

## **POSSIBILITY OF USING BIOFEEDBACK AS A THERAPEUTIC TOOL**

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**Abstract: INTRODUCTION:** The traditional treatment of anxiety, depression and migraine is carried out through medication, but additional alternative methods to traditional therapy are offered, such as biofeedback, (alternative treatment based on the human-computer interaction principle), where the individual is trained to be able to control their physiological responses according to feedback received from machines that transform physiological signals into visual or sound responses. **GOAL:** To evaluate how *biofeedback* can help with health problems as part of self-care. **MATERIAL AND METHODS:** Narrative review of literature published between 2011 and 2021 in PubMed, Virtual Health Library and Web of Science databases. **RESULTS:** Different types of *biofeedback* were analyzed, mainly cardiac variability and neurofeedback, which were applied using different methods. Despite the variety presented in the studies, the results presented were mostly positive regarding the effectiveness of *biofeedback* as a tool in the treatment of anxiety, depression and migraine. **CONCLUSION:** *Biofeedback* can be considered as an additional therapy to the treatment used in cases of anxiety, depression and migraines, and follow-up by a professional proved to be essential to obtain better results. **Keywords:** *Biofeedback*; depression; anxiety; migraine.

## INTRODUCTION

During the COVID-19 pandemic, in 2020, the mental health of the population was significantly affected. Anxiety, depression and stress caused by fear of the disease and social isolation were observed in several countries, indicating an increase of these conditions in the world population. Frontline health professionals with patients also reported high levels of stress and anxiety caused by the high workloads demanded during this period

(BÄUERLE et al. 2020; ELBAY et al. 2020; LIMCAOCO et al. 2020).

According to the Global Burden of Disease (GBD) study conducted in 2013, on the world stage, migraines are the sixth leading cause of years lived with disability (YLD) (GBD, 2013).

A study published in 2016 by the GBD that analyzed the Brazilian scenario, found that migraines are the fourth leading cause of years lived with disability since 1990, and this position was maintained in 2016 (GBD, 2016)

In view of the prevalence of these conditions, alternative treatments to the drugs offered, such as meditation and physical exercises, also began to be considered. Among these techniques, there is *biofeedback*, which allows the patient to voluntarily control their physiological reactions with the help of electronic equipment capable of converting these reactions into signals that can be captured by the senses, helping the individual to control his breathing and, consequently, his heartbeat., promoting relaxation.

The concept of *biofeedback* has been known by some cultures and countries for millennia, being applied in techniques such as pranayama, a breathing technique of Indian origin used in yoga (MOSS, 1998). The theory of cybernetics promoted by Norbert Wiener in 1948, defined by him as “the control and communication of the animal and the machine”, the term *biofeedback* became popular in 1969 after publications disseminated new concepts of feedback between systems (MOSS, 1998). The technique is based on the use of electronic instruments capable of providing information on physiological processes and, in return, the individual gains greater awareness and control over these processes, being able to self-regulate efficiently (MOSS, 1998).

*Biofeedback* is considered a therapeutic alternative or a complement to an existing drug treatment, being a way to improve the results obtained and, in some cases, even eliminate

the administration of drugs without the occurrence of significant or harmful adverse events. The increase and popularization of the use of technologies such as video games and gadgets (eg smartwatches and smartphones) in the last decade have made *biofeedback* more accessible and practical through interactive games and applications capable of detecting and reacting to physiological changes (ECONOMIDES et al. 2020).

Constant positive effects of *biofeedback* have been shown in conditions such as headache, post-prostatectomy urinary incontinence and we can mention, among others, its clinical uses in the management of anxiety or stress, asthma, attention deficit/hyperactivity disorder (ADHD), chronic pain, constipation, fecal incontinence, fibromyalgia, hypertension, irritable bowel syndrome and tinnitus (KONDO et al. 2019). The advantages presented by this technique include the fact that it is a non-invasive method, it makes the individual feel in greater control over their own health and can reduce or even eliminate the use of medication in some cases (MAYO CLINIC, 2019), very important for the practice of self-care.

