RESEARCH ARTICLE

Automatic migraine classification using artificial neural networks [version 1; peer review: 1 approved with reservations]

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Abstract

Background: Previous studies of migraine classification have focused on the analysis of brain waves, leading to the development of complex tests that are not accessible to the majority of the population. In the early stages of this pathology, patients tend to go to the emergency services or outpatient department, where timely identification largely depends on the expertise of the physician and continuous monitoring of the patient. However, owing to the lack of time to make a proper diagnosis or the inexperience of the physician, migraines are often misdiagnosed either because they are wrongly classified or because the disease severity is underestimated or disparaged. Both cases can lead to inappropriate, unnecessary, or imprecise therapies, which can result in damage to patients' health.
Methods: This study focuses on designing and testing an early classification system capable of distinguishing between seven types of migraines based on the patient's symptoms. The methodology proposed comprises four steps: data collection based on symptoms and diagnosis by the treating physician, selection of the most relevant variables, use of artificial neural network models for automatic classification, and selection of the best model based on the accuracy and precision of the diagnosis. **Results:** The neural network models used provide an excellent classification performance, with accuracy and precision levels >97% and which exceed the classifications made using other model, such as logistic regression, support vector machines, nearest neighbor, and decision trees.
Conclusions: The implementation of migraine classification through neural networks is a powerful tool that reduces the time to obtain accurate, reliable, and timely clinical diagnoses.

Keywords

artificial neural networks, migraine, supervised learning, automatic classification techniques

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Introduction

Cephalalgia or headache represents one of the most common types of pain experienced by humans. Headaches usually occur intermittently. The most frequent forms correspond to migraine and tension headache. Migraines are classified as chronic disorders of the nervous system and are characterized by the onset of recurrent symptoms or episodes associated with headache, which can range from moderate to severe pain and includes throbbing or vibrating pain; furthermore, migraines can be experienced unilaterally or bilaterally and can trigger other symptoms, such as nausea, vomiting, weakness, and light and sound sensitivity (Charles, 2013; Deza, 2010; IHS, 2018).

Both chronic and recurrent/relapsing headaches can cause pain and distress, but they rarely reflect a serious health problem. However, any change in the pattern or nature of the headache could be a sign of a serious complication, i.e., change in pain frequency from sporadic to frequent or pain severity from mild to acute; hence, medical attention should be sought as soon as possible (Goadsby *et al*., 2002).

Although headache is generally a benign and transitory disorder that in most cases ceases spontaneously or with the aid of analgesics, it can also be caused by a serious life-threatening illness such as meningitis, brain tumor, hypercholesterolemia, heart problems, or subarachnoid hemorrhage (arteriovenous malformation). On the other hand, certain types of headaches, such as migraines, although benign, cause much suffering in affected individuals and represent an economic burden because of the high number of work-loss hours they cause (Trillos, 2010).

In 1988, the Classification Committee of the International Headache Society (IHS, 2018) published the current classification of headache types, which divides headaches into primary and secondary headaches. Primary headaches include migraines, tension-type headaches, paroxysmal headaches (cluster headaches and paroxysmal hemicrania), and benign miscellaneous headaches. Secondary headaches are those caused by vascular disease, infection, tumors, alteration in cerebrospinal fluid production, cranial trauma, neuralgia, etc.

Discrimination among migraines with and without aura and other types of migraines and headaches is established based on the specific criteria established by the International Headache Society (Charles, 2018; IHS, 2018; Rasmussen & Olesen, 1992; Viana *et al.*, 2017) as follows:

Migraines without aura

A. At least five attacks that meet criteria B to D.

B. Duration from 4 to 72 hours.

C. At least two of the following symptoms: 1. unilateral pain, 2. throbbing pain, 3. moderate-to-severe pain, 4. pain increases with physical activity.

D. During headache, at least one of the following symptoms: 1. nausea and/or vomiting, 2. photophobia or phonophobia.

E. At least one of the following: 1. Medical history that does not suggest secondary headache; 2. clinical history that suggests structural injury but is discarded via appropriate investigation; 3. structural injury exists, but the headache is not related with its presence nor is it related to time.

Migraines with aura

A. At least two attacks that meet criterion B.

B. At least three of the following four characteristics should be met: 1. One or more aura symptoms indicating focal cortical injury and/or brainstem dysfunction; 2. At least one gradually developing aura symptom lasting longer than 4 minutes or two or more successive symptoms; 3. The aura should not last for more than 60 minutes. If there is more than one aura, the duration of its presentation is proportional; 4. Headaches follow aura at intervals no greater than 60 minutes. Pain can be experienced before the aura or at the time of the aura.

C. At least one of the following characteristics should be met: 1. Clinical history and physical and neurological examination that does not suggest secondary structural injury or metabolic disease; 2. If the clinical history or physical or neurological examination suggest secondary injury, this should be discarded via appropriate investigation; 3. In the presence of secondary injury, this does not explain the pain, it has no temporal relationship, and it does not occur for the first time.

