Stroke and Visual Rehabilitation,” vol. 15, no. 1, pp. 27–36, 2008.

[7] L. Wright *et al.*, “Stroke management: Updated recommendations for treatment along the care continuum,” *Intern. Med. J.*, vol. 42, no. 5, pp. 562–569, 2012.

[8] B. E. Wallace, N. Carolina, A. K. Wagner, and E. P. Wagner, “A History and Review of Quantitative Electroencephalography in Traumatic Brain Injury,” vol. 16, no. 2, pp. 165–190, 2001.

[9] T. K. Pogoda *et al.*, “Multisensory impairment reported by veterans with and without mild traumatic brain injury history,” *J. Rehabil. Res. Dev.*, vol. 49, no. 7, p. 971, 2012.

[10] K. Mckenna, D. M. Cooke, J. Fleming, A. Jefferson, and S. Ogden, “The incidence of visual perceptual impairment in patients with severe traumatic brain injury,” vol. 20, no. May, pp. 507–518, 2006.

[11] M. de Salud, “Carga de enfermedad por enfermedades crónicas no transmisibles y discapacidad en Colombia.,” pp. 38–53.

[12] E. By and T. J. Liesegang, “Neurovisual rehabilitation: recent devel- opments and future directions.,” 2000.

[13] World Health Organization, “Neurological disorders: a public health approach,” *Neurol. Disord. public Heal. challenges.*, pp. 41–176, 2006.

[14] F. R. Carrick, “Eye-Movement Training Results in Changes in qEEG and NIH Stroke Scale in Subjects Suffering from Acute Middle Cerebral Artery Ischemic Stroke: A Randomized Control Trial,” vol. 7, no. January, 2016.

[15] G. E. Legge and S. T. L. Chung, “Low Vision and Plasticity : Implications for Rehabilitation.”

[16] et al. Crosson B, Ford A, McGregor KM, “Functional Imaging and Related Techniques: An Introduction for Rehabilitation Researchers.,” *J Rehabil Res Dev*, vol. 47, no. 2, pp. 1–33, 2010.

[17] F. Lopes da Silva, “EEG and MEG: Relevance to neuroscience,” *Neuron*, vol. 80, no. 5, pp. 1112–1128, 2013.

[18] M. R. Borich, K. E. Brown, B. Lakhani, and L. A. Boyd, “Applications of electroencephalography to characterize brain activity: Perspectives in stroke,” *J. Neurol. Phys. Ther.*, vol. 39, no. 1, pp. 43–51, 2015.

[19] S. Finnigan and M. J. A. M. Van Putten, “EEG in ischaemic stroke : Quantitative EEG can uniquely inform (sub-) acute prognoses and clinical management,” *Clin. Neurophysiol.*, vol. 124, no. 1, pp. 10–19, 2013.