Self-care is defined as a regulating human function performed by the individual himself or by another who performs it for him in order to preserve life, health, development and well-being, and when autonomy is achieved and acts in a effective, conscious, controlled and intentional, then, it is designated as a self-care activity (QUEIROS et al. 2014).

In the Brazilian scenario, the complexity of the therapeutic scheme, the cost of medications and adverse events negatively influence patient adherence to treatment, often these patients are unable to do so and end up not adhering to the prescribed treatment (OLIVEIRA et al. 2019; TAVARES et al. 2013).

Thus, alternative treatments offer possibilities for important choices in the

search for quality of life and health.

## **GOAL**

Evaluate how *biofeedback* can help with health problems such as anxiety, depression and migraine as part of self-care, and may be a possibility of a complementary therapeutic alternative.

## **MATERIAL AND METHODS**

### **RESEARCH STRATEGIES**

To carry out the proposed narrative review, searches were carried out in the US National Library of Medicine – National Institutes of Health (PubMed), Web of Science and Virtual Health Library (BVS) databases. The main descriptor used was “*biofeedback*”, combined with the descriptors “anxiety”, “depression” and “migraine” separately. For all databases, terms in English were used exclusively, as the terms in Portuguese did not return results or were a sampling of the results obtained with the search where the descriptors in English were used.

### **SELECTION CRITERIA**

In order to use up-to-date information, articles published in the last 10 years, between 2011 and 2021, that were in Portuguese or English, had the full text, in full and available for free, were selected. Articles that did not meet these criteria were disregarded.

### **DATA COLLECTION AND ANALYSIS**

Publications that met the described criteria were selected or discarded after reading the title and its abstract, in order to identify whether the approach adopted was relevant to the subject of the work. After the previously mentioned selection, the articles were read in full. Whenever possible, the “sort by relevance” option was selected.

As the articles were read, the information

deemed relevant was recorded in a spreadsheet stored on the Google Sheets® site that contained the following columns: name of the article, year, type of article, diseases addressed, type of *biofeedback*, amount of subjects, population, intervention method, evaluation method, results, intervention effectiveness and study problems.

## RESULTS

The research process and the selection of articles are illustrated in Figures 1, 2 and 3, indicating, respectively, the results obtained with the descriptors “anxiety”, “depression” and “migraine” when combined with “*biofeedback*”.

