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Doctorate in Physics

ELECTRICAL AND MAGNETIC STIMULATION FOR THE TREATMENT OF PATIENTS WITH CARDIAC AND NEUROLOGICAL CONDITIONS

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ABSTRACT

Electrical stimulation and electrophysiological signal analysis have proven to be key tools in biomedical research and the development of therapeutic devices. Various studies have explored their application in the modulation of nervous system activity, the treatment of pathologies such as migraines and arrhythmias, and the identification of neuronal biomarkers through EEG. In this context, non-invasive electrical stimulation devices have been developed with the ability to vary key parameters such as frequency, current, and pulse width, allowing personalized adaptation for the research and treatment of conditions related to the vagus nerve. A system has been designed to correct arrhythmias by means of bioelectromagnetic stimulation of the sinus node and cervical sympathetic ganglia, demonstrating a promising response in heart rhythm regulation. Likewise, studies have been conducted on the relationship between brain activity and migraines through the analysis of EEG signals. Interactive games have been designed to induce states of concentration and activate specific brain regions, providing a possible electrophysiological biomarker of migraines. In addition, a neuromodulation device has been developed for the simultaneous stimulation of the vagus and trigeminal nerves, evaluating its effect on pain reduction and cognitive activity by recording EEG signals from the prefrontal lobe. These advances reflect the potential of biomedical technology in the exploration of the nervous system and the development of alternative therapies for various pathologies, offering new perspectives in the research and treatment of neurological and cardiovascular diseases.

1. INTRODUCTION

The vagus nerve plays a central role in the parasympathetic nervous system, contributing to the regulation of vital functions such as heart rate, digestion, and mood [1, 2]. Building on this physiological relevance, non-invasive electrical stimulation of the vagus nerve has emerged as a promising tool in modern medicine. Several studies have demonstrated its effectiveness in treating conditions such as epilepsy, migraines, and depression [1], as well as other disorders related to the autonomic nervous system, including cardiac arrhythmias. This therapeutic approach is particularly valuable for patients in whom conventional pharmacological treatments have proven insufficient.

In the context of cardiac arrhythmia, electrical stimulation of the vagus nerve and magnetic stimulation of the cervical sympathetic ganglia have been proposed as noninvasive methods to correct cardiac rhythm disturbances. Vagus nerve stimulation helps reduce heart rate in patients with tachycardia, while magnetic stimulation of the sympathetic ganglia can increase heart rate in cases of bradycardia [3, 4]. These advances offer patients a less invasive therapeutic alternative with fewer side effects compared to conventional drug treatments, thus improving their quality of life [1, 5].

Furthermore, research on simultaneous stimulation of the vagus and trigeminal nerves has gained relevance, especially in the treatment of migraines. Electrical stimulation of these nerves has shown positive effects when applied independently [6, 7]. However, the goal of some current studies is to combine these techniques into a single device, which would allow for more efficient interventions in migraine treatment. This device also incorporates EEG signal monitoring, allowing for the evaluation of the effects of stimulation on brain activity, particularly in the left prefrontal lobe, an area associated with cognitive processes such as concentration and meditation [8]. This research aims not only to improve migraine symptoms but also to generate new knowledge about the interaction between electrical stimuli and brain activity in real time [9, 10].

In parallel with the study of electrical stimulation, tools such as interactive games designed to induce states of concentration are being explored, allowing for the evaluation of brain oscillations, such as gamma and beta waves, which are related to cognitive functions and the

management of emotional states such as stress and anxiety [8, 11]. Games such as "buzz wire" are useful for inducing changes in brain activity, also functioning as indicators of neurological responses to applied electrical stimulation [9]. Advances in this field suggest that modulating these oscillations could be crucial for the treatment of neurological disorders such as Alzheimer's disease and schizophrenia, offering hope for patients.

In conclusion, the combination of noninvasive electrical stimulation devices and brain signal monitoring using EEG promises to revolutionize the treatment of various neurological pathologies, improving patients' quality of life and expanding the understanding of the brain mechanisms involved in these diseases [1, 2].

2. STATEMENT OF THE PROBLEM

The challenge lies in understanding and controlling electrical and magnetic stimulation focused on the cervical sympathetic ganglia and the vagus and trigeminal nerves, in order to develop potential treatments for patients with cardiac and neurological conditions. This type of practice has shown significant advances in neuromodulation; therefore, the present investigation aims to contribute to this field of research by deepening the understanding of physics associated with the design and construction of devices useful in the treatment of conditions such as migraines and cardiac arrhythmia. Initially, the lack of understanding of the physical principles underlying the electronic control of electric and magnetic fields, as well as their application to the nervous system and the resulting physiological responses, is considered a limitation in the development of effective treatments.

Research Question

How can we generate and apply energy in the form of electric and magnetic fields to stimulate cervical sympathetic ganglia and the vagus and trigeminal nerves, to find potential treatments for patients with cardiac and neurological conditions?

3. THEORETICAL FRAMEWORK

3.1 Transcutaneous electrical stimulation applied to nerves

It consists on the application of pulsed electrical current through the skin using a pair of electrodes located on the outer surface of the epidermis [12]. The parameters used in stimulation are adjusted through programming, and different physiological effects are produced depending on the settings [12]. Stimulation is usually applied using varying frequencies, intensities, and pulse widths. The stimulation frequency is typically classified as high frequency if it is above 50 Hz or low frequency, if it is below 10 Hz; the intensity is generally determined by the patient's sensitivity[13].

The physical foundations that explain the behavior of noninvasive electrical stimulation of nerves begin with the fact that human tissue can be modeled as a heterogeneous conductive medium. The Ohm's law (Equation 1) describes how electrical current flows through the skin, subcutaneous tissue, and nerves. Tissue impedance depends on the signal frequency. At frequencies below 1 kHz, the skin's impedance can vary between tens and hundreds of kilo-ohms (kΩ) [14], At low frequencies, impedance increases due to the capacitance of the cell membrane. Subcutaneous tissue generally has a lower impedance than the skin but higher than that of nerves and muscles. In this sense, nerves have a relatively low impedance compared to skin and subcutaneous tissue due to their high ionic conductivity.

$$V = IR \tag{1}$$

Regarding the movement of electrical charges along the nerve, it can be stated that a potential difference between the electrodes in contact with the skin produces an electric field in the nerves, which, in turn, generates an electric current in the nerve axons. The electric field present in tissues can be represented according to Gauss's law (Equation 2):

$$\oint_s \boldsymbol{E} \cdot d\boldsymbol{A} = \frac{Q}{\varepsilon} \tag{2}$$

Moreover, nerves can be modeled as an electrical cable according to the Hodgkin-Huxley cable equation or its simplified version (Equation 3):

$$\frac{\partial V}{\partial x} = D\frac{\partial^2 V}{\partial x^2} - \frac{V}{\tau} \tag{3}$$

where D is the diffusion coefficient of the potential and τ is the membrane time constant. The external current generated by electrical stimulation depolarizes the nerve membrane, causing the opening of ion channels and generating an action potential that propagates through the nerve. The generation of an action potential is possible as long as the stimulus exceeds the activation threshold.

3.2 Magnetic Stimulation

When a magnetic field comes into contact with the human body, it is possible to induce electrical currents in the nervous system. For the generation of electrical currents in nerves to occur, the magnetic field must be time-varying. Depending on the intensity, frequency, and duration of magnetic stimulation, neuronal activity may be modulated, either by exciting or inhibiting neurons in a specific region. Magnetic stimulation directed toward peripheral nerves is based on Faraday's Law (Equation 4), which states that a time-varying magnetic field induces an electrical current in a conductor[15].

$$\nabla \times \boldsymbol{E} = -\frac{\partial \boldsymbol{B}}{\partial t} \tag{4}$$

If the induced current in the tissue is sufficient to depolarize neuronal membranes, the generation of action potentials in neurons becomes possible. To describe this, it is appropriate to combine electrodynamic principles with nerve conduction models, such as the Hodgkin-Huxley model, which describes the dynamics of the transmembrane voltage $V_m(t)$ of a neuron (Equation 5):

$$C_m \frac{dV_m}{dt} = I_{\text{ext}} - (I_{Na} + I_K + I_L). \tag{5}$$

If the induced current I_{ext} is large enough, the transmembrane voltage V_m will reach the activation threshold (≈ -55 mV), generating an action potential. For magnetic stimulation to trigger neuronal firing, the induced current must exceed the threshold required to open sodium channels:

$$I_{\text{ext}} > I_{\text{threshold}}$$

where the threshold depends on:

- The duration of the magnetic pulse (nerve recruitment time law),
- The resistance of nervous tissue,

- The orientation of the nerve is related to the induced field.

An approximate model for estimating the minimum current required is:

$$I_{\text{threshold}} \approx \frac{\theta C_m}{\tau_m}(V_{\text{threshold}} - V_{\text{rest}})$$

where θ is a shape factor that depends on the geometry of the electric field, and τ_m is the membrane time constant. This approach allows for the design of effective stimulation protocols for therapeutic and experimental applications.

When optimizing application methods, it is important to recognize that various parameters, structures, and techniques affect the efficiency of magnetic field delivery to the body. These include the shape of the coil, the distance between the coil and the nerve, and the frequency and intensity of the magnetic pulses.

3.3 Induced Current in Nervous Tissue

Nervous tissue has σ electrical conductivity and ε permittivity. The density of induced current in the nerve is given by:

$$\boldsymbol{J = \sigma E + \varepsilon\,(\partial E/\partial t)}$$

Where:

- $\boldsymbol{J}$ is the density of induced current (A/m^2),
- $\boldsymbol{\sigma}$ is the conductivity of the nervous tissue (S/m),
- $\boldsymbol{\varepsilon}$ is the electrical permittivity of the tissue $(\varepsilon_r \varepsilon_0)$

For low frequencies, the contribution of $\varepsilon\frac{\partial \boldsymbol{E}}{\partial t}$ It is small, and the Eddy current is approximately:

$$\boldsymbol{J \approx \sigma E}$$

This means that the current induced in the nerve is directly dependent on the induced electric field and the conductivity of the tissue.

3.4 The Vagus Nerve

The vagus nerve is the longest of the cranial nerves and is involved in the endocrine, immune, gastrointestinal, respiratory, cardiovascular, and autonomic systems. Also known as the pneumogastric nerve, the tenth cranial nerve is the most important anatomical structure of

the parasympathetic system and innervates several organs, primarily those located in the thoracic and abdominal regions. Through its diverse innervations, the vagus nerve regulates nutrition, respiration, airway diameter, vascular resistance, blood pressure, and heart rate [16].

3.5 Electrical Stimulation of the Vagus Nerve

This technique involves applying electrical impulses to the vagus nerve. Stimulation can be performed in two ways: invasive and noninvasive. The invasive method involves implanting a device connected to a cable that wraps around the vagus nerve in the neck, while the noninvasive method is performed transcutaneously in the auricular or cervical region. Electrical stimulation of the vagus nerve is believed to contribute to the modulation of neurotransmitters, increase cerebral blood flow, help stabilize abnormal electrical activity patterns in the brain, and promote anti-inflammatory processes.

There are a variety of conditions that could be treated or investigated through vagus nerve electrical stimulation. Listed below are some of the conditions that have been treated with his form of therapy. It can start with hiccups, which can be stopped by this type of stimulation. Persistent hiccups can become a serious problem, particularly in patients requiring artificial ventilation in intensive care units. In such cases, the use of transcutaneous vagus nerve stimulators becomes vital [17].

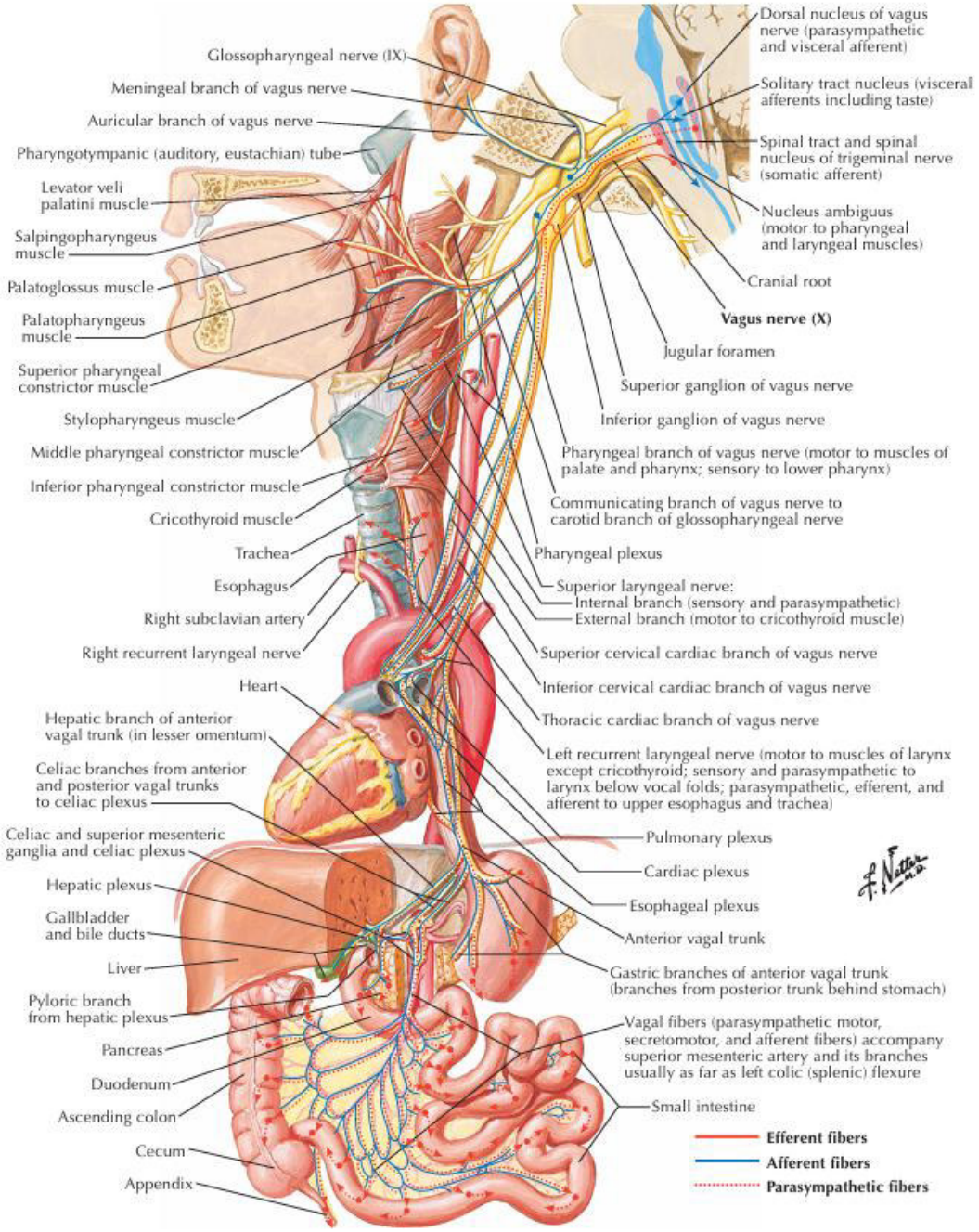


Figure 1. Structure and innervations of the vagus nerve [17].

Another condition is epilepsy, a disease for which medication has been essential. However, there are times when drug treatments are insufficient, and in these cases, electrical stimulation of the vagus nerve has proven to be an effective treatment for epileptic patients with drug resistance[18–21]. Similarly, in cases of migraine, when pharmacological treatments are not sufficient, electrical stimulation of the vagus nerve has shown favorable results[7, 22].

Furthermore, electrical stimulation of the vagus nerve has been found to impact mood states, offering hope for depressed patients who have benefited from this type of treatment [23, 24]. Additionally, its potential application for patients with Parkinson's disease has been proposed. Although the use of vagus nerve stimulation as a new therapy for Parkinson's patients is still preliminary, initial results are promising and ongoing investigations are underway [25].

Diseases associated with dementia and serious mental disorders, such as schizophrenia and Alzheimer's disease, have also been evaluated in the context of vagus nerve stimulation. In schizophrenic patients, stimulation has been well tolerated; although a total improvement in symptoms has not been achieved, variations in symptom patterns suggest that further research is warranted [26]. In Alzheimer's disease, it is believed that the cognitive dysfunction caused by the condition may be counteracted by vagus nerve stimulation, and upcoming clinical trials are expected to provide valuable information about its potential benefits[27]. Finally, it is important to highlight the significant role that electrical biostimulation has played as a potential solution for cardiac [28–31] and even digestive [32] disorders.