[20] K. E. Thornton, “The Role of the Quantitative EEG in the Diagnosis and Rehabilitation of the Traumatic Brain Injured Patients,” pp. 345–361.
[21] J. Sanchez-lopez *et al.*, “Visually evoked responses from the blind field of hemianopic patients,” *Neuropsychologia*, 2017.
[22] E. Mezer, C. A. Westall, G. Mirabella, T. Wygnanski-Jaffe, R. Yagev, and J. R. Buncic, “Measuring recovery of visual function in children with papilledema using sweep visual evoked potentials,” *J. AAPOS*, vol. 20, no. 3, pp. 252–257, 2016.
[23] C. Hemptinne, J. Liu-Shuang, D. Yuksel, and B. Rossion, “Rapid objective assessment of contrast sensitivity and visual acuity with sweep visual evoked potentials and an extended electrode array,” *Investig. Ophthalmol. Vis. Sci.*, vol. 59, no. 2, pp. 1144–1157, 2018.
[24] W. V. Good, C. Hou, and A. M. Norcia, “Spatial contrast sensitivity vision loss in children with cortical visual impairment,” *Investig. Ophthalmol. Vis. Sci.*, vol. 53, no. 12, pp. 7730–7734, 2012.
[25] F. Almoqbel, S. J. Leat, and E. Irving, “The technique, validity and clinical use of the sweep VEP,” *Ophthalmic Physiol. Opt.*, vol. 28, no. 5, pp. 393–403, 2008.
[26] J. P. Kelly, K. Tarczy-Hornoch, E. Herlihy, and A. H. Weiss, “Occlusion therapy improves phase-alignment of the cortical response in amblyopia,” *Vision Res.*, vol. 114, pp. 142–150, 2015.
[27] H. S. M. Kiiski *et al.*, “Delayed P100-Like Latencies in Multiple Sclerosis: A Preliminary Investigation Using Visual Evoked Spread Spectrum Analysis,” *PLoS One*, vol. 11, no. 1, p. e0146084, 2016.
[28] C. Barber and D. Keating, “Comparison of cathode ray tube and liquid crystal display stimulators for use in multifocal VEP,” pp. 115–122, 2014.
[29] M. Molnár *et al.*, “Spectral and complexity features of the EEG changed by visual input in a case of subcortical stroke compared to healthy controls,” *Clin. Neurophysiol.*, vol. 117, no. 4, pp. 771–780, 2006.
[30] M. Gittler and A. M. Davis, “Guidelines for adult stroke rehabilitation and recovery,” *JAMA - J. Am. Med. Assoc.*, vol. 319, no. 8, pp. 820–821, 2018.
[31] M. Ramos-lima, I. Isme, and M. Jose, “Quality of life after stroke : impact of clinical and sociodemographic factors,” pp. 1–7, 2018.
[32] M. C. Leary and H. A. Yacoub, *Chapter 85 – The Heart and Stroke*, Second Edi. Elsevier, 2017.
[33] S. Km, A. Midelfart, L. Thomassen, A. Melms, H. Wilhelm, and H. Jm, “Visual impairment in stroke patients – a review,” vol. 127, pp. 52–56, 2013.
[34] L. Hepworth *et al.*, “Post-stroke Visual Impairment: A Systematic Literature Review of Types and Recovery of Visual Conditions,” *Ophthalmol. Res. An Int. J.*, vol. 5, no. 1, pp. 1–43, 2016.
[35] J. L. Timothy W. Ellis, “TBI and sensory sensitivity: Translational opportunities,” in *Traumatic Brain Injury*, 2017, pp. 163–167.
[36] E. O. Vallejo Agudelo, S. Rendón Villa, A. Colina Vargas, J. Bustamante, and J. C. Suárez-Escudero, “Revisión anatomofuncional de la neurología visual. Reporte de caso: Discapacidad visual neurológica pos-TEC con hematomas subdurales subcrónicos bilaterales parietooccipitales,” *Rev. Mex. Oftalmol.*, vol. 90, no. 1, pp. 33–42, 2016.
[37] I. B. Suchoff, N. Kapoor, K. J. Ciuffreda, D. Rutner, E. Han, and S. Craig, “The frequency of occurrence, types, and characteristics of visual field defects in acquired brain injury: A retrospective analysis,” *Optometry*, vol. 79, no. 5, pp.