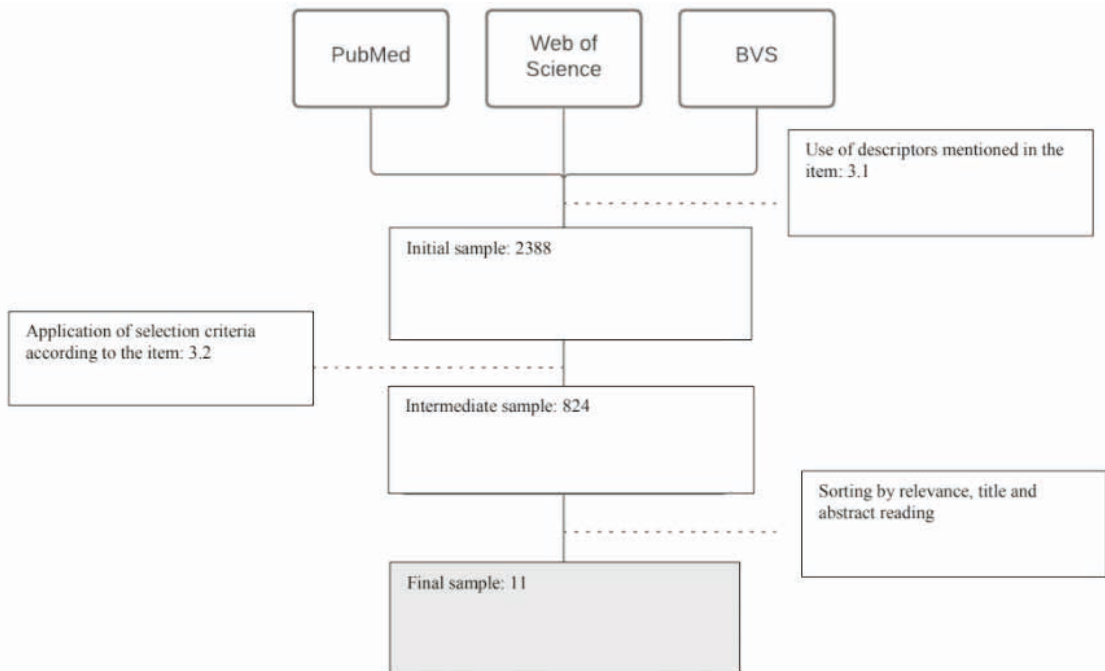


Figure 1. Flowchart illustrating the process of selecting articles with the descriptors “*biofeedback*” and “anxiety” in the US National Library of Medicine – National Institutes of Health (PubMed), Web of Science and Virtual Health Library (VHL) databases.

Source: Scheme developed by the authors (2021).

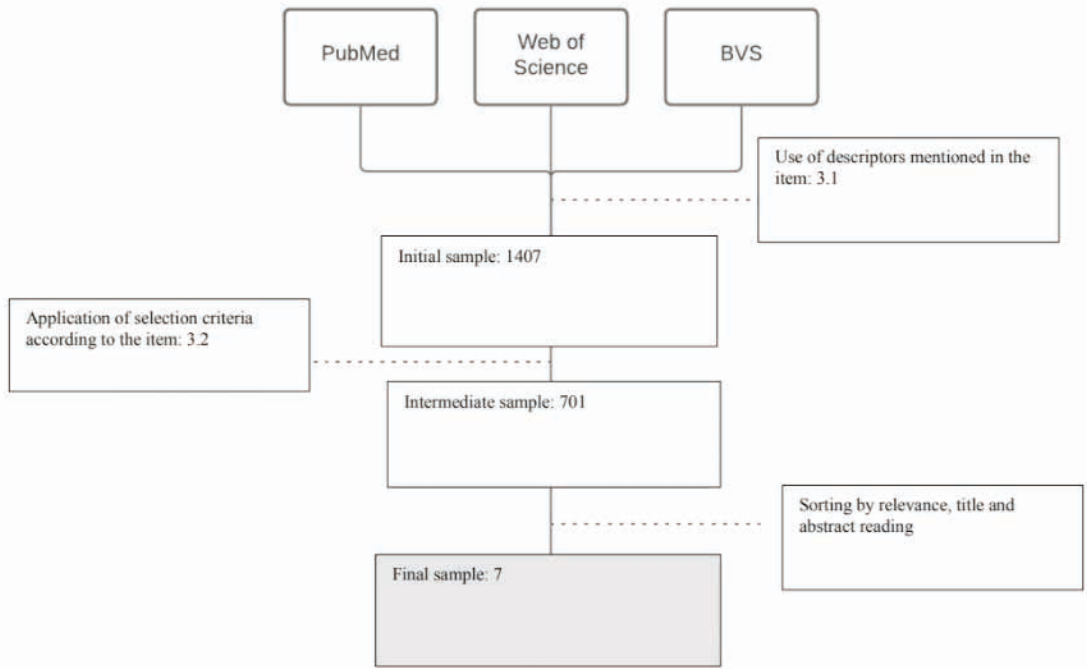


Figure 2. Flowchart illustrating the process of selecting articles with the descriptors “*biofeedback*” and “*depression*” in the US National Library of Medicine – National Institutes of Health (PubMed), Web of Science and Virtual Health Library (VHL) databases.

Source: Scheme developed by the authors (2021).