3.6 Trigeminal Nerve

The trigeminal nerve is identified as the fifth cranial nerve. Its main function is to provide sensory innervation to the face. This nerve divides into three branches: the ophthalmic, maxillary, and mandibular nerves, which converge at the trigeminal ganglion. The ophthalmic nerve is responsible for sensory innervation to the face and skull above the palpebral fissure, as well as the eye and parts of the nasal cavity [33], The maxillary nerve serves as a crucial pathway for sensory perception in the midface and associated structures, having no direct motor function related to facial muscles or mastication. Finally, the mandibular nerve is essential for mastication, sensation in the lower face and tongue, and some functions related to hearing and the temporomandibular joint. Its mixed nature distinguishes it from the other two branches of the trigeminal nerve, which are purely sensory [34].

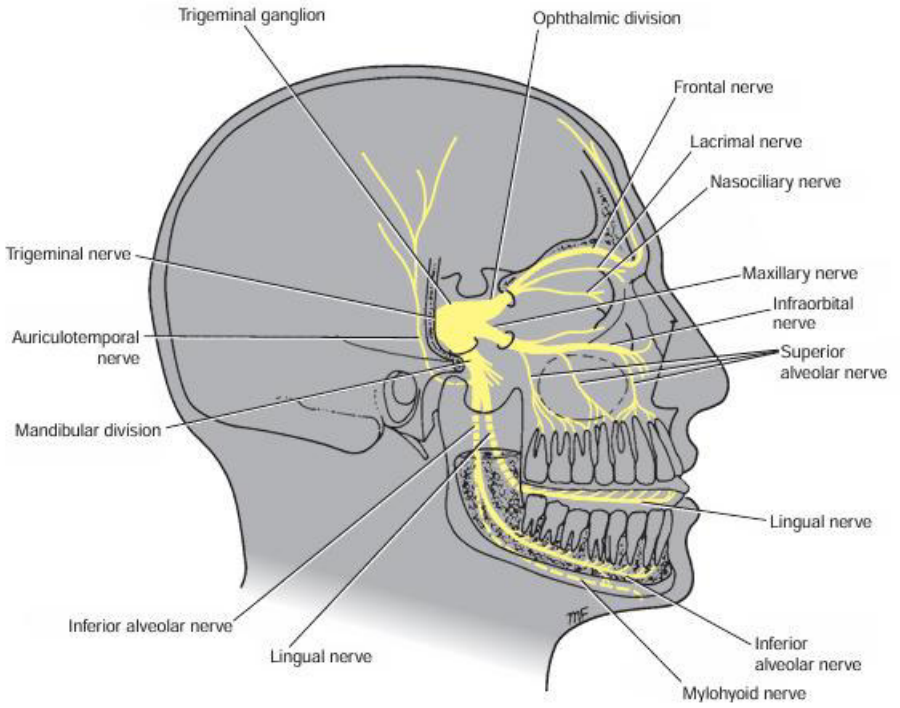


Figure 2. Distribution of the trigeminal nerve [35].

3.7 Cervical Sympathetic Ganglia

They are part of the sympathetic structure for the autonomic nervous system and form a bilateral ganglionic chain located on either side of the neck, following the pathway of the sympathetic trunk, see Figure 3. The cervical sympathetic ganglia are divided into three: the upper cervical, middle cervical, and the lower cervical, which in turn joins the first thoracic ganglion to form the stellate ganglion [35].

The general functions of the cervical sympathetic ganglia include participation in autonomic system actions such as increased heart rate, pupillary dilation, and vasoconstriction in response to fight, flight, or stress events. The cervical sympathetic ganglia also contribute to the coordination of autonomic functions to maintain homeostasis under stress conditions. The postganglionic fibers that emerge from these ganglia innervate various structures in the head, neck, and thorax. In addition to the functions mentioned above, these ganglia contribute to the control of sweat and salivary glands, participate in the formation of the cardiac plexus, and innervate the thyroid gland [36].

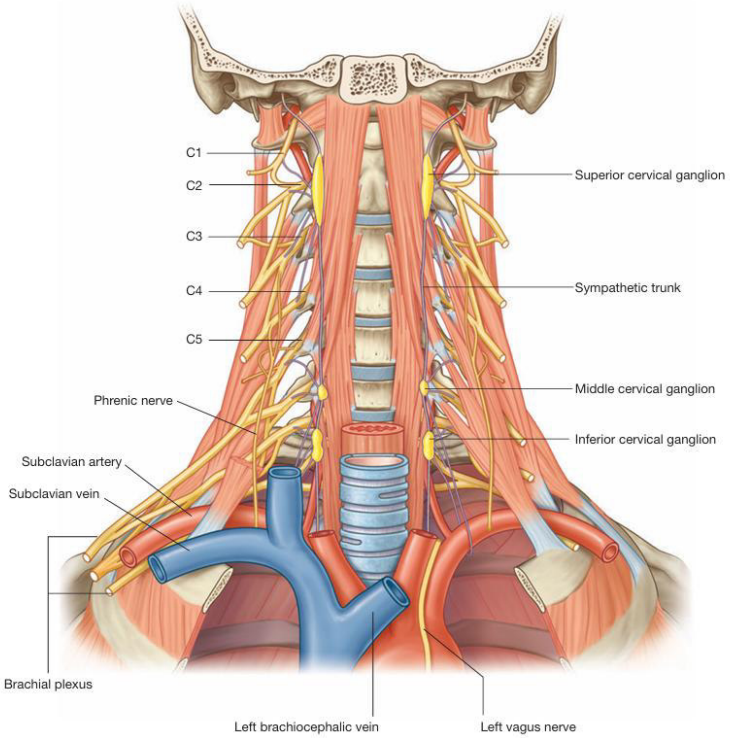


Figure 3. Cervical sympathetic ganglia.

The superior cervical ganglion is the largest and is located adjacent to the C1-C3 vertebrae, the middle cervical ganglion is smaller and is located near the C6 vertebra, the inferior cervical ganglion is located near the C7 vertebra and the first rib[17].

3.8 Migraine

Migraine is a common neurological condition, affecting approximately 10 % of the world's population [37]. It is a disabling disease that reduces productivity and negatively impacts the quality of life of those affected, as well as those close to them. Migraine cases occur more frequently in women; it is estimated to affect one in five women and one in sixteen men. Unfortunately, migraine usually occurs during the most productive stage of life, negatively impacting several aspects: it complicates adequate school dynamics, deteriorates personal relationships, hinders family integration, challenges mental health, and impedes professional development [38].

It is a headache generally characterized by being unilateral and throbbing. The intensity of the pain experienced by patients ranges from moderate to severe, and physical activity can influence its severity [39]. Migraine is an episodic headache with certain associated characteristics, particularly sensitivity to light, sound, odors, and head movement [40].

This type of neurological disorder is characterized by multiple phases: premonitory or prodrome, aura, headache, and postdrome. The premonitory phase can begin up to three days before the headache and allows for early identification of the onset of migraine [41]. The most common symptoms during this particular phase are fatigue, noticeable mood swings, food cravings, yawning, muscle tenderness, and photophobia [42].

A second phase is characterized by the aura, although it does not strictly precede the headache, as it does not occur in all individuals. It is important to recognize that the most common type of aura is visual, characterized by flashes of light, zigzag lines, or other changes in vision. The aura can also manifest through other sensory neurological events that affect speech, motor function, or cause tingling in the hand or face[39].

The third phase of migraine is the most critical because it constitutes the pain stage, which can last from 4 h to 72 h. Finally, during the postdrome or final stage, sensory and gastrointestinal symptoms and general malaise occur, which can prevent the resumption of daily activities. The most reported symptoms during this phase include neck stiffness, difficulty concentrating, fatigue, sensitivity, irritability, pallor, and nausea [43].

3.9 Common Migraine Treatments

An important way to treat migraines is to educate the patient so they can learn to live with the condition. It is advisable to review the patient's lifestyle, with recommendations including regular physical activity, avoiding excess weight, and maintaining a consistent sleep pattern. It is crucial for the patient to identify their specific triggers to help prevent an attack. These triggers are usually individual, and there is no universal cause; for some, triggers might include noise, odors, certain foods, or stress. However, not all patients can tolerate or control migraines through lifestyle management alone, which is when treatment becomes necessary. One of the initial approaches to treating attacks is through the use of analgesics, often combined with sedatives. However, regular use of analgesics can exacerbate migraines. Overuse of analgesics can produce the opposite effect, increasing the excitability of pain-related neurons while inhibiting the activity of neurons that reduce pain. It is estimated that 73 % of patients with chronic migraines overuse analgesics, which significantly worsens the severity of the disease [44].

Various medications are available as preventive measures for migraines, including beta-blockers, neuromodulators, antidepressants, calcium channel antagonists, and even nutraceuticals. Each of these treatments is effective in approximately two out of three patients, but they are not without adverse effects, even at low doses. The existence of side effects is evident, and the lack of efficacy and adverse effects can cause patients to abandon treatment [44].

In addition to medications, non-pharmacological treatments exist. One such method is the use of botulinum toxin (BOTOX), which is administered through injections. This treatment reduces inflammation in sensitive areas, thereby decreasing pain sensitivity. Although BOTOX has adverse effects, they are generally temporary, and its use is restricted in pregnant women. Another novel treatment involves the use of monoclonal antibodies, which have been shown to be both safe and effective. However, further studies, including more prospective variables, are needed to draw generalized conclusions about their efficacy [45]. Medicinal plants, such as Butterbur (Petasita), acupuncture, massage, and physical therapy, have also been reported to reduce the frequency of attacks. However, no definitive conclusions can be drawn regarding the effectiveness of these treatments [44].

Despite the technological advances that have led to therapeutic medications for migraine patients, many people find these treatments ineffective due to intolerance, contraindications, or drug-drug interactions. Research on migraine pathophysiology has advanced, leading to the development of novel neuromodulation techniques based on electrical stimulation for migraine treatment [46]. The growing popularity of neuromodulation treatments is largely due to their effectiveness and minimal risks to patients [47]. Historically, neuron stimulation was often performed invasively through electrode implantation, which posed significant challenges. However, new devices have overcome these obstacles, allowing for noninvasive neuromodulation, a process that involves the excitation of groups of neurons through the application of electrical pulses.

3.10 Physiological Aspects of Vagus Nerve Stimulation in Migraine Patients

Some research indicates that vagus nerve afferents can activate ascending nociceptive pathways in the gray matter and raphe nuclei of the brainstem. The importance of this lies in the fact that the literature also indicates that circuits between the thalamus and cortex play an

important role in mediating pain perception, and that functional and anatomical alterations in thalamocortical circuits are involved in the development and maintenance of migraines [7]. Finally, preliminary studies suggest that the thalamus occupies a relevant perspective in understanding cutaneous allodynia, central sensitization, and photophobia in migraines [48]. On the other hand, other studies have found that other structures such as the locus ceruleus, the nucleus of the solitary tract, and the spinal trigeminal tract are considered to be responsible for the pathophysiology of migraine, and something relevant here is that the vagus nerve can modulate these areas [47].

The rationale behind the use of electrical stimulation of the vagus nerve in patients with headaches is based on the fact that when it is stimulated, specific nerve fibers are activated, among which are some afferent ones that are responsible for the transmission of pain. These specific fibers promote synapses in the zona postrema, in the spinal trigeminal nucleus, as well as in the nucleus of the solitary tract, from where projections emerge towards the locus ceruleus and the periaqueductal gray matter. On the other hand, as previously mentioned, some important projections of the vagus nerve establish a connection with the thalamus, and it is precisely the thalamus, together with the periaqueductal gray matter, that have been described as important agents in the pathophysiology of migraine [46].

Neurostimulation of the vagus nerve has been performed mainly in the auricular and cervical areas. For cases of migraine, studies have been reported in which some transcutaneous neurostimulators are shown where favorable results are presented in patients. These neurostimulators have been designed to contact the vagus nerve through its auricular branch. The regions innervated by this branch are the concha, internal tragus and external auditory canal [1].

In previous works on electrical stimulation of the vagus nerve in patients with migraine, the use of a frequency of 1 Hz stands out. Stimulation performed at this frequency has been safe and efficient. In one of the reviewed works, the efficacy of the treatment was reported after 12 weeks of treatment [6]. In another reported study, functional magnetic resonance imaging shows the comparison between the changes evoked by stimulation performed at a frequency of 1 Hz applied to the cymba of the concha, in contrast to a sham in the helix of the ear that is not innervated by the vagus nerve. There it is concluded that through transcutaneous stimulation of the auricular branch, it is possible to modulate the pain modulation networks,

the activity of the locus ceruleus and the functional connectivity in the resting state, which once again highlights the importance of vagus stimulation performed at 1 Hz in patients with migraine [49].

3.11 Electrical Stimulation of the Trigeminal nerve in Patientes with Migraine

The trigeminal pathway plays an integral role in the pathophysiology of migraine, with the ophthalmic branch of the trigeminal nerve being particularly involved. This branch is innervated by the anterior superior cephalic region, which is a common area for migraine pain distribution [50].

Electrical stimulation of the ophthalmic branch of the trigeminal nerve has been shown to significantly reduce the frequency of migraine attacks [51]. After electrical stimulation, significant hypometabolism was observed in the frontotemporal areas of the brain, particularly in the orbitofrontal and rostral anterior cingulate cortices, in patients with migraine. This hypometabolism was found to decrease further after three months of stimulation, and the reduction in hypometabolism was associated with a significant decrease in the frequency of migraine attacks [51].

Several studies have reported the effectiveness of neuromodulation applied to the trigeminal nerve in patients with migraine. In particular, the use of 60 Hz frequencies has been highlighted in experimental tests [50–53].

3.12 EEG Signal Potentials in Migraine

Electroencephalograms (EEG) are not routinely used to diagnose migraine; however, they can be very useful for investigating cortical alterations in the brain [54]. For an EEG study in patients with migraine to yield relevant conclusions, it must go beyond the traditional visual analysis of the trace, which often shows abnormal recordings. Instead, a quantitative analysis is required, involving the use of computers and power spectrum analysis, typically obtained through a Fourier transform. This approach allows power to be quantified and changes to be verified as a function of frequency [55].

Several studies have provided valuable insights through EEG analysis in migraine patients. One approach involves the analysis of event-related potentials, which has led to important

findings suggesting difficulties in neural processes of inhibition and excitation [55], Additionally, studies using evoked potentials have allowed for the classification of migraines, assessment of the impact of electrical stimulation on the brain, and even identification of cognitive impairments in patients.

Evoked potentials refer to changes in brain electrical activity produced by stimuli perceived through the senses or cognitive functions. These stimuli are transmitted as nerve impulses from sensory organs to the brain, where they are interpreted using brain activity. Various electroencephalographic signal analysis techniques, including Fourier transform and digital filtering, enable the use of EEG potential measurements as a valuable biomarker for studying migraine patients. For instance, signals generated from somatosensory stimuli can distinguish migraine patients in ictal and interictal states from healthy controls [56].

Compared to healthy individuals, migraine patients show abnormalities in visual evoked potentials, particularly in the amplitude values recorded in the signal, which are found to be higher in patients [57, 58]. Other studies have shown that non-invasive stimulation of the vagus and trigeminal nerves in migraine patients can influence laser-evoked potential. This is evidenced by a reduction in cortical potentials evoked by ipsilateral trigeminal stimuli, areas that are affected by electrical stimulation [59, 60]. Regarding cognitive potentials, it has been demonstrated that patients with migraine exhibit anomalies in the generation of P300, a potential known for its high sensitivity to detect alterations in cognitive functioning. This suggests that people with migraine may experience a decline in cortical regions involved in cognitive functions [61].

Considering the above, it can be concluded that studying EEG signal potentials in migraine patients exposed to electrical stimulation of the vagus and trigeminal nerves could provide a valuable tool for understanding the mechanisms of action of the stimulation or gaining more insight into brain activity in migraine patients.

4. METHODOLOGY

Instrumentation, as a fundamental tool in the development of physics, involves the design, construction, and application of instruments that enable precise measurement and control of physical variables, as well as controlled interaction with systems. The history of medicine,

in turn, has been shaped by physics and its methods, in which instrumentation plays a crucial role. The methodology used in this work aligns with this context. Accordingly, one section of the methodology described below presents the process used in the construction of each device. A second section outlines the measurement protocol employed during the implementations carried out on both healthy individuals and patients.

4.1 Device for vagus nerve stimulation capable of parameter adjustment and physiological variable recording

The main objective of the first device was to develop an efficient method for transcutaneous electrical stimulation of the vagus nerve. The aim was to design and build a novel tool with characteristics like those of devices currently on the market, particularly regarding stimulation parameter values accepted by healthcare professionals. In addition to providing stimulation, the device integrates a set of sensors that allow continuous monitoring of physiological variables associated with vagus nerve activity.