259–265, 2008.
[38] G. C. Cockerham *et al.*, “Eye and visual function in traumatic brain injury,” *J. Rehabil. Res. Dev.*, vol. 46, no. 6, pp. 811–818, 2009.
[39] A. A. Brewer and B. Barton, “Visual Field Map Organization in Human Visual Cortex,” *Intech Open Sci.*, vol. 10.5772/51, 2012.
[40] R. F. Dougherty, V. M. Koch, A. A. Brewer, J. Modersitzki, and B. A. Wandell, “Visual field representations and locations of visual areas V1 / 2 / 3 in human visual cortex,” pp. 586–598, 2003.
[41] B. A. Wandell, S. O. Dumoulin, and A. A. Brewer, “Review Visual Field Maps in Human Cortex,” no. 1893, pp. 366–383, 2007.
[42] T. H. Donner, M. Siegel, R. Oostenveld, P. Fries, M. Bauer, and A. K. Engel, “Population Activity in the Human Dorsal Pathway Predicts the Accuracy of Visual Motion Detection,” *J Neurophysiol 98*, vol. 98, pp. 345–359, 2007.
[43] S. Prasad and S. L. Galetta, *Anatomy and physiology of the afferent visual system*, 1st ed., vol. 102, no. 617. Elsevier B.V., 2011.
[44] W. Health Organization, *Informe mundial sobre la visión*. 2019.
[45] S. Stevens, “How to measure distance visual acuity,” *Eye Heal. J.*, p. 2014, 2014.
[46] F. Ejzenbaum, A. Berezovsky, and P. Y. Sacai, “Age norms for monocular grating acuity measured by sweep-VEP in the first three years of age,” vol. 71, no. 3, pp. 7–8, 2008.
[47] B. H. Hospital and B. H. Hospital, “Improving outcome in stroke patients with visual problems,” no. July, pp. 560–565, 2006.
[48] F. Ricci, C. Cedrone, and L. Cerulli, “Review article Standardized measurement of visual acuity,” no. 9100119, pp. 1990–1995, 1998.
[49] Y. Kim, “Cortical sources of Vernier acuity in the human visual system : An EEG-source imaging study,” vol. 17, pp. 1–12, 2017.
[50] S. Ajami, A. Mahnam, and V. Abootalebi, “Development of a practical high frequency brain–computer interface based on steady-state visual evoked potentials using a single channel of EEG,” *Biocybern. Biomed. Eng.*, vol. 38, no. 1, pp. 106–114, 2018.
[51] F. M. Almoqbel, E. L. Irving, and S. J. Leat, “Visual Acuity and Contrast Sensitivity Development in Children : Sweep Visually Evoked Potential and Psychophysics,” vol. 94, no. 8, 2017.
[52] M. Bach, J. P. Maurer, and M. E. Wolf, “Visual evoked potential-based acuity assessment in normal vision, artificially degraded vision, and in patients,” *Br. J. Ophthalmol.*, vol. 92, no. 3, pp. 396–403, 2008.
[53] A. S. Hawkins, J. P. Szlyk, Z. Ardickas, K. R. Alexander, and J. T. Wilensky, “Comparison of contrast sensitivity, visual acuity, and Humphrey visual field testing in patients with glaucoma,” *J Glaucoma*, vol. 12, pp. 134–138, 2003.
[54] D. G. Pelli and P. Bex, “Measuring contrast sensitivity,” pp. 10–14, 2014.
[55] L. J. Balcer *et al.*, “Contrast letter acuity as a visual component for the Multiple Sclerosis Functional Composite,” vol. 000, pp. 1367–1374, 2003.
[56] K. Boyd, “Visual Field Test,” 2019. [Online]. Available: https://www.aao.org/eye-health/tips-prevention/visual-field-testing.
[57] J. G. Romano, P. Schulz, S. Kenkel, and D. P. Todd, “Visual field changes after a rehabilitation intervention: Vision restoration therapy,” vol. 273, pp. 70–74, 2008.
[58] E. Kasten, U. Bunzenthal, and B. A. Sabel, “Visual field recovery after vision restoration therapy (VRT) is independent of eye movements : An eye tracker