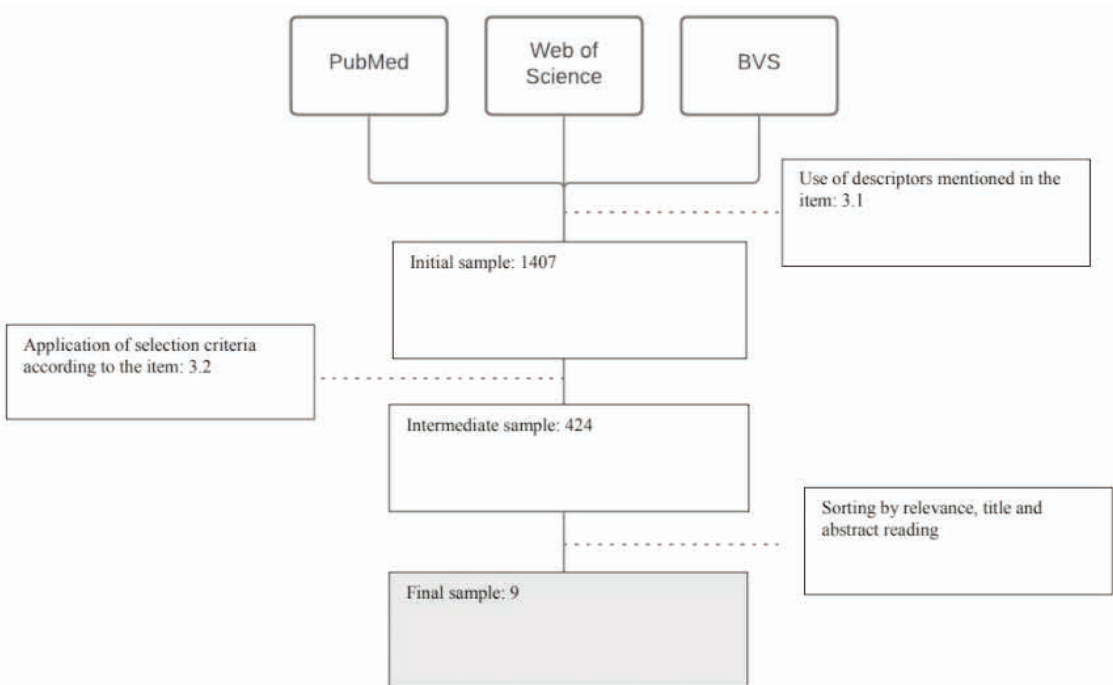


Figure 3. Flowchart illustrating the process of selecting articles with the descriptors “*biofeedback*” and “*migraine*” in the US National Library of Medicine – National Institutes of Health (PubMed), Web of Science and Virtual Health Library (VHL) databases.

Source: Scheme developed by the authors (2021).

Using the descriptors “anxiety”, “depression” and “migraine” combined with “*biofeedback*” and applying the selection criteria, the final sample of 11 articles related to anxiety, 7 related to depression and 9 related to migraine was obtained. There were four articles of the literary review type that were not limited to illnesses, addressing psychiatric illnesses in general or aspects of health and quality of life that influence conditions, serving mostly as a basis for concepts.

## **DISCUSSION**

### **BIOFEEDBACK IN THE TREATMENT OF ANXIETY AND DEPRESSION**

The type of biofeedback commonly used in the treatment of anxiety and depression is heart rate variability (HRV, and heart rate variability) through breathing techniques, with the advantages of being an easy-to-learn technique and without the need of intense physical exercise. HRV is measured by the time between two heartbeats (R-R intervals) and a low HRV has been shown to be associated with some psychopathological states such as anxiety, while a high HRV has been shown to be related to a reduction in negative emotions during acute stress situations (GOESSL et al. 2017).

Mehra and Grover (2020) reported in India the case of a 27-year-old pregnant woman with frequent panic attacks and anxiety symptoms. Before pregnancy, drug treatment with paroxetine and clonazepam was performed, but discontinued use with medical guidance. In the first trimester she started experiencing anxiety which gradually turned into frequent panic attacks. We then opted for biofeedback through breathing techniques. With regular monitoring of the severity of symptoms through the General Anxiety Disorder scale (GAD-7), the sessions began with a frequency of two to three per week lasting from 30 to 45 minutes for 3 weeks, which resulted in a

decrease in Initial GAD-7 from 13 to 7. The frequency of sessions was reduced to once a week and a GAD-7 of 3 was observed. In two months, the patient started having sessions once or twice a month. The pregnancy was completed and a healthy baby was born without complications.