Procedure used in the construction of the device

a) Identification of the different methods, signals, variables, and parameters frequently used by healthcare professionals and the scientific community when performing non-invasive electrical stimulation of the vagus nerve. To carry out this part of the work, a review of the work was conducted, which is summarized in the table 1.
b) Design and construction of the device for stimulation and obtaining physiological signals.

The diagram shown in Figure 4 illustrates how the device's components interact. Using the NXP-MKL05Z32VLC microcontroller, it is possible to program a PWM signal that allows the amplitude, period, and pulse width to be adjusted. Next, there is an H-bridge similar to that used in a motor, which seeks to maintain the positive and negative portions of the signal. After the H-bridge, there is a transformer that increases the voltage value.

Table 1. Previously performed work using biphasic signal [62].

Autor	Intensity [mA]	Frequency [Hz]	Pulse width	Time	Object of study or condition of interest
Aihua Liu[20]	It starts with 4 mA, then increases 2 mA per week, until the patient cannot tolerate it	10	200 sec	20 minutes three times a day for 6 months	Refractory Epilepsy
Hermann Stefan[21]	Selected by the patient according to tolerance level	10	300 μs	1 hour in the morning, 1 hour at noon and another hour in the afternoon for 9 months	Epilepsy
William L. Schuerman[63]	0.1-0.4	10 or 30	100 or 250 μs	Pulse trains of 11 seconds, followed by a rest period of 8 seconds, for 10 minutes	Observe cortical activity during stimulation
Charlotte Keatch[64]	0.2-2	6, 24 or 25	1, 4 and 10 ms	4 different protocols were carried out, each lasting 10 minutes	Measurement of the brain response to electrical stimulation of the vagus nerve
Petteri Hyvärinen[65]	0.5	25	500 μs	6 minutes	Tinnitus
Peder S. Olofsson[66]	2.5	10	200 and 250 μs	60 seconds	Reduction of tumor necrosis in endotoxemia, test in mice and rats

An ESP32 microcontroller, a NEXTION 3224T024 touchscreen, a power supply, and sensors for heart rate, skin conductivity, and electromyography are added to the board assembly. The complete device is illustrated in Figure 5. The objective of integrating a new ESP32 microcontroller device is to read and process the signal from each of the sensors. Furthermore, with the ESP32, it was also possible to establish communication via UART between the NEXTION screen and the NXP-MKL05Z32VLC microcontroller. From the screen, it is possible to adjust the frequency, pulse width, and stimulation time.

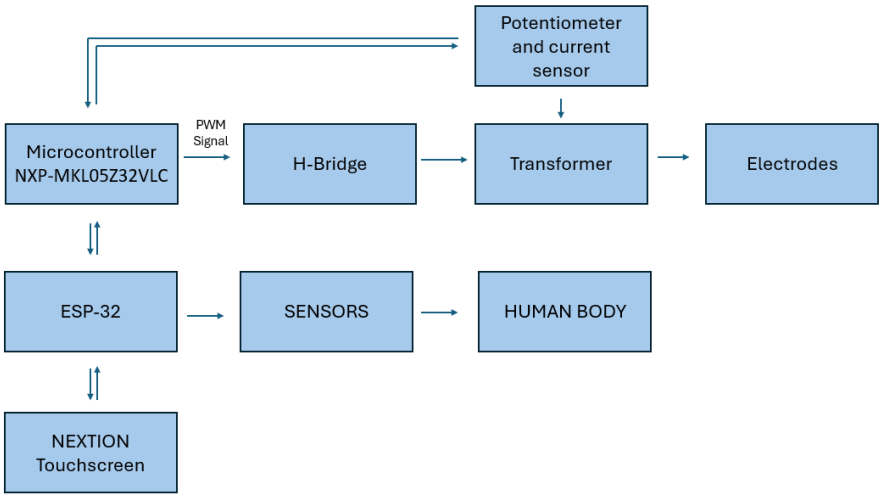


Figure 4. Electrical circuit diagram.

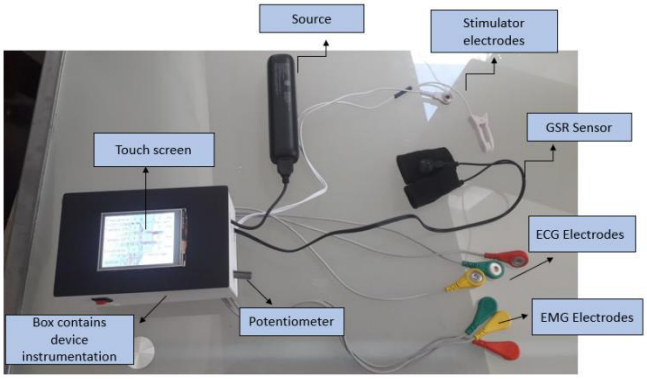


Figure 5. Device for stimulation of the auricular branch of the vagus nerve.

c) Recording physiological variables in real time.

Due to the influence of the vagus nerve on heart rate [5], the need to include a record of this physiological variable was considered during this work. To this end, the AD8232 sensor was used, which allows measurement of the heart's electrical activity. This is done by locating three electrodes on the person's body. The electrodes can be positioned according to any of the configurations associated with Einthoven's triangle. However, test measurements were performed with electrodes placed on the upper extremities of the thorax and lateral abdomen[62].

Furthermore, electrical stimulation of the vagus nerve has a certain relationship with the neuromodulation of cognitive processes related to noradrenergic activity, and the acoustic

startle response constitutes an interesting biomarker. This variable can be recorded by electromyographic recording of the orbicularis oculi muscle [67]. To obtain this signal, it was necessary to use a sensor to record electrical muscle activity and place three electrodes in the orbicularis oculi region.

Another variable of interest associated with electrical stimulation of the vagus nerve is cutaneous conductance [67–69]. To measure this variable, a sensor that detects the galvanic response of the skin was chosen. As for the appropriate location for detection, a pair of electrodes were placed on two fingers of the same hand.

Once the physiological variables were defined, as well as the instrumentation necessary to make the recordings, it was necessary to build a graphical interface that would allow the data obtained using the sensors to be received and graphed through the ESP32. The process of presenting dynamic signals in a graphical interface begins with the acquisition of analog signals through the sensors, then a digital and analog low pass filtering of each of the signals is performed independently [62].

4.2 Arrhythmia correction device

The proposal is based on anatomical, physiological, physical, and electronic foundations. This interdisciplinary approach focuses on the use of electrical and magnetic stimulation to stabilize heart rate in people experiencing arrhythmia episodes. The device presented here embodies this proposal. Each component of the device is described in detail below.

Arrhythmia Detector

This section of the work focuses on the interaction of light with biological tissues, specifically with blood. The intensity of the light reflected or absorbed by the blood depends on volume changes in the capillaries responsible for their transport. These volume changes occur due to variations in blood pressure generated by heartbeats. This principle is directly related to a technique that involves positioning a light-emitting source to target peripheral blood vessels and placing a photodetector in front of the tissue to detect changes in the intensity of the light

reflected by the blood. This measurement technique is known as photoplethysmography, and the arrhythmia detector is based on this method [70].

The arrhythmia detector uses the MAX30102 sensor, see Figure 6, which not only performs photoplethysmography but also includes the electronics necessary for signal amplification, filtering, and a 16-bit ADC. In addition, the sensor has an internal temperature sensor to compensate for the effects of temperature on the measurement. The sensor is placed on the earlobe, which offers two advantages: good blood perfusion and the ability to keep the sensor in a fixed position, minimizing motion artifacts that could interfere with the measurement. During testing, movement of the sensor or the measurement area could induce errors.

Figure 6. MAX30102 sensor attached to an adjustable headband that allows the sensor to remain in position.

The obtained photoplethysmography signal is characterized by points representing systole, the phase of the cardiac cycle in which the heart contracts and pushes blood through the circulatory system. An algorithm detects systolic peaks and the time between consecutive peaks, allowing the heart rate to be calculated. The ESP32 microcontroller is used to control the sensor and execute the algorithm. If the heart rate exceeds or falls below a stable range, an alert is triggered, and communication is established with the automatic discerner described in the next section.

Electric Stimulator

Currently, vagus nerve stimulation has become a common practice with positive results in the treatment of various conditions. Its significant impact on parasympathetic activity has been shown to influence autonomic parameters, such as heart rate variability. As a result of stimulation, heart rate may decrease, which is believed to be related to the activation of parasympathetic nerve fibers affecting the sinoatrial and atrioventricular ganglia. This stimulator works based on these physiological principles [70]. The effects of stimulation on heart rate have been observed under specific stimulation parameters. It is known that the frequency should be around 20 Hz and the pulse width approximately 500 µS. The developed instrumentation allows electrical stimulation to be delivered within these parameters, see Figure 7.

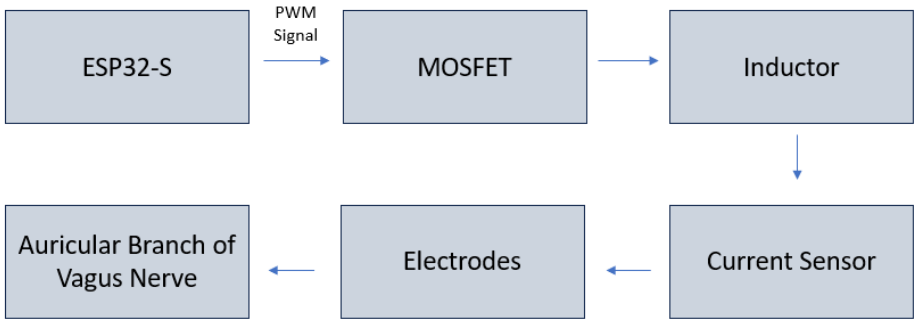


Figure 7. Flowchart illustrates the general structure of the electrical stimulator.

The device incorporates several electronic components that condition the signal and generate stimulation. The most relevant components are described below, in Figure 8. The ESP32-S microcontroller generates a PWM signal with a fixed frequency of 20 Hz, which is transmitted to an inductor through a MOSFET that acts as a switch to control the current flow. The inductor stores and releases energy based on the PWM duty cycle, allowing for stable voltage and current output [70].

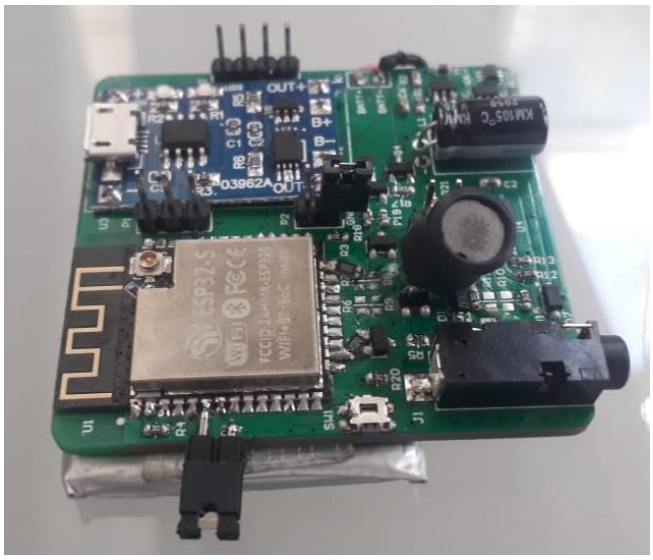


Figure 8. Electronic card containing the electrical stimulator.

To generate a pulse signal at the circuit output that aligns with the stimulation characteristics reported in the literature, a couple of simulations were performed in Simulink, see Figure 9, to guide the circuit design, the arrangement of components, and the conditioning of magnitude values for each circuit element.

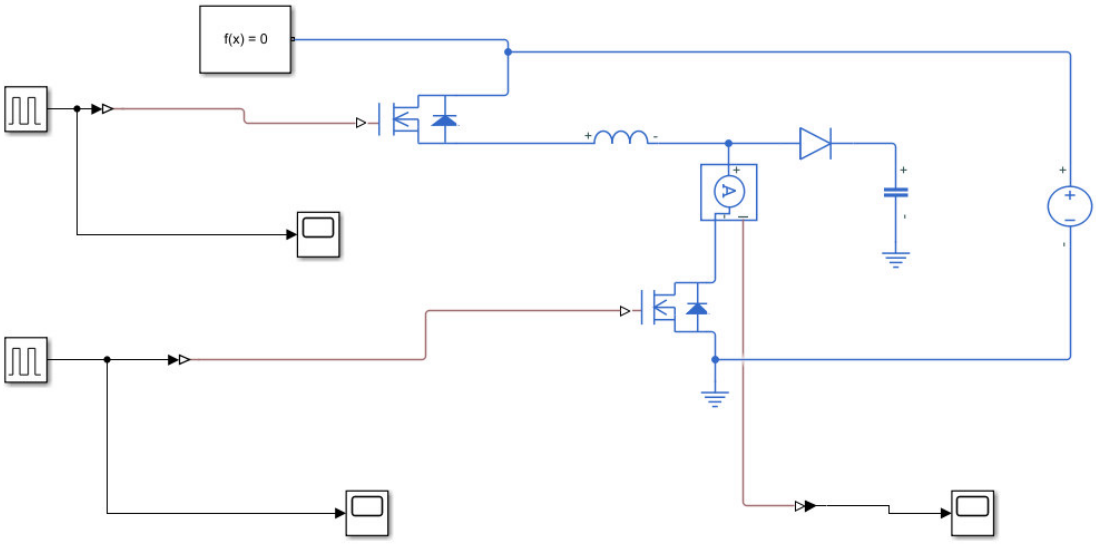


Figure 9. Simulaciones de circuitos en Simulink.

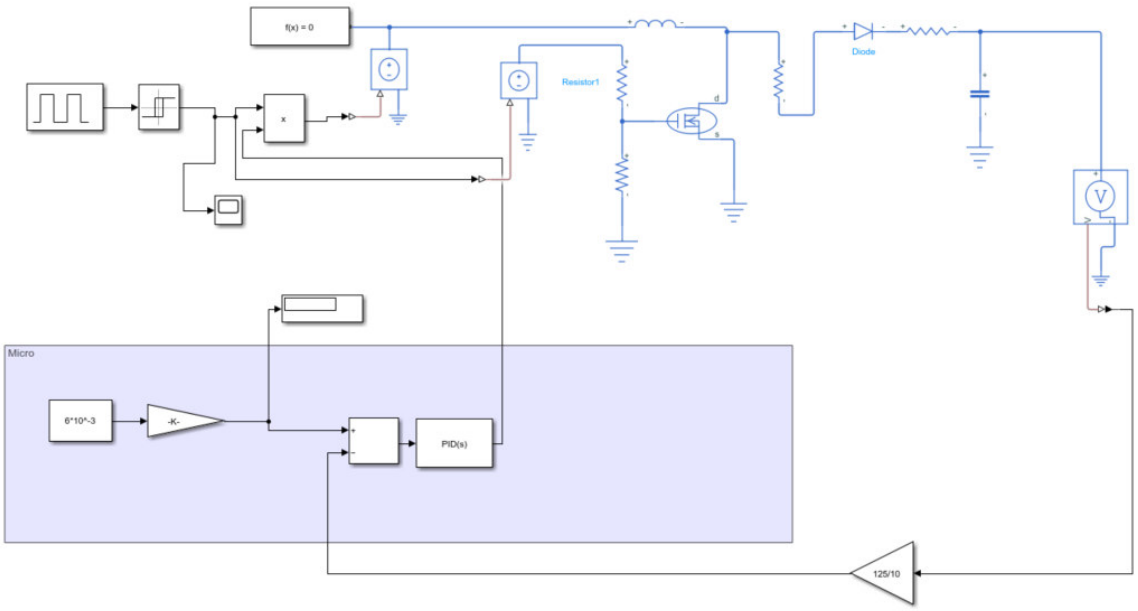


Figure 9a. Simulaciones de circuitos en Simulink.

The selection of the body part for stimulation was carefully considered in the design of the stimulator, see Figure 10. After an anatomical review, it was found that the vagus nerve has a branch that reaches the auricular area, innervating parts of the ear such as the inner surface of the tragus, the concha, and the external auditory meatus. Previous studies have performed vagal stimulation in these areas with favorable results.

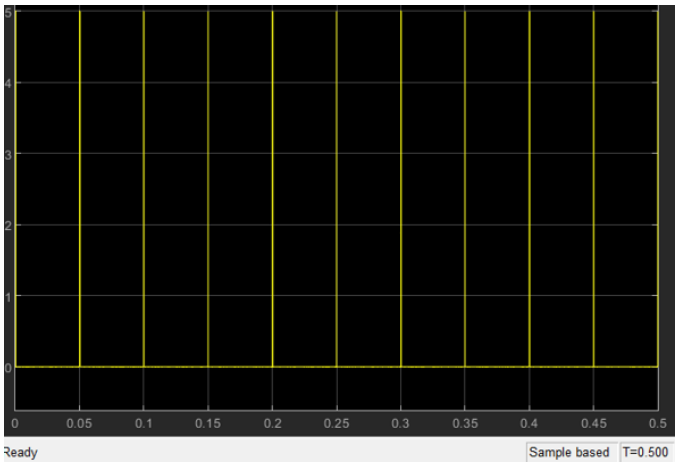


Figure 10. Signal generated theoretically from the simulation, (voltage versus time).