study," vol. 175, pp. 18–26, 2006.
[59] I. Mueller, H. Mast, and B. A. Sabel, "Recovery of visual field defects : A large clinical observational study using vision restoration therapy," vol. 25, pp. 563–572, 2007.
[60] A. Borst and M. Egelhaaf, "Principles of visual motion detection," pp. 297–306, 1989.
[61] V. Walsh, A. Ellison, L. Battelli, and A. Cowey, "Task-specific impairments and enhancements induced by magnetic stimulation of human visual area V5," vol. 5, no. November 1997, 1998.
[62] L. M. Hamm, J. Black, S. Dai, and B. Thompson, "Global processing in amblyopia: a review," vol. 5, no. June, pp. 1–21, 2014.
[63] J. E. Raymond, "Attentional modulation of visual motion perception," vol. 4, no. 2, pp. 42–50, 2000.
[64] F. Rocchi and B. S. Webb, "Criterion-free measurement of motion transparency perception at different speeds," vol. 18, pp. 1–12, 2018.
[65] S. O. Murray, D. Kersten, B. A. Olshausen, P. Schrater, and D. L. Woods, "Shape perception reduces activity in human primary visual cortex," *PNAS*, vol. 99, p. 23, 2002.
[66] T. W. James, J. Culham, G. K. Humphrey, A. D. Milner, and M. A. Goodale, "Ventral occipital lesions impair object recognition but not object-directed grasping : an fMRI study," 2003.
[67] I. Kurki and J. Saarinen, "Investigating shape perception by classification images," *J. Vis.*, vol. 14, pp. 1–19, 2014.
[68] B. J. B. Nicole M. Gage, *Fundamentals of Cognitive Neuroscience (Second Edition)*. 2018.
[69] H. O. Karnath, J. Rüter, A. Mandler, and M. Himmelbach, "The anatomy of object recognition - Visual form agnosia caused by medial occipitotemporal stroke," *J. Neurosci.*, vol. 29, no. 18, pp. 5854–5862, 2009.
[70] G. W. A. James C. Grotta, *Stroke. Pathophysiology, Diagnosis, and Management*. 2016.
[71] P. Kok and F. P. De Lange, "Shape perception simultaneously up- and downregulates neural activity in the primary visual cortex," *Curr. Biol.*, vol. 24, no. 13, pp. 1531–1535, 2014.
[72] C. Terms, "Color Vision," vol. 41, no. 3, 2000.
[73] K. Seymour, C. W. G. Clifford, and N. K. Logothetis, "The Coding of Color , Motion , and Their Conjunction in the Human Visual Cortex," *Curr. Biol.*, vol. 19, no. 3, pp. 177–183, 2009.
[74] S. Zeki and A. Bartels, "The clinical and functional measurement of cortical (in) activity in the visual brain , with special reference to the two subdivisions (V4 and V4 a) of the human colour centre," 1999.
[75] S. E. Bouvier and S. A. Engel, "Behavioral Deficits and Cortical Damage Loci in Cerebral Achromatopsia," *Cereb. Cortex*, no. February, pp. 183–191, 2006.
[76] M. A. Crognale, C. S. Duncan, D. J. Peterson, and M. E. Berryhill, "The locus of color sensation : Cortical color loss and the chromatic visual evoked potential," *Vision*, vol. 13, pp. 1–11, 2013.
[77] D. J. Mckeefry and S. Zeki, "The position and topography of the human colour centre as revealed by functional magnetic resonance imaging," pp. 2229–2242, 1997.
[78] G. Kerkhoff, "Restorative and compensatory therapy approaches in cerebral blindness – a review," vol. 15, pp. 255–271, 1999.