Causes: Many researchers agree that migraines have a genetic cause; however, there are a number of triggering factors, including stress; anxiety; hormonal imbalances in women; exposure to bright or flashing lights, loud noises, and strong odors; medications; inappropriate amount of sleep; sudden weather or environmental changes; overexertion (too much physical activity); tobacco or caffeine intake (consumption or withdrawal); skipping meals; medication overuse (taking migraine medication too often); and certain foods and food additives, such as alcohol, chocolate, ripened cheese, monosodium glutamate, some fruits and nuts, fermented or pickled products, yeast, and cured or processed meats (Evans, 2009).

Epidemiological studies examining various types of populations show that people suffering from migraines share a very hectic social and work life, and as these individuals do not usually observe orderly resting times or practice other activities that help clear the mind, they are under stress, with migraine being a sign of work and emotional burden (Dodick, 2018; Parikh & Silberstein, 2019). Migraines also cause indirect damage to companies because they involve loss in labor productivity; annual losses in the United States are estimated at billions of dollars; such effects also apply to countries such as Colombia (Burch *et al.*, 2018; Deza, 2010; Ramírez & Urrea, 2012).

Phases: Migraines generally involve four phases (Burch, 2019; Katsarava *et al.*, 2012):

- Prodromic phase (previous): This phase begins up to 24 hours before you have a migraine. Early signs and

symptoms include food cravings, unexplained mood swings, uncontrollable yawning, fluid retention, and increased urination.

- Aura: If you are in this phase, you may see flashing or bright lights or criss-crossing lines. You may experience muscle weakness or a feeling of being touched or grabbed. Aura can occur just before or during a migraine.

- Headache phase: In general, a migraine gradually begins and then becomes more severe. It often causes throbbing or vibrating pain, usually unilaterally. However, you can experience a migraine without experiencing a headache. Other migraine symptoms may include increased sensitivity to light, noise, and odor; nausea and vomiting; pain that worsens with movement; coughing; and sneezing.

- Postdromal phase (after headache): You may feel exhausted, weak, and confused after a migraine. This can last up to 1 day.

Migraines are more common during mornings. People often wake up suffering from migraines. Others experience migraines at predictable times, such as before menstruation or on weekends after a stressful work week (Kelman, 2007).

Diagnosis: To diagnose migraines, the patient's medical history and symptoms are assessed and a physical and neurological examination is performed; these are sometimes accompanied by specialized examinations such as magnetic resonance imaging, tomography, electroencephalogram, and lumbar puncture (Evans, 2019). An important part of diagnosing migraines is discarding other medical conditions that could be causing the symptoms (Altintop *et al*., 2017; Diamond *et al*., 2007; Giffin *et al.*, 2003; Goadsby & Holland, 2019; Karsan & Goadsby, 2018; Maniyar *et al*., 2015).

Treatment: There is no cure for migraines; therefore, treatment focuses on relieving symptoms and preventing further attacks. There are various types of medicines to relieve symptoms, such as triptans, ergotamine, and painkillers. The sooner these medications are administered, the more effective they are. In addition, to relieve symptoms, you can rest with your eyes closed in a quiet and dark room, place a cold cloth or ice pack on your forehead, or drink liquids (Burch, 2019; Charles, 2018; Diamond *et al*., 2007; Evans, 2009; Viana *et al.*, 2017). Similarly, lifestyle changes can be adopted to control stress or other triggering factors. Furthermore, natural treatments can be used (May & Schulte, 2016).

Some studies report that approximately 15% of United States citizens and 12% of the world's population suffer from migraines (Burch, 2019; Burch *et al.*, 2018; Chen *et al.*, 2019; Diener *et al*., 2012; Dodick, 2018; Parikh & Silberstein, 2019). Migraines can affect anyone, but their prevalence increases in women, i.e., women are three times more likely to suffer from migraines than men. Migraines also have a high prevalence in those with a family history of migraines or those who suffer from medical conditions such as depression, anxiety, bipolar disorder, sleep problems, and epilepsy.

Isaza *et al.* (1997) conducted a statistical study in mid-1981 and 1989 in Colombia and showed that 11.6% of women and 3.4% of men suffered from migraines. Similarly, Ramírez & Urrea (2012) reported that in 1997, of 3,401 patients assessed in Colombia in the outpatient department of the neurology service, 848 (24.93%) were due to primary headache, which is an important reason for outpatient consultation. Migraines occurred in 617 (18.14%) patients, with aura in 255 (7.5%) and no aura in 362 (10.64%).