A randomized controlled clinical trial by ZWAN et al. (2019) in the Netherlands analyzed the effectiveness of HRV biofeedback in a population of 50 women between 18 and 40 years old, including 20 pregnant women. The participants were divided into training groups that performed the HRV biofeedback sessions together and into groups in the waiting condition. The study intervention consisted of five weekly meetings lasting between 60 and 90 minutes each, with training given by two people, following the VFC biofeedback protocol developed by Lehrer, Vaschillo and Vaschillo, in 2000, and common stress management techniques ; additionally, instructions were given for the participants to perform daily breathing exercises at home, increasing the duration each week.

It was observed that women in the biofeedback intervention condition and in the waiting condition had fewer complaints regarding stress and depression, but there were no significant effects on sleep or anxiety. Women in the biofeedback intervention condition showed more significant improvements than those on hold, these improvements being maintained at the six-week follow-up. It was also observed that the anxiety-reducing effect was greater among pregnant women (ZWAN et al. 2019).

In addition to being a potential alternative to drug treatments, biofeedback is also an additional tool for more traditional methods of dealing with anxiety, such as counseling. In order to analyze this tool on heart rate variability as a complement to the traditional method, Ratanasiripong et al. (2019)



conducted a study with college students that compared participants who received only brief counseling versus participants who received brief counseling and biofeedback training. The instrument used was the Beck Anxiety Inventory (BAI). The students were divided into two groups, the placebo group and the biofeedback group. The placebo group received four counseling sessions over four weeks, while the biofeedback group received the same counseling sessions with the addition of four 30-minute sessions. After analyzing the collected data, it was noted that both groups had a significant reduction in BAI scores, however, the group that received the additional biofeedback treatment showed greater decreases in anxiety symptoms compared to the placebo group, evidencing that the biofeedback training improves the effectiveness of the traditional counseling method (RATANASIRIPONG et al. 2019).

Lin et al. (2019) evaluated the effect of HRV biofeedback on depressive patients with sleep disorders in a study with 48 adult and elderly patients aged up to 75 years suffering from these conditions. Participants were divided into two groups, control and intervention, both receiving standard medical care and the intervention group receiving an additional one-hour biofeedback session weekly for six weeks. The biofeedback protocol was followed on autonomic balance through slow breathing, including muscle relaxation training, diaphragmatic breathing, paced breathing, pursed-lip breathing, depression regulation psychoeducation, and 10 minutes daily at home. The statistical analyzes by Lin et al. (2019) indicated that participants showed a significant decrease in depression and anxiety in addition to improvement in insomnia symptoms, and this result was maintained at follow-up after one month.

A possible explanation presented is related to the effect of HRV biofeedback on the

vagal afferent pathway to areas of the brain, such as the amygdala and the orbitofrontal cortex, affecting the emotional regulation process. Another work, developed in Brazil, by Maynard et al. (2020) also evaluated biofeedback in the treatment of depression in a randomized, parallel, open-label study. Thirty-four individuals were divided into two groups, the control group received traditional treatments for depression while the other group underwent six sessions of biofeedback training, lasting from 10 to 30 minutes. The results were measured in two stages, before the test and after the test. Statistical analyzes showed a significant improvement in the levels of depression in the group treated with biofeedback, demonstrating the potential of the technique for treating this disorder.

Another scenario in which biofeedback is an interesting alternative is in the younger population, such as children and adolescents. Anxiety disorders are among the most frequent psychological problems in this age group and generally persist into adulthood, often manifesting themselves through physiological reactions such as headaches, stomach aches and sleep disturbances (KNOX et al., 2011).

In the Netherlands, Bossenbroek et al. (2019) conducted a study with adolescents to evaluate the effectiveness of a virtual biofeedback game and the impact of the intervention on disruptive behaviors in the classroom. Eight teenagers who attended a special secondary school for students with psychiatric and behavioral problems participated in the study. The biofeedback tool analyzed was the virtual reality video game DEEP, where players explore a fantasy world underwater by controlling their diaphragmatic breathing in an immersive and relaxing way, since there are no objectives to be fulfilled in the game and inhaling and exhaling movements were detected by a special belt-like control that wrapped around the abdomen.