To establish a connection with the areas innervated by the vagus nerve in the auricular region, a pair of electrodes was designed, see Figure 11. These electrodes feature a clip that attaches to the concha of the ear and a cone that is inserted into the ear canal, ensuring constant contact

with the inner walls of the tragus and the ear canal. The cone-shaped electrode is coated with conductive silver paint on its surface to ensure efficient electrical charge transfer.

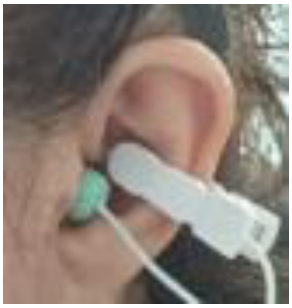


Figure 11.The probe is illustrated with the pair of electrodes and their location in the auricular area.

Magnetic Stimulator

It is possible to influence the sympathetic system using magnetic stimulation to increase heart rate. Tests in both humans and animals have shown that this type of stimulation can increase heart rate. In magnetic stimulation studies, short pulses of 100–300 mS are typically used, although the exact duration can vary depending on the experimental protocol. To induce a physiological response, the magnetic field must be strong enough to activate sympathetic nerve fibers. With this device, the stimulation is intended to be applied progressively until the desired effects on heart rate are achieved. Furthermore, precise placement of stimulation in the ganglia is essential to influence cardiac activity [70].

The ESP32-S3, see Figure 12 is programmed to generate a PWM signal with the values necessary to activate sympathetic nerve fibers 100–300 µS. An H-bridge and a coil are then connected to the ESP32-S3. The H-bridge allows the direction of the current passing through the coil to be changed. By controlling the PWM signal applied to the H-bridge, the strength of the magnetic field can be adjusted, since an increase in the duty cycle results in a larger average current flowing through the coil, which in turn generates a stronger magnetic field.

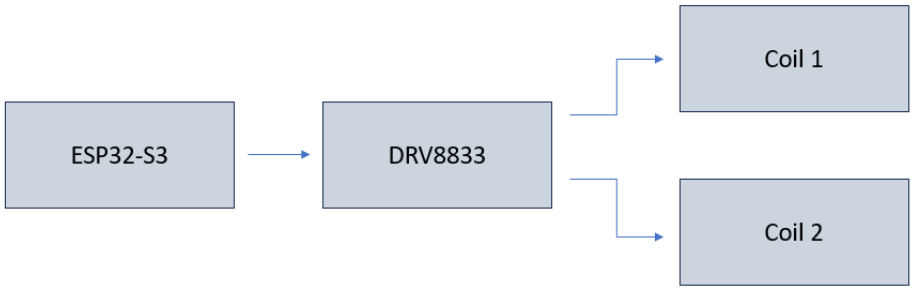


Figure 12. Flowchart illustrates the general structure of the magnetic stimulator.

In this configuration, two 12.3 mH air-core coils were used, coupled to a DVR8833 driver containing two H-bridges, see figure 13. The components are mounted on an electronics board held by an adjustable base around the neck, with leather and foam terminals acting as the field applicator.

Figure 13. Magnetic field applicator.

Automatic Discerner

This is part of the code loaded into Microcontroller 1 of the arrhythmia detector, which is responsible for activating the electrical stimulator or adjusting the stimulation intensity based on data from the arrhythmia detector. This section of code also communicates with the magnetic stimulator, allowing the arrhythmia detector to interact with this second stimulator and activate stimulation as needed.

4.3 Electrical stimulator for the vagus and trigeminal nerves

Previously developed devices for vagus nerve stimulation are a fundamental pillar for the construction of this third device. However, the stimulation parameters vary, as does the instrumentation that complements the device. For this implementation, two stimulators are required, one acting on the trigeminal nerve and the other directed toward the vagus nerve. Each of these stimulators is described below:

Electrical stimulator for the vagus nerve, aimed at patients diagnosed with migraine

Based on the positive results obtained, stimulation is performed at 1 Hz, 2 mA, and (0.2-0.3) mS with instrumentation similar to that used in the arrhythmia correction device.

Electrical stimulator for the trigeminal nerve: It has a structure similar to that of the vagus nerve, but some changes are made to the inductor and a PID is built to ensure that the current is always the same. This is also characterized by its soft start.

A current sensor was used to ensure that the same current was always delivered. Because human impedance varies, the incorporation of this sensor was necessary and key to the PID.

Figure 14. Electrodes for vagus and trigeminal nerve stimulation.

Description of the buzz wire

The buzz wire game involves guiding a small-diameter conductive ring along an irregular path defined by a conductive wire connected to a voltage source. The objective of the game is to avoid contact between the wire and the ring, which is connected to the opposite terminal of the source. If contact occurs, a buzzer connected in series is activated. The game aims to stimulate brain areas associated with concentration, motor activity, and visual and auditory processing. Adjustments have been made to the game, including changes to its dimensions, route regularity, and stability, to increase its difficulty and ensure replicability. Figure 15 illustrates the assembly.

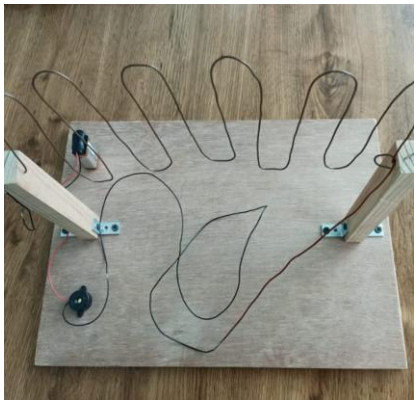


Figure 15. The buzz wire game.

Figure 16 illustrates the dimensions used in constructing the assembly. The curves follow ellipsoidal trajectories and, analogous to the model of a transverse wave, the setup consists of six valleys and five crests. The power supply provides 9 V, the conducting wire has a diameter of 1.25 mm, and the buzzer operates at a frequency of 3,600 Hz with a sound intensity of 75 dB. The ring has a diameter of 0.8 cm, and the wire length from the buzzer to the handle's base is 70 cm, facilitating maneuverability.

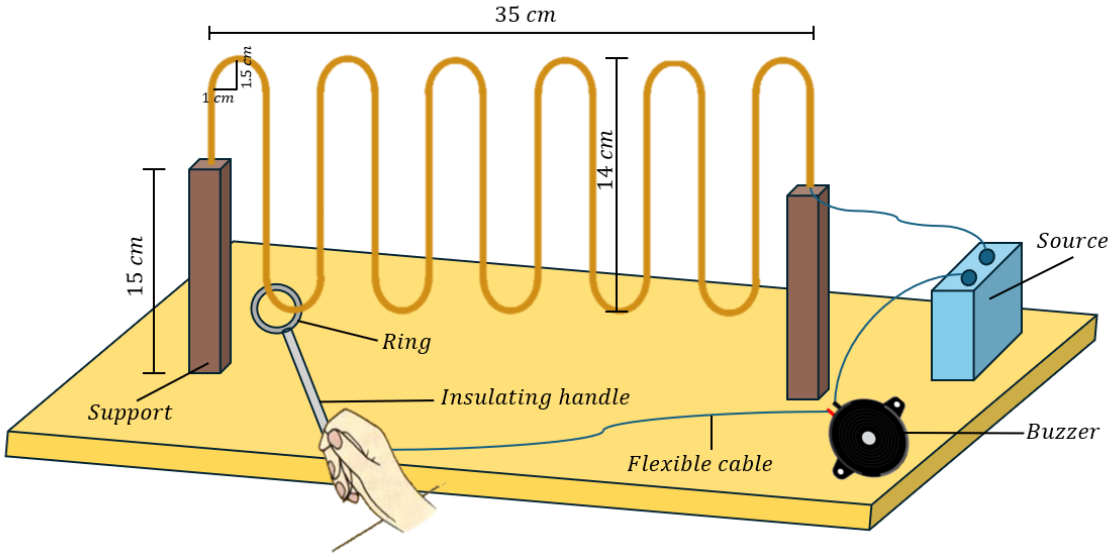


Figure 16. Dimensions of the game.

4.4 Device Implementation

Based on the findings to date, three stimulation devices and three measurement systems were developed:

i) A device for electrical stimulation of the vagus nerve, with adjustable parameters, integrated into a physiological variable monitoring system. This device was tested on four healthy volunteers. Details of this study—aimed at validating the efficacy and safety of controlled vagus nerve stimulation—are presented in the Results chapter.

ii) A device designed for both magnetic and electrical stimulation to control arrhythmias, integrated with an arrhythmia detection system. This device has not yet been tested on patients due to associated risks. However, the Results and Analysis chapter describes the planned steps for future validation.

iii) A device for electrical stimulation of the vagus and trigeminal nerves, intended for patients diagnosed with migraine. A separate system is available for recording electroencephalographic (EEG) signals during a concentration task, although it is not directly connected to the stimulation device. This device has been tested in patients, and the methodology and protocol are described below.

Methodological Design for Implementation of Electrical Stimulation of the Vagus and Trigeminal Nerves in Migraine Patients

This section of the methodology demonstrates the procedure used to obtain data for analyzing potential changes in brain activity, as well as the effectiveness of noninvasive and simultaneous electrical stimulation of the vagus and trigeminal nerves in migraine patients. This approach is based on questionnaires using a VAS scale and analysis of EEG signals obtained from the left prefrontal lobe during concentration activities.

Inclusion Criteria:

- Adult patients aged 18 to 50 years with a history of migraine meet the diagnostic criteria listed in ICHD-III, excluding complicated migraine cases such as hemiplegic migraine, migraine with brainstem aura, ophthalmoplegic migraine, migraine infarction, and basilar

migraine. Patients with pain are also excluded from the trial; in the frontal, retro- or periorbital regions, on one or both sides.

- Migraine must have occurred in the individual for a period of 12 months or more.

Exclusion Criteria:

- Complicated cases of migraine such as hemiplegic migraine, migraine with brainstem aura, ophthalmoplegic migraine, migraine infarction, or basilar migraine. Cases of pain in the frontal, retro-, or periorbital regions, on one or both sides, are also excluded from the trial.
- Pregnancy, breastfeeding, or planned pregnancy.
- Treatment with neurotoxins, for example, botulinum toxin in the head, in the previous 4 months.
- Supraorbital or auricular nerve block in the previous 4 months.
- Diagnosis of other primary or secondary headache disorders, excluding medication overuse headache.
- Headache located solely in the temporal or occipital region.
- Intolerance to supraorbital or auricular neurostimulation.
- Previous cerebrovascular events or neurosurgical interventions.
- Having experienced brain or facial trauma within the previous 3 months.
- Skin lesions or inflammation at the electrode site.
- Drug abuse or alcoholism (2 alcohol equivalents).
- Implantation of metallic or electrical devices in the head, not including dental implants.
- Use of a cardiac pacemaker or implanted or portable defibrillator.
- Diagnosis of epilepsy, personality disorder, somatoform disorder, or other severe neurological or psychiatric disorder.
- Intracranial lesions or severe headaches.
- In women, it is important that the attacks are not related to the menstrual cycle.

Procedure:

Eleven patients diagnosed with migraine who met the inclusion criteria were included. One of them also had a diagnosis of gastritis and colitis.

The eleven patients received stimulation three times a week for one month in 30-minute sessions, completing a total of 12 sessions. At the beginning, before the first application, and

at the end of the 12th session of treatment, a concentration challenge using The Buzz Wire game was performed, and EEG potential signals were recorded for 3 minutes.

A clinical history was taken regarding the patient's current migraine health status, using the pain scale illustrated in Figure 17 as a reference. Patients were also asked about the frequency of attacks experienced during the previous month.

The objective of these questions was to identify the initial pain intensity experienced during a migraine attack before undergoing the stimulation experience. Similar questions were asked at the end of treatment, and the same questions were followed up with one and two months after the completion of treatment.

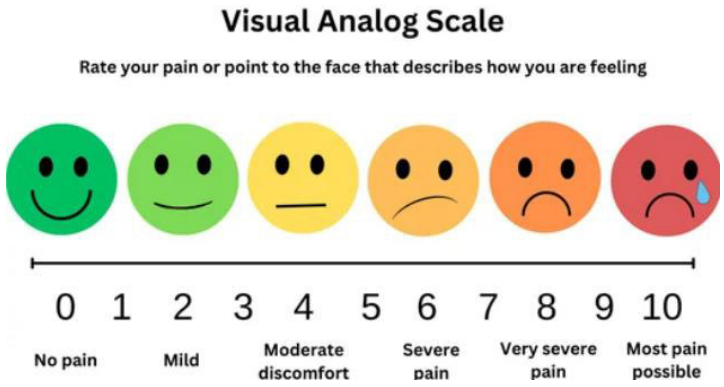


Figure 17. Visual pain scale (https://www.etsy.com/es/listing/1699498673/).

Electrical Stimulation:

a) Patients receive stimulation in a quiet and comfortable location, free from noise and extreme electromagnetic pollution.

b) Electrical stimulation is performed using two devices connected to the patient via two pairs of electrodes: one pair is located on the forehead and the other pair is placed on the ear. The devices are lightweight and comfortable to wear. Table 2 illustrates the parameters used during stimulation.

Table 2. These data are based on references from previous work on electrical stimulation of the vagus and trigeminal nerves.

Stimulation Parameters				
Nerves	**Frequency**	**Current**	**Pulse Width**	**Place of stimulation**
Trigeminal	60 Hz	[4] mA	[0.2 – 0.3] mS	Front in supraorbital and supratrochlear nerves.
Vagus	1 Hz	[2] mA	[0.2 – 0.3] mS	Cymba, tragus and internal auditory canal.

Performing simultaneous stimulation of both the vagus and trigeminal nerves offers the potential to optimize treatment, as they are two sources of stimulation, and in terms of the amount of net charge transferred, the values used in treatments designed for 3 or even 6 months can be achieved. Furthermore, it is important to highlight that 12 sessions over a period of one month is the minimum period reported in the literature with favorable results.

c) At the end of the electrical stimulation, the electrodes and the device are removed.

Figure 18. Device for stimulation.

The device consists of two parts, each contained in a box. The first part establishes a connection with the vagus nerve through a pair of electrodes connected to the cymba and internal auditory canal. The second part connects to the trigeminal nerve through two electrodes attached to an adjustable swing that allows contact to be established with the supraorbital nerve, which is innervated by the trigeminal nerve.

Concentration test and EEG potential recording

This test is performed twice (baseline and final): at the beginning before receiving electrical stimulation and at the end after the entire treatment has been completed.

Once the measuring instrument is placed, the patient is asked to practice with the pulse test, while simultaneously recording EEG signals associated with concentration stimuli.

EEG recording is performed using a single channel using the Neurosky Mindwave sensor, which is attached to a comfortable and lightweight headband that simultaneously allows contact between an electrode and the left prefrontal lobe. Two reference nodes are also maintained with gentle pressure clamps located in the auricular area.

Figure 19. Headband for recording EEG potentials.

During the measurement, two recordings of 2 minutes each are made.

The procedure is as follows:

- First recording: In this measurement, the person being measured is not performing any relaxation exercises or concentrating on anything in particular.
- Second recording: The person in charge of the measurement explains the pulse game instructions to the patient, and then, while the patient uses the game, the signal is recorded.

5. RESULTS

5.1 Results of vagus nerve stimulation in healthy people

Trial 1: This trial is carried out without electrical stimulation. It consists of placing the detectors on the person's body and then proceeding to monitor the physiological variables. Figure 20, illustrates the corresponding signals with the three variables recorded in a basal state and in response to stimuli.

Trial 2*:* Electrical stimulation is performed on four healthy male volunteers aged 24, 26, 29, and 30, respectively.

The parameters were as follows:

- ✓ Frequency (Hz): [21, 22, 23, and 24]
- ✓ Current: Values less than 1mA, without reaching the pain threshold
- ✓ Pulse width: 100 ms

Procedure**:** Detectors are placed to record physiological variables in addition to the electrodes used for stimulation. The test completion time is 28 minutes, as illustrated in Table 3.