[79] R. J. Nudo, “Recovery after brain injury: mechanisms and principles,” *Front. Hum. Neurosci.*, vol. 7, no. December, pp. 1–14, 2013.
[80] A. Pascual-leone, A. Amedi, F. Fregni, and L. B. Merabet, “The Plastic Human Brain Cortex,” 2005.
[81] A. T. Toosy, “Valuable Insights Into Visual Neuroplasticity After Optic Neuritis,” pp. 1–2, 2018.
[82] I. Mueller *et al.*, “Vision restoration therapy after brain damage : Subjective improvements of activities of daily life and their relationship to visual field enlargements to visual field enlargements,” vol. 5167, no. January 2016, 2009.
[83] G. K. V, D. Strasse, and D.- München, “Neurovisual rehabilitation : recent developments and future directions,” pp. 691–706, 2000.
[84] L. F. Nicolas-Alonso and J. Gomez-Gil, “Brain computer interfaces, a review,” *Sensors*, vol. 12, no. 2, pp. 1211–1279, 2012.
[85] S. S. and J. A. Chambers, *EEG Signal Processing*. 2007.
[86] X. Lei *et al.*, “Identification of EEG features in Stroke Patients based on Common Spatial Pattern and Sparse Representation Classification,” pp. 114–117, 2017.
[87] Encyclopedia, *Medical Devices and Human Engineering*, vol. 5. 2006.
[88] J. Leon-carrion, J. F. Martin-rodriguez, J. Damas-lopez, J. Manuel, and M. R. Dominguez-morales, “Clinical Neurophysiology Delta – alpha ratio correlates with level of recovery after neurorehabilitation in patients with acquired brain injury,” *Clin. Neurophysiol.*, vol. 120, no. 6, pp. 1039–1045, 2009.
[89] M. I. Vanegas *et al.*, “Altered dynamics of visual contextual interactions in Parkinson’s disease,” *npj Park. Dis.*, vol. 5, no. 1, 2019.
[90] M. I. Vanegas, A. Blangero, and S. P. Kelly, “Electrophysiological indices of surround suppression in humans,” *J. Neurophysiol.*, vol. 113, no. 4, pp. 1100–1109, 2015.
[91] M. I. Vanegas, A. Blangero, and S. P. Kelly, “Exploiting individual primary visual cortex geometry to boost steady state visual evoked potentials,” *J Neural Eng.*, vol. 23, no. 1, pp. 1–7, 2013.
[92] A. Mora-Cortes, K. R. Ridderinkhof, and M. X. Cohen, “Evaluating the feasibility of the steady-state visual evoked potential (SSVEP) to study temporal attention,” *Psychophysiology*, no. June, 2017.
[93] X. Gao, D. Xu, M. Cheng, and S. Gao, “A BCI-based environmental controller for the motion-disabled,” *IEEE Trans. Neural Syst. Rehabil. Eng.*, vol. 11, no. 2, pp. 137–140, 2003.
[94] A. M. Norcia, L. G. G. Appelbaum, J. M. J. M. Ales, B. R. B. R. Cottereau, and B. Rossion, “The steady-state visual evoked potential in vision research: a review,” *J. Vis.*, vol. 15, no. 6, p. 4, 2015.
[95] Y. Wang, X. Gao, B. Hong, C. Jia, and S. Gao, “Brain-Computer Interfaces Based on Visual Evoked Potentials,” *Ieee Eng. Med. Biol. Mag.*, vol. 27, no. 5, pp. 64–71, 2008.
[96] J. A. G. Heckenlively, *Principles and practice of clinical electrophysiology of vision.* 2006.
[97] S. J. Leat, L. M. Head, and E. L. Irving, “Effects of sweep VEP parameters on visual acuity and contrast thresholds in children and adults,” *Graefes Arch Clin Exp Ophthalmol*, pp. 613–623, 2011.

[98] Julius O. Smith III. Welch's Method. 2011, ISBN 978-0-9745607-3-1.

[99] S. Stathopoulou, “EEG Changes in Traumatic Brain Injured Patients After Cognitive Rehabilitation,” *J. Neurother.*, vol. 8, no. 2.

[100] M. Pharmacology, P. Health, and L. Angeles, “Early and persistent impaired percent alpha variability on continuous electroencephalography monitoring as predictive of poor outcome after traumatic brain injury,” *J Neurosurg*, vol. 97, pp. 84–92, 2002.

[101] E. Pereda, R. Q. Quiroga, and J. Bhattacharya, “Nonlinear multivariate analysis of neurophysiological signals,” *Prog. Neurobiol.*, vol. 77, no. 1–2, pp. 1–37, 2005.

[102] X. Guo, Z. Jin, X. Feng, and S. Tong, “Enhanced effective connectivity in mild occipital stroke patients with hemianopia,” *IEEE Trans. Neural Syst. Rehabil. Eng.*, vol. 22, no. 6, pp. 1210–1217, 2014.

[103] J. Wu *et al.*, “Connectivity measures are robust biomarkers of cortical function and plasticity after stroke,” *Brain*, vol. 138, no. 8, pp. 2359–2369, 2015.

[104] J. D. Lewine *et al.*, “Quantitative EEG Biomarkers for Mild Traumatic Brain Injury,” *J. Clin. Neurophysiol.*, vol. 36, no. 4, pp. 298–305, 2019.

[105] L. Cutillo, *Encyclopedia of Bioinformatics and Computational Biology - Parametric and Multivariate Methods*. 2019.

[106] R. Kuehl, *Diseño de experimentos*. 2001.