Visual feedback of the players breathing is given through circles, which expand during inhalation and contract with exhalation. After six sessions of DEEP, the authors observed a small decrease in daily levels of anxiety and disruptive behavior. At an individual level, strong evidence was found in five participants of an average reduction in anxiety levels over the course of the intervention. The results appeared to last approximately two hours after the sessions.

These authors concluded that DEEP reduces daily levels of anxiety and, although the effects do not last for a full school day, it can be an important method in certain situations that provoke anxiety, such as exams or seminars.

In the United States of America, Knox et al. (2011) analyzed the effect of a game-based biofeedback approach in children and adolescents with twenty-seven participants aged between 9 and 17 years, and the evaluation of the effects was performed using the MASC (Multidimensional Anxiety Scale for Children), this way, the participants were helped to detect signs of anxiety, as well as events and thoughts that could trigger anxiety. The analyzed games were Freeze-Framer 2.0 and Journey to the Wild Divine: The Passage, both software that use images and sounds to aid relaxation, where the player needs to accomplish certain objectives that are achieved with the decrease of tension and breathing spacing. The results indicated that the method can be effective in reducing anxiety for children and adolescents, however, the greatest effect of the study was on depression, although they were referred due to anxiety, a correlation between the two disorders was observed in the population. young.

Due to greater accessibility to available technology, the practice of biofeedback has become easier for those who do not have the time or resources to constantly travel

to specialized centers or clinics. Rosenberg and Hamiel (2020) analyzed the effect of a portable biofeedback device (CalmiGo®) that helps control breathing and consequently heart variability, with the aim of reducing the effects of anxiety and stress in students during exams. The device used uses an algorithm and provides feedback in the form of light, sounds and vibrations according to the user's breathing until the ideal exhalation time is reached. The 34 participants were divided into three groups, one receiving the CalmiGo®, the second receiving instructions for self-control of breathing and the third receiving only a leaflet with information about exam-related anxiety.

The results showed that the participants who used the device showed a significant decrease in all scales of the TAI (Test Anxiety Inventory) even with little time to practice, proving to be effective in reducing anxiety symptoms. One explanation is that with the aid of the device, the individual has a more accurate feedback during expiration while the other groups did not have any feedback. It was also observed that the biofeedback group performed training more frequently than the other groups, but no correlations were found between the amount of practice time and therapeutic effects. Another study by Ratanasiripong et al. (2015) evaluated the effectiveness of HRV biofeedback using a portable device in university nursing students in Thailand. Sixty people participated in the study and were divided into two groups, one for control and the other for the biofeedback intervention, the intervention group received training on how to use the device and were instructed to perform breathing training with the equipment three times a day during four weeks. Levels of stress, anxiety, and depression were assessed using the Perceived Stress Scale, State Anxiety Scale, Center for Epidemiological Study-Depression Scale, as



well as a brief demographic questionnaire. At the end of the period, it was observed that the control group had higher scores than the initial ones, while the intervention group had a significant decrease in symptoms.

Another option for portable devices are mobile applications, as smartphones are widely used by a large part of the population and, with the advancement of technology, become a viable option. Economides et al. (2020) determined whether remote biofeedback training in addition to therapy was possible and effective for symptoms of depression. The Meru Health app received a HRV-based biofeedback component. A group of 48 adults with at least moderate depressive symptoms participated in the study and were divided into two groups, both underwent eight intervention modules applied over a period of eight weeks with known practices, such as Mindfulness-Based Stress Reduction (MBSR), Mindfulness-Based Cognitive Therapy (MBCT), Cognitive-Behavioral Therapy (CBT) etc. using texts, videos, audios, meditation exercises, among others. One of the groups performed an additional exercise with the Meru Health application in its biofeedback component, connected to a bluetooth heart sensor called HeartMath®.

Results showed that participants in the biofeedback group completed fewer meditations than the other group but participated more in the behavioral activation therapy/cognitive behavioral therapy exercises, also, patients in the group with the additional biofeedback intervention were more likely to experience clinically significant improvements than the other group. Therefore, the combination of biofeedback therapy with other known and applied techniques can improve treatment results when performed remotely.