Table 3. Sequence of applied stimulation, from 21 Hz to 24 Hz

Time (min)	Frequency (Hz)
1	No stimulation
6	21
1	No stimulation
6	22
1	No stimulation
6	23
1	No stimulation
6	24

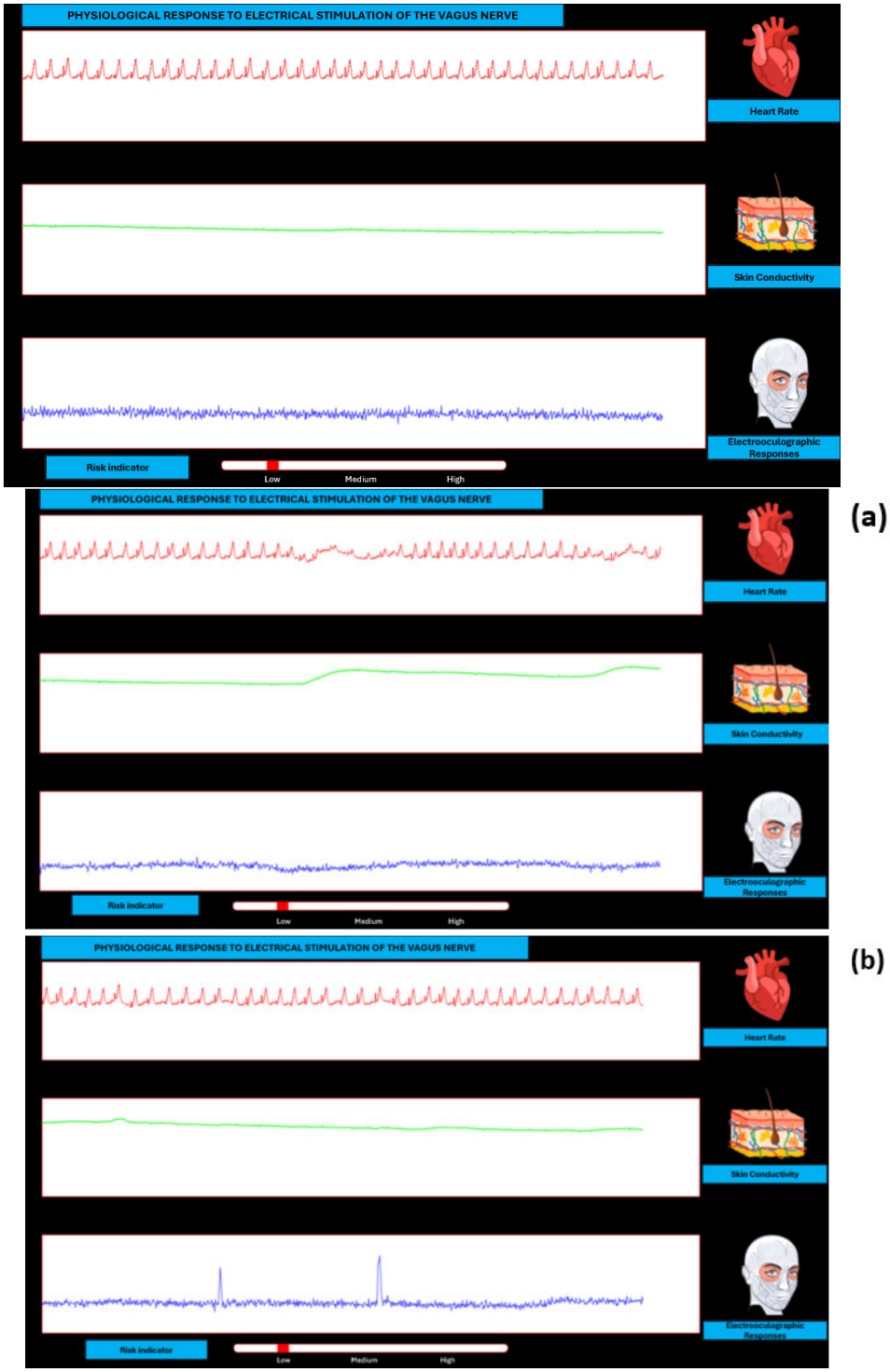
The idea of this trial was to identify the response in the records of physiological variables based on frequency variations. To evaluate the changes, a break was made between frequency changes so that the stimulation for each frequency started from a basal state. The stimulation was initiated gradually, ensuring that volunteers remained unaware of the onset of changes. Volunteers described their perception as a subtle, occasionally fleeting tingling sensation. Each participant was informed of the 28-minute duration of stimulation but remained unaware of the specific moments and variations. The intensity was systematically increased from low to high, facilitating adaptation to incremental changes in frequency.

Figure 20 shows the graphical interface of the device through which it is possible to view the monitoring of physiological variables: heart rate, skin conductivity and electromyography of the orbicularis oculi muscle.

During stimulation at different frequencies, the following results were obtained:

Heart Rate: Throughout the stimulation process, the heart rate was observed to exhibit minimal variation, remaining constant within the predefined ranges as described below:

Figure 20. Physiological variable signals in basal state.



In (a), The recording is made as a result of a couple of deep inhalations, and in (b), the signal is shown as a result of two strong voluntary blinks.

Volunteer 1: [78-83], Volunteer 2: [83-86], Volunteer 3: [63-67], Volunteer 4: [63-75]. This could be an indication that the system is safe, as it does not drastically alter heart rate.

Skin Conductance: Figure 21 illustrates how conductance values decrease as frequency increases during stimulation, showing an upward trend. This result is consistent with the general finding that vagus nerve stimulation can cause a temporary decrease in skin conductance due to activation of the parasympathetic nervous system, which can induce a relaxation response in the body. However, it is important to note that the GSR response is variable, and not all individuals showed the same response pattern.

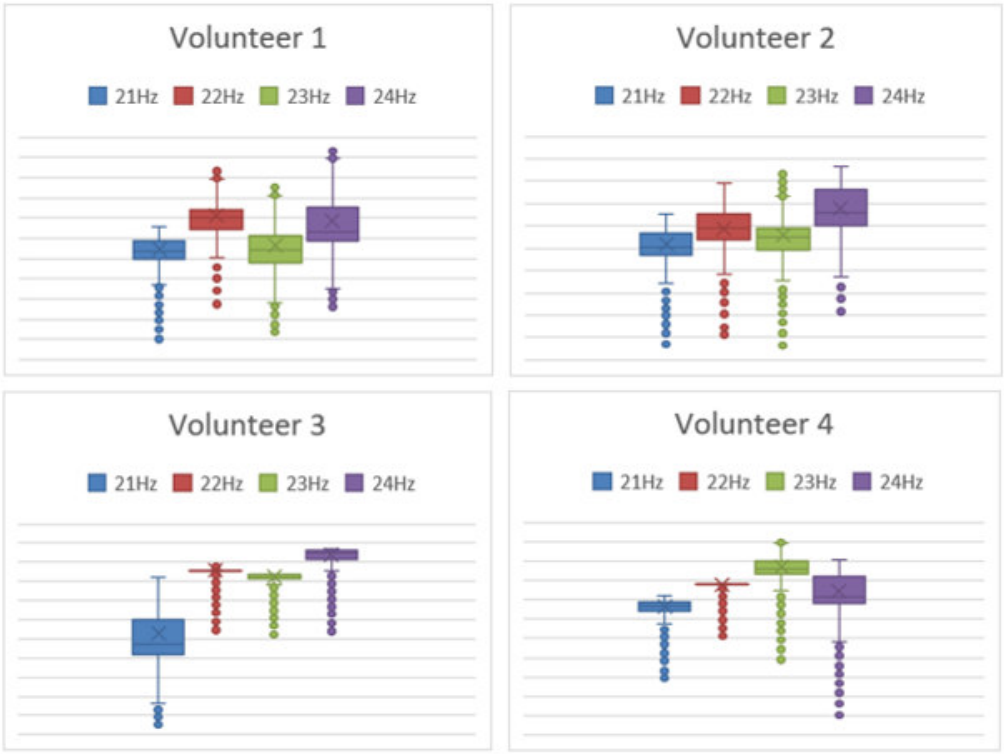


Figure 21. The distribution of values is inverse with the conductance.

Electrical activity of the orbicularis oculi muscle**:** Table 4 shows that increases in frequency are related to decreases in voltage, indicating a decrease in muscle electrical activity. This decrease is associated with the action of the vagus nerve, which is part of the autonomic nervous system and regulates involuntary functions such as muscle contraction.

5.2 Results of the implementation carried out in patients diagnosed with migraine

Data processing and results obtained in the implementation of patients diagnosed with migraine:

Initially, the EEG signal illustrated in Figure 22 is obtained from the frontal lobe and is a noisy signal.

Table 4. Voltage expressed in mV as a function of frequency

Frequency (Hz)	Volunteer 1	Volunteer 2	Volunteer 3	Volunteer 4
21	442.0	443.0	456.3	442.9
22	441.9	441.6	442.2	441.8
23	441.7	441.5	443.1	442.6
24	441.9	441.4	442.5	442.5

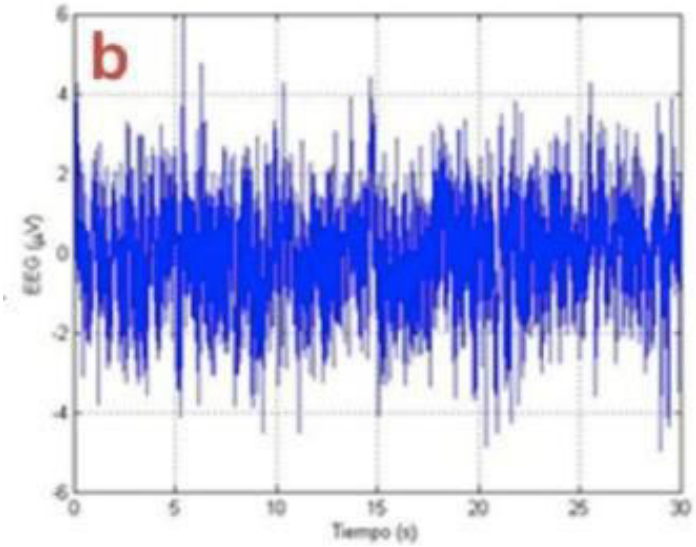


Figure 22. The EEG signal.

The signal is made up of signals from different areas of the brain that oscillate at different frequencies. After applying the Fourier transform, it is possible to decompose the signal into its frequency components. This allows the data to be classified by bands, as illustrated in Table 5.

After data extraction, a signal distribution diagram is constructed by frequency, showing the percentage of signal distribution for each band. Figure 23 illustrates, as an example, what this distribution looks like for one of the patients in a baseline state, which is associated with a resting state in which individuals are not receiving major stimuli.

Table 5. Signal decomposition into bands.

delta	high_alpha	high_beta	low_alpha	low_beta	low_gamma	mid_gamma	theta
26839	16160	3601	18277	15302	9198	2121	15862
707638	3129	9888	8194	15648	4119	2040	32263
156297	15702	10828	11914	16049	9946	1704	95411
814463	24660	5488	16752858	15447	3967	3518	127641
150658	1302	3661	8992	3555	1309	787	12867
17966	4972	11205	16748634	5790	11476	2527	16758980
25095	21500	7244	10793	12846	12469	3663	16745421
1683845	29121	20063	27069	16763447	9910	6136	656578
262634	6337	3245	6735	2205	2774	836	20135
1637633	14348	12437	16752445	14227	4388	2650	144306

Table 5 shows a representative sample of the data collected during the measurements. It should be noted that the total amount of data recorded for each band was considerably higher, as the sensor operates at a sampling rate of 512 Hz.

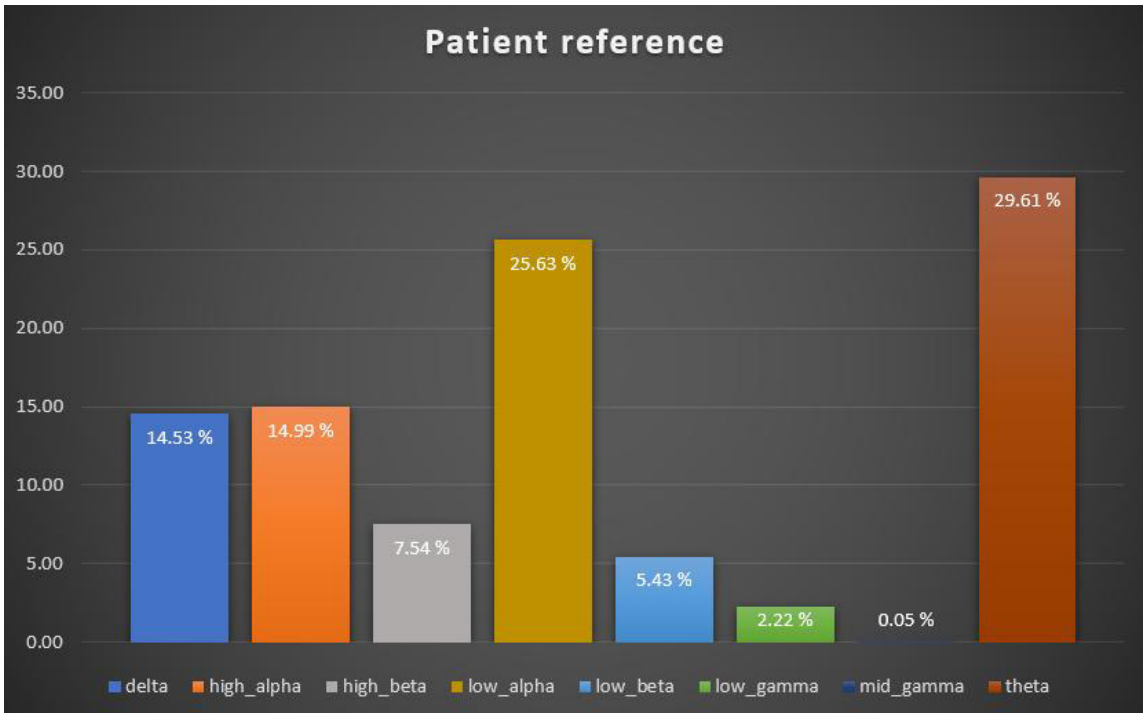


Figure 23. Patient reference.

Distribution of the EEG signal by signal percentage,
where 100 % of the signal is observed distributed among the different frequency bands.

For each subject, there were two types of data: the first were baseline data without experience with the pulse game and recorded brain activity in a baseline state. The second showed ongoing brain activity superimposed on that induced through practice with the pulse game. The measurements taken are illustrated in Table 6.

Table 6. Measurements made on healthy people and patients before and after receiving electrical stimulation.

Measurement	Healthy person	Pearson diagnosed with migraine	Using the pulse game
Baseline or reference state without the use of pulse set and without electrical stimulation. (initial records)	X	X	
Baseline state + buzz wire game induced activity without electrical stimulation. (final records)	X	X	X
Baseline or reference state without use of the pulse set and after electrical stimulation treatment. (initial records)		X	
Baseline state + buzz wire game induced activity following electrical stimulation treatment. (final records)		X	X

For each of the measurements illustrated in Table 4, a band decomposition was performed by applying the Fourier transform as shown in Table 3. After separating the signal into frequency bands, a percentage distribution calculation is made as illustrated in Figure 24. The magnitude of each percentage depends on the amplitude of the signal for each frequency and represents the preponderance of each oscillation over the total EEG signal obtained. Figure 25 shows the behavior for one of the bands in relation to the participants.

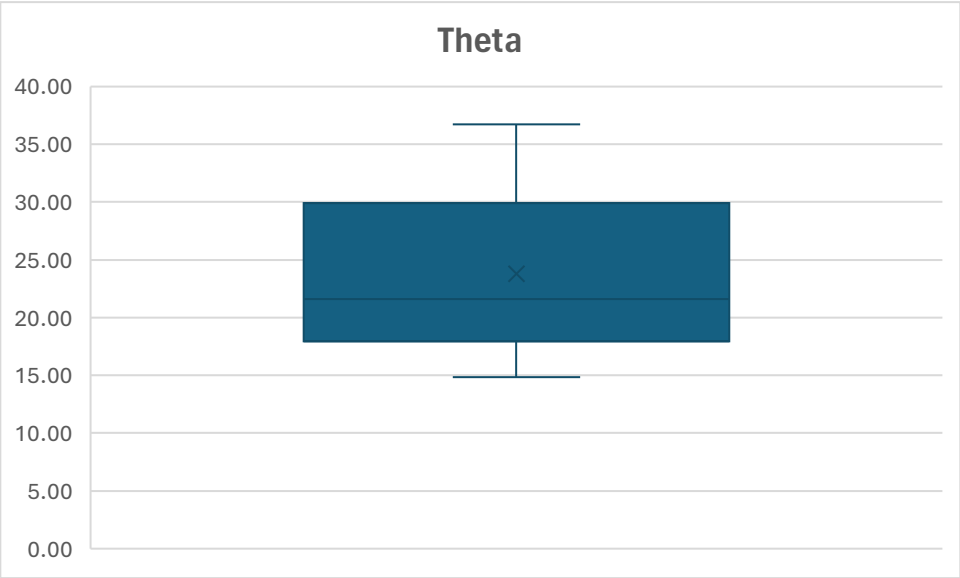


Figure 24. It shows the percentage distribution of the signal for the theta band in patients before receiving electrical stimulation and in a basal state without using the pulse set.