[107] M. Dempster, *A Research Guide for Health and Clinical Psychology*. 2011.

[108] A. M. Skoczenski and A. M. Norcia, “Development of VEP Vernier Acuity and Grating Acuity in Human Infants,” *Invest. Ophthalmol. Vis. Sci.*, 2018.

[109] C. Hou, W. V Good, and A. M. Norcia, “Detection of Amblyopia Using Sweep VEP Vernier and Grating Acuity,” *Investig. Ophthalmol. Vis. Sci.*, 2018.

[110] W. H. Ridder, I. I. I. Anna, and T. Floresca, “Reliability of acuities determined with the sweep visual evoked potential (sVEP),” *Doc Ophthalmol*, pp. 99–107, 2012.

[111] J. M. L. De Faria, O. Katsumi, M. Arai, and T. Hirose, “Objective measurement of contrast sensitivity function using contrast sweep visual evoked responses,” *Br. J. Ophthalmol.*, pp. 168–173, 1998.

[112] A. L. Ely *et al.*, “Degradation of Swept-Parameter VEP Responses by Neutral Density Filters in Amblyopic and Normal Subjects,” *Investig. opthalmology Vis. Sci.*, 2018.

[113] H. Ja, “A comparison of the performance of three visual evoked potential-based methods to estimate visual acuity,” *Doc Ophthalmol*, pp. 45–56, 2013.

[114] E. M. Santos, E. K. Gnang, and E. Kowler, “Anticipatory smooth eye movements with random-dot kinematograms,” vol. 12, pp. 1–20, 2012.

[115] “OpenBCI shop,” *https://shop.openbci.com/products/cyton-biosensing-board-8-channel?variant=38958638542*. .

[116] R. Oostenveld and P. Praamstra, “The five percent electrode system for high-resolution EEG and ERP measurements,” *Clin. Neurophysiol.*, vol. 112, no. 4, pp. 713–719, 2001.

[117] R. J. Barry, A. R. Clarke, S. J. Johnstone, C. A. Magee, and J. A. Rushby, “EEG differences between eyes-closed and eyes-open resting conditions,” vol. 118, pp. 2765–2773, 2007.

[118] L. Li, “The Differences among Eyes-closed , Eyes-open and Attention States : An EEG Study,” no. Nsfc 30800242, 2010.

[119] R. Nakayama, I. Motoyoshi, and T. Sato, “Discretized Theta-Rhythm

Perception Revealed by Moving Stimuli," *Sci. Rep.*, vol. 8, no. 1, pp. 2–10, 2018.
[120] S. Cochin, C. Barthelemy, B. Lejeune, S. Roux, and J. Martineau, "Perception of motion and qEEG activity in human adults," *Electroencephalogr. Clin. Neurophysiol.*, vol. 107, no. 4, pp. 287–295, 1998.
[121] A. Yoto, T. Katsuura, K. Iwanaga, and Y. Shimomura, "Effects of Object Color Stimuli on Human Brain Activities in Perception and Attention Referred to EEG Alpha Band Response," 1999.

12 Supplementary material

Appendix 1
Demographics information for healthy participant

Code	Dominat eye	Age	Gender
S1	Left	25	F
S2	Right	30	F
S3	Left	19	F
S4	Left	24	M
S5	Right	43	F
S6	Right	24	M
S7	Right	25	M
S8	Right	25	F
S9	Right	35	M
S10	Left	20	F
S11	Right	22	M
S12	Left	24	F
S13	Left	24	M
S14	Left	19	M
S15	Left	25	F
S16	Right	28	M
S17	Right	29	M
S18	Right	39	M
S19	Right	22	F
S20	Left	27	M
S21	Left	35	M
S22	Right	25	M
S23	Right	22	M
S24	Right	22	F
S25	Right	23	F
S26	Right	23	M
S27	Right	23	M
S28	Left	24	M
S29	Right	29	M
S30	Right	53	F
S31	Right	24	M
S32	Left	22	M
S33	Left	25	M
S34	Left	25	F
S35	Left	25	F
S36	Right	35	M

S37	Right	22	F