The results and conclusions obtained in the analyzed works are in accordance with

the consulted meta-analyses (GOESSL et al., 2017; PINTER et al., 2019; LEHRER et al., 2020) which show that the use of heart rate variability biofeedback for the treatment of anxiety and depression is effective and safe for relieving symptoms and may be used as an adjunct or alternative therapy for cases in which the administration of medication is not recommended (eg pregnant women) or individuals refractory to drug treatment, showing positive and significant results in different populations.

Heart rate variability biofeedback is the most prevalent modality for treating anxiety, but another important method is neurofeedback. In this type of biofeedback, the activity of the central nervous system is monitored in real time by means of an electroencephalogram and, depending on the psychophysical state of the individual, the brain waves are modified (MARKIEWICZ, 2017).

In order to report the effects of neurofeedback on anxiety, a case study was carried out by Moradi et al. (2011) with two patients who had anxiety, aggressiveness and nervousness among other disorders. Both patients had unsuccessful pharmacological interventions in the past, and the researchers used neurofeedback, which consisted of weekly 50-minute sessions for 10 weeks, and electroencephalogram recordings. Before the intervention, they indicated anxiety, restlessness, lack of concentration and sleep disturbances in the individuals. After one year, treatment and follow-up, both patients showed improvement in symptoms related to anxiety and aggressive behavior, in addition to an increase in motivation. The results were maintained after one year, and no relapses were reported by any of the participants. The authors concluded that neurofeedback is an effective modality for the treatment of anxiety.

Hou et al. (2020) analyzed the effectiveness of neurofeedback on symptoms of anxiety and

depression in a study involving 26 patients who were divided into two groups, one group would receive training for the left parietal lobe of the brain while the other would receive training for the right parietal lobe. The questionnaires and measures used were: State-Trait Anxiety Inventory, Beck Depression Scale and Insomnia Severity Index. The sessions started with a recording of the participant's baseline and then performed three trials of biofeedback training, with a two-minute break between them. Analysis of the results indicated that the treatment was effective, decreasing anxiety, depression and insomnia scores. Improvement in insomnia symptoms was correlated with improvement in anxiety symptoms and the authors concluded that neurofeedback training in the parietal lobe is effective, but long-term follow-up is needed to confirm the result.

### **BIOFEEDBACK IN THE TREATMENT OF MIGRAINE**

In the treatment of migraine, behavioral treatments can be used as a way to prevent episodes and secondary consequences that impact the patient's quality of life, which include relaxation training, thermal biofeedback combined with relaxation training, electromyography biofeedback and cognitive-behavioral therapy, being used in multiple stages of care. In addition to improving treatment results, the incorporation of these techniques also promotes independence, can reduce medical expenses and improve adherence to medical strategies. Different biofeedback modalities are used for certain conditions, often being combined, and those with the strongest evidence for the treatment of migraine include thermal biofeedback, electromyography or muscle tension, and blood pulsation (SINGER, 2015).

Stubberud et al. (2020) worked on the development of an application called mHealth,

aimed at biofeedback treatment that uses an algorithm that uses three physiological parameters: HRV, muscle tension and skin temperature. At the end of 2020, the authors conducted a study with 16 adolescents to evaluate the performance and effectiveness of mHealth as a primary treatment, therefore, participants would not be using medication for prophylaxis. This study consisted of four weeks of baseline observation followed by an eight-week intervention period with either the mHealth biofeedback app or a sham biofeedback app. The mHealth treatment group received biofeedback training, instructions on how to do it themselves, and a migraine diary. Participants were told that the aim of the sessions was to increase skin temperature and decrease muscle tension and heart rate. Suggestions were given on how to achieve the goals, such as relaxation strategies. The app sent daily notifications informing them to complete the diary and complete a 10-minute session. The fake application had its algorithm modified by adding fluctuations of the sine curve to the correct feedback signal and, this way, there was a partial interruption of the connection between the input of physiological parameters and the feedback. The same sensors used in the usability study were used, connected via Bluetooth to a cell phone, and the primary result was the change in the frequency of migraine days comparing the baseline days with the end of treatment. The result observed by the authors was a decrease of approximately 20% in the frequency of migraines, which is smaller than the effect of the traditionally performed biofeedback treatment. The method addressed in the study has a great difference compared to the traditional method, where there are regular sessions with therapists and adjuvant behavioral therapies such as relaxation and stress management and there is direct help from the professional to promote self-control.