For each frequency band, patients are compared with healthy subjects from the perspective that generates the two possible states of brain activity: the baseline state and that induced by the pulse pattern. An example of these comparisons is illustrated in Figure 25.

Figure 26 allows us to compare the difference between reference states and induced EEG activity for healthy and patients for the theta band.

Table 7 presents the results obtained from the comparison between healthy subjects and patients diagnosed with migraine without electrical stimulation. It can be observed that for some bands, the activity in people with migraine tends to remain the same, decrease or increase with respect to healthy people. The variations recorded in Table 5 are statistically supported by Student t tests that allowed comparing means between healthy subjects and patients for each of the bands. The value representing the level of variation is obtained from the difference: $0.05 - P(T \leq t)$.

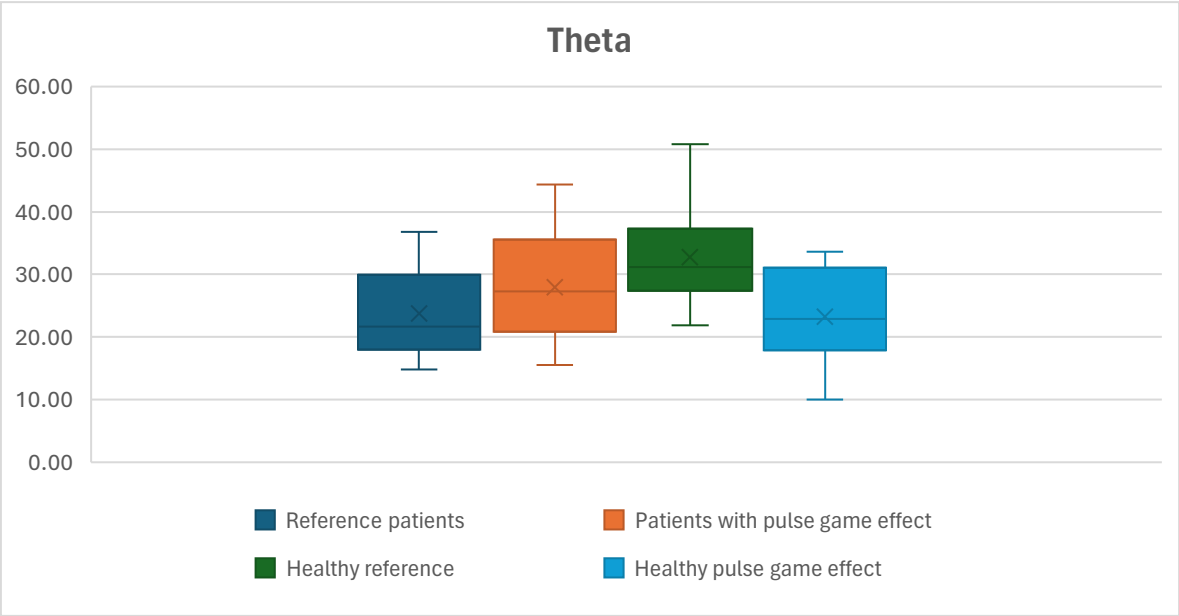


Figure 25. Comparison of results for the theta band.

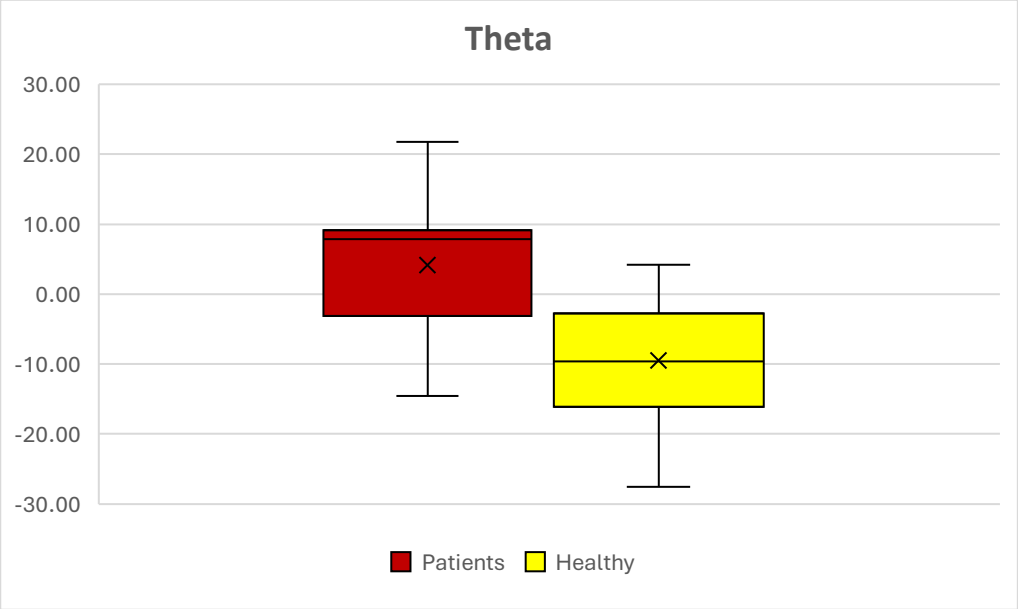


Figure 26. Patients vs Healthy.

There is an increase in theta oscillations, while in healthy individuals the activity for this band tends to decrease.

Table 8 presents the results obtained from the comparison between healthy subjects and patients diagnosed with migraine after the application of electrical stimulation treatment. It can be observed that for the low alpha, low beta and high beta bands, there are no statistically

significant changes compared to those observed before the patients received electrical stimulation treatment.

Table 7. Statistically significant changes for the bands $\delta, \theta, \alpha, \beta, \Upsilon$.

Band	Outcome in patients compared to people without a migraine diagnosis	Level of variation
Delta (0.1-3)Hz	INCREASE	0.04924292 ******
Theta (4-7)Hz	INCREASE	0.04900521 *****
Low Alpha (8-9)Hz	DECREASES	0.00454146 *
High Alpha (10-12)Hz	EQUIVALENT	-0.03033059
Low Beta (13-17)Hz	DECREASES	0.03546246 **
High Beta (18-30)Hz	DECREASES	0.03910792 ***
Low Gamma (31-40)Hz	DECREASES	0.04708995 ****
Mid Gamma (40-60)Hz	EQUIVALENT	-0.22329867

Table 8. Effects of stimulation.

Band	Healthy patients without electrical stimulation *vs.* patients with electrical stimulation treatment	Level of variation
Delta (0.1-3)Hz	Increase	0.040632505
Theta (4-7)Hz	Increase	0.044860091
Low Alpha (8-9)Hz	Equivalent	-0.56141002
High Alpha (10-12)Hz	Equivalent	-0.185218689
Low Beta (13-17)Hz	Equivalent	-0.20771627
High Beta (18-30)Hz	Equivalent	-0.161028
Low Gamma (31-40)Hz	Decreases	0.040378109
Mid Gamma (40-60)Hz	Equivalent	-0.063471152

Each of the patients who participated in the treatment was given a two-question test at different times: before the treatment, after the treatment, and one and two months after receiving the electrical stimulation treatment. Figures 27 and 28 illustrate the responses provided by the patients.

The boxplot in figure 27 illustrates the distribution of migraine attack frequency among 11 patients across four time points. A marked reduction in both the median number of attacks and the variability is evident immediately after treatment. At 1 and 2 months, the median remains low, indicating sustained therapeutic benefit. One outlier appears at 2 months, suggesting variability in long-term individual responses.

The figure 28 illustrates the distribution of pain intensity reported by 11 patients before treatment, immediately after treatment, and at one and two months of follow-up. A clear reduction in median pain intensity is observed after the intervention, with most patients reporting lower pain levels that remained relatively stable during the follow-up period. Despite some variability among patients, the overall trend indicates a sustained decrease in perceived pain following treatment.

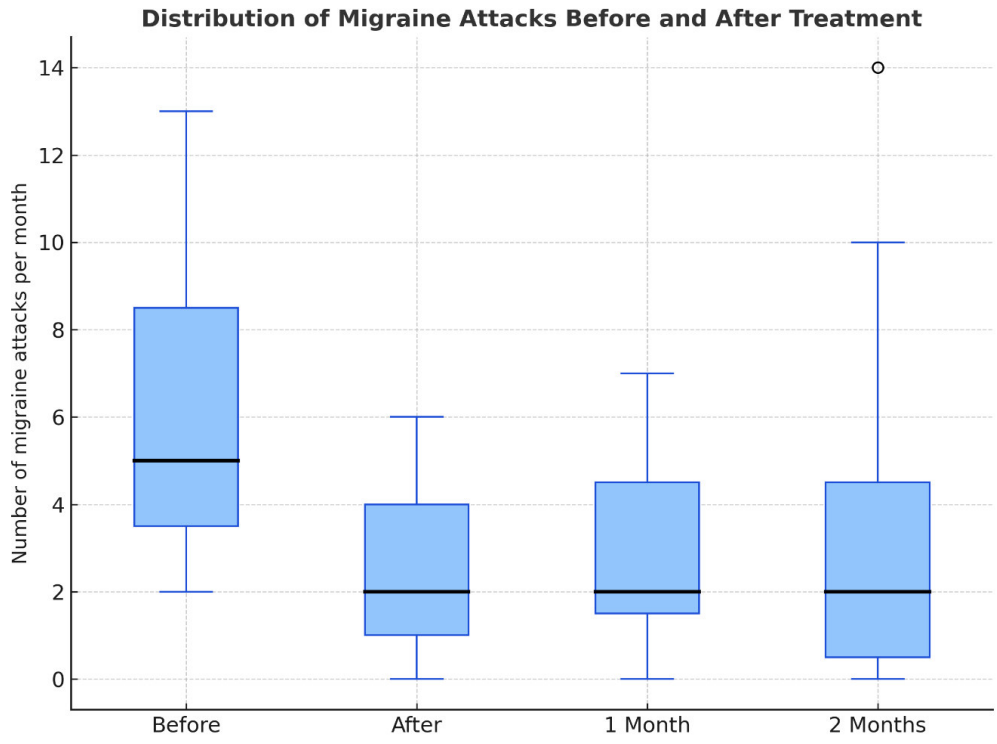


Figure 27. Answers to the question: How many migraine attacks have you had this month?

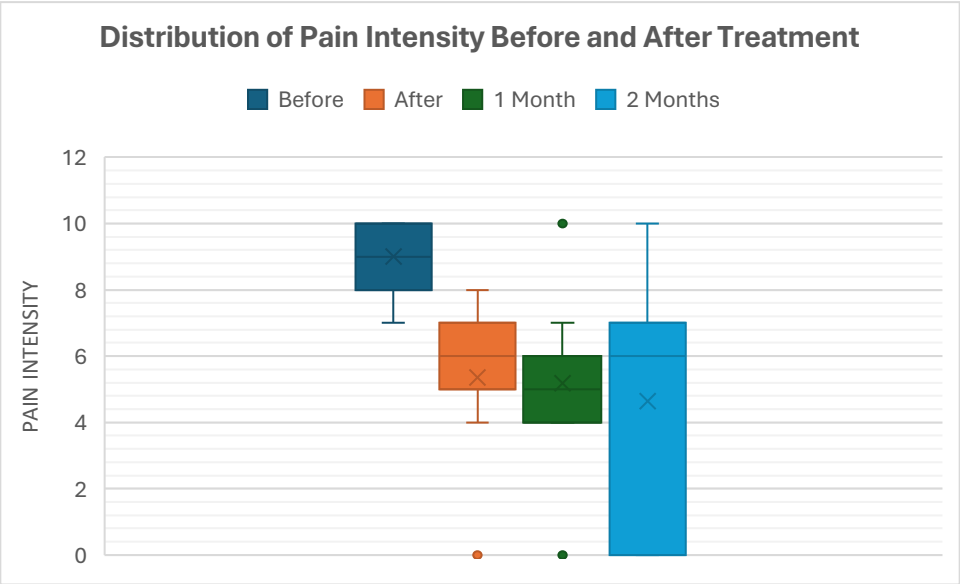


Figure 28. Responses to a question using an analog scale about the intensity of pain experienced during crises experienced this month.

6. Results and Discussion

6.1 Arrhythmia detector analysis

Given the difficulty and risk associated with this type of treatment, trials in controlled in vitro or animal settings, followed by human testing, remain the subject of ongoing research and debate. Initially, interventions are planned in pigs and/or canines due to their anatomical similarities with humans. For example, when comparing nervous structures, both species have an auricular branch of the vagus nerve. Similarly, vagus nerve stimulation in pigs can induce a decrease in heart rate. Furthermore, the cervical sympathetic ganglia in both humans and canines share similarities, and, as in humans, stimulation of these ganglia can significantly increase heart rate.

The objective of this work was to inform the scientific community about the development of a device designed to help restore heart rhythm in individuals experiencing an arrhythmia episode. The use of two stimulators, combined with the ability to automate stimulation using an arrhythmia detector, supports a novel approach with anatomical and physiological foundations that have not been implemented in other devices to date. It is anticipated that the

described methodology will establish the device as an effective tool for managing arrhythmia episodes.

6.2 Analysis of electrical stimulation results in people diagnosed with migraine

The treatment applied to patients diagnosed with migraine proved generally effective: 9 out of 11 patients experienced a reduction in either the frequency or intensity of attacks. To assess the effects of the stimulation on brain activity, electroencephalographic (EEG) recordings were analyzed.

Delta:

During the tests performed, the increase in intensity in the delta band in patients diagnosed with migraine was evident, delta waves are the result of an interaction between cortical and subcortical networks, mainly in the cerebral cortex and thalamus[71]. In previous studies performed on migraine patients, it was found for example that during attacks with disturbed consciousness and hemiplegic migraine, people presented abnormal activity of the delta waves. These results may offer valuable information about the underlying mechanisms of these specific types of migraine [72].

In another investigation [73] it was found that the increase in delta power in the frontocentral region is significant and a correlation was found between delta power and migraine severity, which highlights the importance of understanding how alterations in brain activity can influence the experience of pain. The frontocentral area is associated with pain perception, from the correlation presented with migraine severity it is possible to suggest that delta activity may be a marker of pain intensity in these patients, and may even have implications for the treatment and management of migraine [73]. In another work carried out previously [74], it was found that during migraine attacks the EEG pattern presents an increase for the delta band. This may be related to neuronal excitability and dysfunction in brain networks. These findings are important to understand the underlying mechanisms of migraine and could also have implications in the treatment and management of the disease [74]. In an electroencephalographic study focusing on bioelectrical abnormalities observed in migraine patients it was also found that there was an increase in delta activity during attacks [75], the findings of the study indicate that a significant percentage of migraine patients have abnormalities in their EEG recordings. This suggests that migraine may be associated with

changes in brain activity that are detectable through electroencephalography. Identifying these abnormalities is crucial to better understand the pathophysiology of migraine and its relationship to other neurological disorders [75].

On the other hand in [76] the observed relationship between delta activity and headache severity suggests that changes in brain activity may reflect migraine intensity. This could have implications for treatment, as clinicians could use delta activity as an indicator of migraine severity and adjust treatment accordingly. This relationship also highlights the importance of a personalized approach in migraine management [76]. Finally, in a study that investigated broadband EEG findings in migraine patients, analyzing their correlation with clinical variables. It was observed that EEG may be a useful biomarker to understand migraine pathology, highlighting the importance of sub delta and delta focal slow waves [77].

Theta:

During the tests performed, the increase in intensity in the theta band in patients diagnosed with migraine was evident, these waves are generated mainly in the hippocampus [78], medial prefrontal cortex [79] and in other areas that are part of the limbic system [80]. The intrinsic oscillatory properties of hippocampal neurons are fundamental for the generation of theta oscillations. These properties allow neurons to synchronize and generate rhythmic activity patterns. Understanding these properties is essential to unravel the mechanisms underlying brain activity.

Alterations in theta oscillations have been linked to several neurological disorders, which is why the implications of research on theta oscillations are significant for the understanding of neurological disorders. As research progresses, it is expected that new therapeutic strategies based on the modulation of theta oscillations will be identified [78].

A similar behavior to that obtained with the pulse game for the theta band was found in [75] where it was found that there was an increase in theta activity during attacks. Increased activity in the theta band during migraine attacks indicates a change in neuronal excitability. These changes may reflect the complexity of the mechanisms underlying migraine and how the brain responds to painful stimuli [75].

In another work, theta activity observed in migraine patients and its relationship with the absence of visual disturbances suggests that this type of brain activity could be associated with specific characteristics of migraine. This highlights the need to further investigate how theta activity relates to migraine symptoms and whether it can be used as a marker to predict the onset of certain symptoms, such as visual disturbances [76].

Low Alpha:

During the tests performed, the intensity of the low Alpha band decreased in patients diagnosed with migraine. These waves are generated mainly in the occipital and parietal cortex, although they are also observed in other cortical areas, such as the frontal lobe. In the absence of other studies that allow validating the conclusions in [81], a correlation was found between the increase in alpha power and the intensity of pulsating pain. The synchrony observed between alpha power oscillations and pulsating rhythm indicates that there is a dynamic relationship between brain activity and the experience of pain. The idea that pulsating pain has a neurophysiological representation is a significant advance in the understanding of pain [81].

In [82] the differences in visual perception between migraine and control groups are explored, focusing on alpha band oscillations in a resting state. Differences in alpha band activity between migraine and control groups are examined there and the implications of these findings for understanding hypersensitivity to visual stimuli in migraine patients are discussed. The results indicating that the migraine group showed greater power in the low alpha band are significant, as they suggest that brain oscillations may be altered in these patients. This greater power may be related to a longer temporal integration of visual information, which could contribute to hypersensitivity to visual stimuli [82].

High y Low Beta

During the tests carried out, an increase in the intensity in the beta band was observed for both high and low frequencies. When consulting with other experiences carried out in which the behavior of the beta band is evaluated, it was found that in [83] the relationship between the patent foramen ovale (PFO) and brain activity in patients with migraine is explored,

analyzing how the PFO can alter cortical excitability and functional connectivity, which could influence the severity of migraine episodes. The work emphasizes the complexity of understanding the relationship between the PFO and migraine and highlights the need for more research. However, interesting results are obtained for the beta band because greater activity was presented in people with PFO who also a diagnosis of migraine have compared to those people who do not have these two diagnoses together. Finally, in this work carried out, it was found that the power spectral density for the beta band correlates with the severity of the migraine [83].

In another work consulted [84], cyclic fluctuations in sensory processing in migraine patients were examined, using beta event-related desynchronization (beta-ERD) measurements through electroencephalography (EEG). Differences in cortical activity during the preictal, ictal, and interictal phases were analyzed, revealing an increase in cortical excitability before migraine attacks [84].

The increase in beta-ERD in the preictal phase suggests that the brain of migraine patients becomes more reactive to sensory stimuli before an attack. This finding is significant because it indicates that there are changes in cortical excitability that may predispose patients to experience headache [84].

7. CONCLUSIONS

The results of these studies demonstrate the promising potential of non-invasive neurostimulation techniques, specifically, electrical stimulation of the vagus and trigeminal nerves, as well as magnetic stimulation of the cervical sympathetic ganglia, for therapeutic and research applications. Non-invasive vagus nerve stimulation (nVNS) has been consistently shown to be safe and well-tolerated, with encouraging outcomes across a range of clinical conditions. The present research supports its utility in both therapeutic and experimental contexts, highlighting the importance of responsible parameter adjustment and the use of conductive gel to ensure effective stimulation. Researchers and clinicians are advised to consult the relevant literature when defining stimulation protocols and to suspend stimulation if unexpected physiological responses occur.

Additionally, a novel device for the management of cardiac arrhythmias has been introduced, integrating dual-site stimulation and automated triggering based on arrhythmia detection.

This approach offers a new physiological and anatomical strategy for restoring heart rhythm, with potential clinical applications not yet explored in existing literature.

Finally, the combined electrical stimulation of the vagus and trigeminal nerves has shown favorable preliminary results in the treatment of migraine. Simultaneous charge delivery to both sites may reduce the number of treatment sessions required. Optimal outcomes are associated with patient-tailored stimulation based on individual impedance and pain thresholds. This underscores the need for future development of automated, adaptive stimulation systems to personalize and enhance therapeutic efficacy.

Together, these studies contribute to the growing evidence base supporting bioelectronic medicine and emphasize the importance of individualized, parameter-sensitive approaches in neuromodulation therapies.

The work conducted with migraine patients was where the most progress was made. The most relevant conclusions are presented below. It is important to note that these generalizations are preliminary so far due to the small number of patients treated.

Clinical effectiveness:

The electrical stimulation treatment produced a significant clinical improvement in most patients diagnosed with migraine, as evidenced by a reduction in both the frequency and intensity of attacks in 9 out of 11 participants. These findings suggest that the applied stimulation protocol effectively modulates neural activity involved in migraine generation and maintenance.

EEG markers of cortical modulation:

The analysis of EEG recordings revealed characteristic changes in brain oscillatory activity after treatment. In particular, alterations in delta, theta, alpha, and beta bands indicate a modulation of cortical and subcortical circuits, possibly reflecting reduced cortical hyperexcitability—a hallmark of migraine pathophysiology.

Delta and theta activity as indicators of migraine severity:

The observed increase in delta and theta power before or during migraine episodes aligns with previous evidence linking these bands to pain perception, cortical–thalamic dysregulation, and neuronal excitability. The correlation between delta power and pain intensity supports the hypothesis that slow-wave activity may serve as a neurophysiological marker of migraine severity.

Alpha desynchronization and sensory hypersensitivity:

The decrease in low-alpha activity after treatment may be related to improved cortical inhibition and reduced hypersensitivity to sensory stimuli. Since alpha oscillations are known to regulate thalamocortical excitability, their reduction could reflect a normalization of neural dynamics associated with visual and somatosensory processing.

Beta-band modulation and cortical excitability:

The increase in beta activity observed after treatment may represent compensatory mechanisms linked to enhanced sensorimotor integration and cortical regulation. Given that preictal beta desynchronization has been associated with increased cortical excitability, these results could indicate a shift toward a more stable excitatory–inhibitory balance following stimulation.

Neurophysiological implications:

Overall, the combined clinical and electrophysiological evidence supports the view that electrical stimulation induces beneficial modulation of brain networks implicated in migraine. The EEG findings highlight potential biomarkers (particularly in the delta and beta ranges) that could guide future optimization of stimulation protocols and individualized therapeutic strategies.

8. REFERENCES

1. Butt MF, Albusoda A, Farmer AD, Aziz Q (2020) The anatomical basis for transcutaneous auricular vagus nerve stimulation. J Anat 236:588–611. https://doi.org/10.1111/joa.13122
2. Yap JYY, Keatch C, Lambert E, et al (2020) Critical Review of Transcutaneous Vagus Nerve Stimulation: Challenges for Translation to Clinical Practice. Front. Neurosci. 14
3. Malik V, Shivkumar K (2024) Stellate ganglion blockade for the management of ventricular arrhythmia storm. Eur Heart J 45:834–836. https://doi.org/10.1093/eurheartj/ehae083
4. Killu AM, Yang M, Naksuk N, et al (2023) Stellate ganglia stimulation counteracts vagal stimulation by significantly increasing heart rate and blood pressure. J Interv

Card Electrophysiol. https://doi.org/10.1007/s10840-023-01516-w

5. Ardesch JJ, Buschman HPJ, van der Burgh PH, et al (2007) Cardiac responses of vagus nerve stimulation: Intraoperative bradycardia and subsequent chronic stimulation. Clin Neurol Neurosurg 109:849–852. https://doi.org/10.1016/j.clineuro.2007.07.024
6. Straube A, Ellrich J, Eren O, et al (2015) Treatment of chronic migraine with transcutaneous stimulation of the auricular branch of the vagal nerve (auricular t-VNS): a randomized, monocentric clinical trial. J Headache Pain 16:. https://doi.org/10.1186/s10194-015-0543-3
7. Zhang Y, Huang Y, Li H, et al (2021) Transcutaneous auricular vagus nerve stimulation (taVNS) for migraine: An fMRI study. Reg Anesth Pain Med 46:145–150. https://doi.org/10.1136/rapm-2020-102088
8. Díaz HM, Cid FM, Otárola J, et al (2019) EEG Beta band frequency domain evaluation for assessing stress and anxiety in resting, eyes closed, basal conditions. Procedia Comput Sci 162:974–981. https://doi.org/10.1016/j.procs.2019.12.075
9. Başar-Eroglu C, Strüber D, Schürmann M, et al (1996) Gamma-band responses in the brain: A short review of psychophysiological correlates and functional significance. Int J Psychophysiol 24:101–112. https://doi.org/10.1016/S0167-8760(96)00051-7
10. Guan A, Wang S, Huang A, et al (2022) The role of gamma oscillations in central nervous system diseases: Mechanism and treatment. Front Cell Neurosci 16:1–15. https://doi.org/10.3389/fncel.2022.962957
11. Chen PL, Chen YC, Tu PH, et al (2022) Subthalamic high-beta oscillation informs the outcome of deep brain stimulation in patients with Parkinson's disease. Front Hum Neurosci 16:. https://doi.org/10.3389/fnhum.2022.958521
12. Amer-Cuenca JJ, Goicoechea C, Lisón JF (2010) Which physiological response triggers the application of the transcutaneous electrical nerve stimulation technique? Rev la Soc Esp del Dolor 17:333–342. https://doi.org/10.1016/j.resed.2010.09.001
13. Sluka KA, Walsh D (2003) Transcutaneous electrical nerve stimulation: Basic science mechanisms and clinical effectiveness. J Pain 4:109–121. https://doi.org/10.1054/jpai.2003.434

14. Lizarde A, Guerrero M (2007) Medición de impedancia eléctrica de la piel en el rango de frecuencia de 5 a 1,000 Hz. Rev Mex Ing Biomédica 28:
15. Wang Y (2023) Therapeutics of Neural Stimulation for Neurological Disorders
16. Yuan H, Silberstein SD (2016) Vagus Nerve and Vagus Nerve Stimulation, a Comprehensive Review: Part i. Headache 56:71–78. https://doi.org/10.1111/head.12647
17. Schulz-Stübner S, Kehl F (2011) Treatment of persistent hiccups with transcutaneous phrenic and vagal nerve stimulation. Intensive Care Med 37:1048–1049. https://doi.org/10.1007/s00134-011-2150-3
18. Aihua L, Lu S, Liping L, et al (2014) A controlled trial of transcutaneous vagus nerve stimulation for the treatment of pharmacoresistant epilepsy. Epilepsy Behav 39:105–110. https://doi.org/10.1016/j.yebeh.2014.08.005
19. González HFJ, Yengo-Kahn A, Englot DJ (2019) Vagus Nerve Stimulation for the Treatment of Epilepsy. Neurosurg Clin N Am 30:219–230. https://doi.org/10.1016/j.nec.2018.12.005
20. Liu A, Rong P, Gong L, et al (2018) Efficacy and safety of treatment with transcutaneous vagus nerve stimulation in 17 patients with refractory epilepsy evaluated by electroencephalogram, seizure frequency, and quality of life. Med Sci Monit 24:8439–8448. https://doi.org/10.12659/MSM.910689
21. Stefan H, Kreiselmeyer G, Kerling F, et al (2012) Transcutaneous vagus nerve stimulation (t-VNS) in pharmacoresistant epilepsies: A proof of concept trial. Epilepsia 53:115–118. https://doi.org/10.1111/j.1528-1167.2012.03492.x
22. Straube A, Ellrich J, Eren O, et al (2015) Treatment of chronic migraine with transcutaneous stimulation of the auricular branch of the vagal nerve (auricular t-VNS): a randomized, monocentric clinical trial. J Headache Pain 16:. https://doi.org/10.1186/s10194-015-0543-3
23. Austelle CW, O'Leary GH, Thompson S, et al (2022) A Comprehensive Review of Vagus Nerve Stimulation for Depression. Neuromodulation 25:309–315. https://doi.org/10.1111/ner.13528
24. Fang J, Egorova N, Rong P, et al (2017) Early cortical biomarkers of longitudinal transcutaneous vagus nerve stimulation treatment success in depression. NeuroImage

Clin 14:105–111. https://doi.org/10.1016/j.nicl.2016.12.016

25. Sigurdsson HP, Raw R, Hunter H, et al (2021) Noninvasive vagus nerve stimulation in Parkinson's disease: current status and future prospects. Expert Rev Med Devices 18:971–984. https://doi.org/10.1080/17434440.2021.1969913
26. Hasan A, Wolff-Menzler C, Pfeiffer S, et al (2015) Transcutaneous noninvasive vagus nerve stimulation (tVNS) in the treatment of schizophrenia: a bicentric randomized controlled pilot study. Eur Arch Psychiatry Clin Neurosci 265:589–600. https://doi.org/10.1007/s00406-015-0618-9
27. Vargas-Caballero M, Warming H, Walker R, et al (2022) Vagus Nerve Stimulation as a Potential Therapy in Early Alzheimer's Disease: A Review. Front Hum Neurosci 16:1–9. https://doi.org/10.3389/fnhum.2022.866434
28. Liu C, Jiang H, Yu L, Po SS (2020) Vagal stimulation and arrhythmias. J Atr Fibrillation 13:89–97. https://doi.org/10.4022/JAFIB.2398
29. De Ferrari GM (2014) Vagal stimulation in heart failure. J Cardiovasc Transl Res 7:310–320. https://doi.org/10.1007/s12265-014-9540-1
30. Olshansky B (2016) Vagus nerve modulation of inflammation: Cardiovascular implications. Trends Cardiovasc Med 26:1–11. https://doi.org/10.1016/j.tcm.2015.03.016
31. Chen M, Li X, Yang H, et al (2020) Hype or hope: Vagus nerve stimulation against acute myocardial ischemia-reperfusion injury. Trends Cardiovasc Med 30:481–488. https://doi.org/10.1016/j.tcm.2019.10.011
32. Veldman F, Hawinkels K, Keszthelyi D (2025) Efficacy of vagus nerve stimulation in gastrointestinal disorders: a systematic review. Gastroenterol Rep 13:1–13. https://doi.org/10.1093/gastro/goaf009
33. Daly THLJWDT (2022) Neuroanatomy, Cranial Nerve 5. National Library of Medicine
34. Netter FH (2014) ATLAS OF HUMAN ANATOMY, 6th editio. Elsevier
35. Akesson Stewart W-P (1997) Autonomic Nerves. BC Decker
36. Snell RS (1980) Clinical Neuro Anatomy
37. Jensen R, Stovner LJ (2008) Epidemiology and comorbidity of headache. Lancet Neurol 7:354–361. https://doi.org/10.1016/S1474-4422(08)70062-0

38. Qubty W, Patniyot I (2020) Migraine Pathophysiology. Pediatr Neurol 107:1–6. https://doi.org/10.1016/j.pediatrneurol.2019.12.014
39. Olesen J (2018) Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia 38:1–211. https://doi.org/10.1177/0333102417738202
40. Akerman S, Goadsby PJ (2014) Migraine, Pathophysiology of. Encycl Neurol Sci 67–71. https://doi.org/10.1016/B978-0-12-385157-4.01087-3
41. Dodick DW (2018) A Phase-by-Phase Review of Migraine Pathophysiology. Headache 58:4–16. https://doi.org/10.1111/head.13300
42. Giffin NJ, Ruggiero L, Lipton RB, et al (2003) Premonitory symptoms in migraine: An electronic diary study. Neurology 60:935–940. https://doi.org/10.1212/01.WNL.0000052998.58526.A9
43. Bose P, Karsan N, Goadsby PJ (2018) The Migraine Postdrome. Contin Lifelong Learn Neurol 24:1023–1031. https://doi.org/10.1212/CON.0000000000000626
44. R. Belvís SS (2020) Migraña, 20 preguntas que siempre quisiste hacer a tu neurólogo. AEMICE, SEN
45. Muñoz-Vendrell A, Campoy S, Caronna E, et al (2023) Effectiveness and safety of anti-CGRP monoclonal antibodies in patients over 65 years: a real-life multicentre analysis of 162 patients. J Headache Pain 24:1–9. https://doi.org/10.1186/s10194-023-01585-2
46. Moreno-Ajona D, Hoffmann J, Akerman S (2022) Devices for Episodic Migraine: Past, Present, and Future. Curr Pain Headache Rep 26:259–265. https://doi.org/10.1007/s11916-022-01024-y
47. Blech B, Starling AJ (2020) Noninvasive Neuromodulation in Migraine. Curr Pain Headache Rep 24:1–7. https://doi.org/10.1007/s11916-020-00914-3
48. Younis S, Hougaard A, Noseda R, Ashina M (2019) Current understanding of thalamic structure and function in migraine. Cephalalgia 39:1675–1682. https://doi.org/10.1177/0333102418791595
49. Zhang Y, Liu J, Li H, et al (2019) Transcutaneous auricular vagus nerve stimulation at 1 Hz modulates locus coeruleus activity and resting state functional connectivity in patients with migraine: An fMRI study. NeuroImage Clin 24:1–8.