Another factor pointed out by the authors was the low adherence obtained, in the biofeedback group an adherence of 79% was observed in the first four weeks and 48% in the last four weeks; in the false biofeedback group these values were 65% and 30%, respectively. Previous studies indicate that there is a correlation between adherence and efficiency, which corroborated the observation that there was a greater reduction in the frequency of migraines in the first weeks.

Stubberud et al. (2016) concluded that more comprehensive instructions, guidelines and guides during sessions and adjunct therapies must be included in sessions, in addition to strategies to increase adherence and motivation of participants such as reminders and even gamification, creating a personalized experience for each individual.

In Japan, Odawara et al. (2015) proposed a prospective randomized study with 32 subjects - divided into biofeedback and control groups - to investigate the effects of real-time intervention in the treatment of migraine. The intervention group underwent eight guided sessions of biofeedback with electromyogram and temperature, accompanied by home training for ten weeks and, during the intervention, all groups were allowed to use pain medications, if necessary. Four weeks before and after the biofeedback treatment, participants carried a palmtop to record inputs into a system in real time, and statistical analyzes showed that the control group had reduced intensity and frequency of migraine attacks. The authors concluded that this result is in agreement with previous meta-analyses, but its differential was the use of the system, which generates greater reliability than the questionnaires commonly used in other studies.

A study by Tommaso and Delussi (2017) sought to compare the efficiency of the biofeedback intervention compared to drug

treatment with topiramate in preventing seizures. The biofeedback was the nociceptive blink reflex. Reduced habituation of the nociceptive blink reflex is considered to be a marker for genetic predisposition to migraine, habituation being defined as a decrease in response as a result of repeated stimulation and its lack is an abnormality found between migraine attacks. 33 participants who had migraines without the presence of aura were recruited, followed up prior to the test for three months and subsequently divided into three groups: group 1, biofeedback treatment; group 2, biofeedback and topiramate treatment; group 3, treatment of only topiramate. The evaluation of the nociceptive reflex was performed using nociceptive electrical stimulation through a customized electrode. The biofeedback training consisted of sessions three times a week for three months, where the individual visualized the responses of his own nociceptive reflex in order to reduce this indicator, thus leading to habituation. The results indicated that biofeedback training was as effective as topiramate for migraine prevention, but the association of both did not lead to a better result than each method individually.

*Biofeedback* can also be used in other conditions associated with migraine, as shown in the study by Haggiag and Speciali (2020), where it was evaluated for migraine related to bruxism. By monitoring the interocclusal space with an intraoral device for 90 days, patients received real-time information on unconscious tension in the teeth and jaw, thus promoting relaxation. An improvement in pain as early as the first week was observed for both bruxism and the parallel related migraine, suggesting that this type of treatment may be effective for patients suffering from both conditions.

The findings in the analyzed studies are in line with the consulted literature (PENZIEN et

al., 2015; STUBBERUD et al., 2016; KONDO et al., 2019) which suggest that *biofeedback* in the prophylactic treatment of migraine is a safe method and effective, with results comparable to those of pharmacological therapies. However, in the work of Tommaso and Delussi (2017) it was found that the association of drugs with *biofeedback* did not bring significant difference when compared to individual methods, contradicting what is generally observed in the literature, which indicates that the combination brings better results than the individual ones.

## CONCLUSION

According to the analyzes of the studies addressed in this work, *biofeedback* is an additional therapy to the treatment traditionally used in cases of anxiety,

depression and migraines, in some specific occasions it may be an alternative for refractory patients or with restrictions on drug treatment. Appropriate guidance on the procedure by a professional proved to be essential in order to obtain the greatest effectiveness.

From the sample of selected articles, only one reports not having presented the expected results due to the low adherence of the participants to the treatment, culminating in a smaller effect than in the traditional treatment. However, a common point observed in all evaluated studies was that *biofeedback* is a promising technique, but there is still a need for more studies with greater control so that its effectiveness is studied with a larger number of research participants.

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