https://doi.org/10.1016/j.nicl.2019.101971

50. Lauritsen CG, Silberstein SD (2019) Rationale for electrical parameter determination in external trigeminal nerve stimulation (eTNS) for migraine: A narrative review. Cephalalgia 39:750–760. https://doi.org/10.1177/0333102418796781
51. Magis D, D'Ostilio K, Thibaut A, et al (2017) Cerebral metabolism before and after external trigeminal nerve stimulation in episodic migraine. Cephalalgia 37:881–891. https://doi.org/10.1177/0333102416656118
52. Gamboa BI, Sotelo ME, Fajreldines HMD, Beltramone DA (2016) Prototipo experimental de electroestimulación trigeminal. Una aproximación inicial al tratamiento de la migraña crónica. 1–6. https://doi.org/10.1109/argencon.2016.7585331
53. Schoenen J, Coppola G (2018) Efficacy and mode of action of external trigeminal neurostimulation in migraine. Expert Rev Neurother 18:545–555. https://doi.org/10.1080/14737175.2018.1488588
54. Magis D, Vigano A, Sava S, et al (2013) Pearls and pitfalls: Electrophysiology for primary headaches. Cephalalgia 33:526–539. https://doi.org/10.1177/0333102413477739
55. Rodr E, Gabriela O, Calder O, et al (2016) Correlatos electroencefalográficos en la migraña y su impacto en la calidad de vida electroencephalographic correlates with migraine and its quiality of life impact. 1:118–134
56. Zhu B, Coppola G, Shoaran M (2019) Migraine classification using somatosensory evoked potentials. Cephalalgia 39:1143–1155. https://doi.org/10.1177/0333102419839975
57. Lisicki M, D'Ostilio K, Coppola G, et al (2018) Brain correlates of single trial visual evoked potentials in migraine: More than meets the eye. Front Neurol 9:15–17. https://doi.org/10.3389/fneur.2018.00393
58. Gawel M, Connolly JF, Rose FC (1983) Migraine Patients Exhibit Abnormalities in the Visual Evoked Potential. Headache J Head Face Pain 23:49–52. https://doi.org/10.1111/j.1526-4610.1983.hed2302049.x
59. Vecchio E, Gentile E, Franco G, et al (2018) Effects of external trigeminal nerve stimulation (eTNS) on laser evoked cortical potentials (LEP): A pilot study in

migraine patients and controls. Cephalalgia 38:1245–1256. https://doi.org/10.1177/0333102417728748

60. Vecchio E, Bassez I, Ricci K, et al (2018) Effect of non-invasive vagus nerve stimulation on resting-state electroencephalography and laser-evoked potentials in migraine patients: Mechanistic insights. Front Hum Neurosci 12:1–17. https://doi.org/10.3389/fnhum.2018.00366
61. Titlic M, Mise NI, Pintaric I, et al (2015) The event-related potential P300 in patients with migraine. Acta Inform Medica 23:339–342. https://doi.org/10.5455/aim.2015.23.339-342
62. Fernando E, Calvo R, Olivas HP, et al Monitoring physiological variables and controlled electrical stimulation on the vagus nerve
63. Schuerman WL, Nourski K V., Rhone AE, et al (2021) Human intracranial recordings reveal distinct cortical activity patterns during invasive and non-invasive vagus nerve stimulation. Sci Rep 11:1–14. https://doi.org/10.1038/s41598-021-02307-x
64. Keatch C, Lambert E, Woods W, Kameneva T (2022) Measuring brain response to transcutaneous vagus nerve stimulation (tVNS) using simultaneous magnetoencephalography (MEG). J Neural Eng 19:. https://doi.org/10.1088/1741-2552/ac620c
65. Hyvarinen P, Yrttiaho S, Lehtimaki J, et al (2015) Transcutaneous Vagus Nerve Stimulation Modulates Tinnitus-Related Beta-and Gamma-Band Activity. Ear Hear 36:e76–e85. https://doi.org/10.1097/AUD.0000000000000123
66. Olofsson PS, Levine YA, Caravaca A, et al (2015) Single-Pulse and Unidirectional Electrical Activation of the Cervical Vagus Nerve Reduces Tumor Necrosis Factor in Endotoxemia. Bioelectron Med 2:37–42. https://doi.org/10.15424/bioelectronmed.2015.00006
67. Colzato L, Beste C (2020) A literature review on the neurophysiological underpinnings and cognitive effects of transcutaneous vagus nerve stimulation: Challenges and future directions. J Neurophysiol 123:1739–1755. https://doi.org/10.1152/jn.00057.2020
68. Burger AM, Verkuil B, Fenlon H, et al (2017) Mixed evidence for the potential of

non-invasive transcutaneous vagal nerve stimulation to improve the extinction and retention of fear. Behav Res Ther 97:64–74. https://doi.org/10.1016/j.brat.2017.07.005

69. Lerman I, Davis B, Huang M, et al (2019) Noninvasive vagus nerve stimulation alters neural response and physiological autonomic tone to noxious thermal challenge. PLoS One 14:1–26. https://doi.org/10.1371/journal.pone.0201212
70. Rodríguez Calvo EF, Pérez Olivas H, Córdova Fraga T, et al (2024) Heart Rhythm Correction Device Using Non-invasive Stimulation of Vagus Nerve and Cervical Sympathetic Ganglia. Digit Med Healthc Technol 3:1–11. https://doi.org/10.5772/dmht.20240017
71. Steriade M, McCormick DA, Sejnowski TJ (1993) Thalamocortical oscillations in the sleeping and aroused brain. Science (80-) 262:679–685. https://doi.org/10.1126/science.8235588
72. Abdurrahman L, Keane M (2024) Understanding Migraine: Epidemiology, EEG Abnormalities, and the Potential of Neurofeedback Training. NeuroRegulation 11:184–190. https://doi.org/10.15540/nr.11.2.184
73. Ojha P, Panda S (2024) Resting-state Quantitative EEG Spectral Patterns in Migraine During Ictal Phase Reveal Deviant Brain Oscillations: Potential Role of Density Spectral Array. Clin EEG Neurosci 55:362–370. https://doi.org/10.1177/15500594221142951
74. Ehteshamzad S, Shkreli R (2023) Abnormalities in EEG as migraine marker: a mini review. J Biol Stud 6:220–229. https://doi.org/10.62400/jbs.v6i1.7791
75. Alberti A, Mazzotta G, Galletti F, Sarchielli P (2004) Electroencephalographic brain mapping and migraine. J Headache Pain 5:50–53. https://doi.org/10.1007/s10194-004-0107-4
76. Smyth VOG, Winter AL (1964) The EEG in migraine. Electroencephalogr Clin Neurophysiol 16:194–202. https://doi.org/10.1016/0013-4694(64)90038-0
77. Hosokawa K, Usami K, Tatsuoka Y, et al (2024) Novel and reappraised wide-band EEG findings in migraineurs: Its correlation with several clinical variables. Clin Neurophysiol 166:166–175. https://doi.org/10.1016/j.clinph.2024.07.020
78. Bazsaki G (2002) Theta oscillations in the hippocampus. Neuron 33:325–340

79. Ishii R, Shinosaki K, Ukai S, et al (1999) Medial prefrontal cortex generates frontal midline theta rhythm. Neuroreport 10:675–679. https://doi.org/10.1097/00001756-199903170-00003

80. Vertes RP, Kocsis B (1997) Brainstem-diencephalo-septohippocampal systems controlling the theta rhythm of the hippocampus. Neuroscience 81:893–926. https://doi.org/10.1016/S0306-4522(97)00239-X

81. Squire LR (2009) Does throbbing pain have a brain signature? Neuron 61:1–7. https://doi.org/10.1016/j.pain.2013.02.013.Does

82. O'Hare L, Menchinelli F, Durrant SJ (2018) Resting-State Alpha-Band Oscillations in Migraine. Perception 47:379–396. https://doi.org/10.1177/0301006618755639

83. Lei X, Wei M, Qi Y, et al (2023) The patent foramen ovale may alter migraine brain activity: A pilot study of electroencephalography spectrum and functional connectivity analysis. Front Mol Neurosci 16:1–10. https://doi.org/10.3389/fnmol.2023.1133303

84. Mykland MS, Bjørk MH, Stjern M, et al (2019) Fluctuations of sensorimotor processing in migraine : a controlled longitudinal study of beta event related desynchronization.

UNIVERSIDAD DE GUANAJUATO

Oficio: JMBO/2025-010
Asunto: Aprobación de TESIS para Presentar Examen Recepcional

León, Gto., 22 de septiembre de 2025

DR. MODESTO ANTONIO SOSA AQUINO
DIRECTOR DE LA DIVISIÓN DE CIENCIAS E INGENIERÍAS
UNIVERSIDAD DE GUANAJUATO
CAMPUS LEÓN

Por medio de la presente le manifiesto que he leído el manuscrito presentado por la Mtro. Edwin Fernando Rodríguez Calvo, titulado "ELECTRICAL AND MAGNETIC STIMULATION FOR THE TREATMENT OF PATIENTS WITH CARDIAC AND NEUROLOGICAL CONDITIONS", para sustentar su examen para obtener el título de DOCTOR EN FÍSICA. Después de revisarlo a fondo considero que cumple con los requisitos y no tengo objeción alguna en que presente su examen a la fecha y hora que le convenga a la solicitante.

Sin más por el momento quedo a sus órdenes para cualquier asunto.

ATENTAMENTE
"LA VERDAD OS HARÁ LIBRES"

Dr. José Marco Balleza Ordaz
Profesor de la División de Ciencias e Ingeniería
Universidad de Guanajuato – Campus León.

UNIVERSIDAD DE GUANAJUATO

Aceptación de Tesis
León, GTO, 12 de octubre de 2025

Dr. Modesto Antonio Sosa Aquino
Director de la División de Ciencias e Ingenierías
Universidad de Guanajuato campus León

Por este conducto comunico que el M.sc. Edwin Fernando Rodríguez Calvo, me compartió su trabajo de tesis de doctorado en Física titulada: ***Electrical and Magnetic Stimulation for the Treatment of Patients with Cardiac and Neurological Conditions***, para sustentar la defensa del proyecto.

Después de revisarlo a fondo considero que cumple con los requisitos y no tengo objeción alguna en que presente su examen a la fecha y hora que le convenga al solicitante.

Se extiende un cordial y afectuoso saludo.

A t e n t a m e n t e:
"La Verdad os hará libre"

Universidad de Guanajuato: 80 años de ser la Universidad Pública del Estado

Dr. Huetzin Aarón PÉREZ OLIVAS

UNIVERSIDAD DE GUANAJUATO

Aceptación de Tesis
León, GTO, 1 de octubre de 2025

Dr. Modesto Antonio Sosa Aquino
Director de la División de Ciencias e Ingenierías
Universidad de Guanajuato campus León

Por este conducto comunico que el M.sc. Edwin Fernando Rodríguez Calvo, me compartió su trabajo de tesis de doctorado en Física titulada: ***Electrical and Magnetic Stimulation for the Treatment of Patients with Cardiac and Neurological Conditions***, para sustentar la defensa del proyecto.

Después de revisarlo a fondo considero que cumple con los requisitos y no tengo objeción alguna en que presente su examen a la fecha y hora que le convenga al solicitante.

Se extiende un cordial y afectuoso saludo.

A t e n t a m e n t e:
"La Verdad os hará libre"

Universidad de Guanajuato: 80 años de ser la Universidad Pública del Estado

Dr. Rafael GUZMÁN CABRERA

UNIVERSIDAD DE GUANAJUATO

Oficio número: FMVL-25-09
Asunto: Aprobación Tesis, Edwin Fernando Rodríguez Calvo

León, Gto., Septiembre 01, 2025

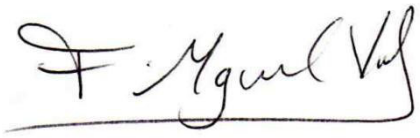
Dr. Modesto Antonio Sosa Aquino
Director
División de Ciencias e Ingenierías

Por medio de la presente me permito informar que he revisado el trabajo titulado "**Electrical and Magnetic Stimulation for the Treatment of Patients with Cardiac and Neurological Conditions**" que para obtener el grado de **Doctor en Física** presenta el Maestro **Edwin Fernando Rodríguez Calvo.**

Considero que el trabajo tiene el nivel y calidad suficiente para obtener dicho grado por lo que no tengo inconveniente en que se realicen los procedimientos necesarios para su presentación ante el comité respectivo.

Sin otro en particular me despido quedando a sus órdenes para cualquier aclaración al respecto.

ATENTAMENTE
"LA VERDAD OS HARÁ LIBRES"



Dr. Francisco Miguel Vargas Luna
Profesor Titular B

C.c.p. Edwin Rodríguez
C.c.p. Archivo FMVL

DEPARTAMENTO DE INGENIERÍA FÍSICA,
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Asunto: Revisión de Tesis
León, Gto., a 15 de septiembre del 2025

DR. MODESTO ANTONIO SOSA AQUINO
DIRECTOR
DIVISIÓN DE CIENCIAS E INGENIERIAS
CL -UNIVERSIDAD DE GUANAJUATO

A través de la presente constato que he revisado la tesis del Mtro. **Edwin Fernando Rodríguez Calvo** con el fin de obtener el grado de Doctor en Física. El trabajo de tesis se titula **"Electrical and magnetic stimulation for the treatment of patients with cardiac and neurological conditions"**. En este proyecto de investigación realizado por Edwin se realizó el desarrollo de varios prototipos para la estimulación del nervio vago para el tratamiento de personas bajo condiciones enfermedades neurológicas. Además, realizó el estudio de campo en personas sanas y con neuropatías, también cabe destacar que tramitó las patentes. El trabajo de titulación satisface con la completez y solidez de un proyecto de titulación a nivel doctorado. También Edwin ha realizado las correcciones pertinentes al documento de la tesis. Además, he cuestionado a Edwin sobre los temas relacionados a su trabajo de tesis, demostrando su dominio en los temas abordados en su trabajo de tesis. Por lo que considero que ya se puede proceder con la disertación de tesis.

Sin más por el momento le envío saludos cordiales.

Atentamente

Dr. Carlos Herman Wiechers Medina
Profesor Titular A
Departamento de Física
División de Ciencias e Ingenierías
Campus León
Universidad de Guanajuato
Tel. +52 (477) 7885100 Ext. 3867
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e-mail 1: carherwm@fisica.ugto.mx
e-mail 2: ch.wiechers@ugto.mx

Asunto: Carta Sinodal

León, GTO, 19 de septiembre de 2025

Dr. Modesto Antonio Sosa Aquino
Director De División De Ciencias E Ingenierías,
Universidad De Guanajuato Campus León

Estimado Dr. Modesto

Por este medio le notifico que he leído y dado mis comentarios **al Mtro. Edwin Fernando Rodríguez Calvo** (NUA 427453) sobre su trabajo de tesis titulado "**ELECTRICAL AND MAGNETIC STIMULATION FOR THE TREATMENT OF PATIENTS WITH CARDIAC AND NEUROLOGICAL CONDITIONS**". El Mtro. Rodríguez realizo los cambios sugeridos y tomando en cuenta cada detalle sobre su trabajo de tesis.

Por lo tanto, confirmo que el Mtro. Edwin Fernando Rodríguez Calvo puede realizar los trámites para presentar su trabajo de tesis en las fechas que se establezcan.

Sin más por el momento me despido de usted agradeciendo su atención y quedo a sus órdenes.

ATENTAMENTE

DR. ANGÉLICA HERNÁNDEZ RAYAS
Coordinadora Ecosistema VIDA UG Campus León
Sinodal

UNIVERSIDAD DE
GUANAJUATO

Aceptación de Tesis
León, GTO, 30 de octubre de 2025

Dr. Modesto Antonio Sosa Aquino
Director de la División de Ciencias e Ingenierías
Universidad de Guanajuato campus León

Por este conducto comunico que el M.sc. Edwin Fernando Rodríguez Calvo, me compartió su trabajo de tesis de doctorado en Física titulada: ***Electrical and Magnetic Stimulation for the Treatment of Patients with Cardiac and Neurological Conditions***, para sustentar la defensa del proyecto.

Después de revisarlo a fondo considero que cumple con los requisitos y no tengo objeción alguna en que presente su examen a la fecha y hora que le convenga al solicitante.

Se extiende un cordial y afectuoso saludo.

A t e n t a m e n t e:
"La Verdad os hará libre"

Universidad de Guanajuato: 80 años de ser la Universidad Pública del Estado

Dra. Blanca Olivia Murillo Ortiz
Jefa de la Unidad de Investigación en Epidemiologia Clínica
OOAD Guanajuato IMSS