Previous studies on migraine classification focused on the neurological or genetic aspects of the disease, leading to investigations that allowed for the classification of various types of migraines based on the study of encephalograms (Akben *et al.*, 2012; Akben *et al.*, 2010; Akben *et al.*, 2016; Alkan & Akben, 2011; Altintop *et al*., 2017; Bellottia *et al*., 2007; Martins-Oliveira *et al*., 2017; Subasi *et al.*, 2018), signals emitted by body temperature sensors, blood oxygen, heart rate, and electrodermal activity data (Chong *et al*., 2017; Koskimäki *et al*., 2017; Schwedt, 2013), or genetic analysis (Gormley *et al*., 2016). Although these studies attempted to classify migraines with precision levels of >70%, the methods used required a direct measurement of the variables using medical devices connected to the patient, which can cause variation in the data; lead to long waiting times for the appointment of specialized examinations, particularly in Latin American countries; or result in a lack of availability of medical equipment in rural regions. As stated previously (Alkan & Akben, 2011), numerous investigations have attempted to develop automatic diagnostic methods for migraines. However, no definitive diagnostic method for migraines has yet been accepted by the authorities on the subject (IHS).

Currently, there is a recurrent problem in the diagnosis and treatment of migraines, which includes, among others, the following needs: (i) proper reading and identification of the patient's primary and secondary symptoms, (ii) precise and timely identification of the type of migraine, (iii) continuous monitoring of the symptoms, and (iv) adequate treatment. In the early stages of the pathology, patients visit the emergency services or outpatient consultation departments, where timely identification largely depends on the expertise of the treating physician and the continuous monitoring of the patient (Burch *et al.*, 2018; Burch, 2019; Deza, 2010; Evans & Johnston, 2011; Trillos, 2010; Wang *et al*., 2019). However, owing to the scarcity of time to establish a diagnosis, the inexperience of the physician, or shortcomings in the patient–physician communication of symptoms, the pathology is often misdiagnosed or the severity of the disease is underestimated, leading to inappropriate, unnecessary, or imprecise therapies, which can result in complex damages to patients' health (Evans & Johnston, 2011). Migraines can be misdiagnosed as tension headache, sinus headache, or other types of headache. A diagnosis of migraine should be considered when there are recurrent and debiliting headaches without secondary warning signs (Burch *et al.*, 2018; Burch, 2019; Wang *et al*., 2019). Therefore, misdiagnosis or incorrect classification of the type of migraine and inadequate treatment of the pathology constitute the underlying problem associated with migraines (Deza, 2010; Trillos, 2010).

This article seeks to contribute to the early identification of different types of migraines through the use of supervised learning techniques based on artificial intelligence, which allow overcoming the difficulties encountered. The purpose of this study is to develop a classification model that allows the determination of the type of migraine a patient suffers based on the analysis of its symptoms and medical history. The novelty, significance, and relevance of this study are outlined as follows:

• An indirect method aimed at classifying the type of migraine experienced by a patient, which, unlike existing methodologies, does not use procedures requiring brain wave measurement or the use of sensors.

• The systematic migraine classification process used includes the stages of data collection based on symptoms and diagnosis by the treating physician, selection of the most relevant features, use of different classification models, and selection of the most suitable model based on the accuracy and precision of diagnosis.

Methods

Proposed methodology for migraine classification

The strategy developed here is based on a systemic approach oriented to the specification of neural network models for the classification of migraines with and without aura, highlighting the relevance of considering key aspects that lead to strong implications in their application, such as the selection of variables and the performance measures that allow for the selection of the best model.

Starting from the existence of a data source that includes various typical symptoms of patients with migraines, Figure 1 outlines the steps in the classification of patients with migraines and the comparison model (García-González *et al.*, 2019; Sánchez-Sánchez *et al.*, 2019b).

The elements included in Figure 1 are discussed below.

1. Selection: The data selection phase is directed toward the preliminary analysis of the various data sources (if any), their features, and aspects related to the environment in which they are obtained. This selection can be defined as a process of approximation to the available information through subjective analysis and statistical treatment in order to infer the hidden structure of data.

Knowing the goals and the data that will enable this process are key factors for a successful selection process.

2. Processing: Data processing consists of analyzing and transforming the input variables with the aim of minimizing noise, highlighting important relationships, and detecting errors to enable the recognition of hidden patterns. Processing comprises four types of processes: the first aimed at minimizing noise via the transformation of the object data and the elimination of irregular patterns (atypical data; poor typing; blank, incomplete, and inconsistent data, etc.); the second aimed at scaling the large-sized object data; the third aimed at considering the syntactic transformations of the object data and facilitating its handling, without leading to changes in the results; and the fourth aimed at the selection of the variables, characteristics, or attributes that will be taken into account. This selection largely depends on the knowledge that the data modeler has on the data sources, and it is his/her task to decide whether to include each variable in the model following some previously established criteria. Typically, not all potential variables are equally informative as they may be correlated, present noise, or have no meaningful relationship with the classification.

The importance of making an adequate selection lies in the difficulties of convergence in learning, which can involve the inclusion of irrelevant variables and poor performance of models. Hota & Shrivas (2014), and Londoño & Sánchez (2015)

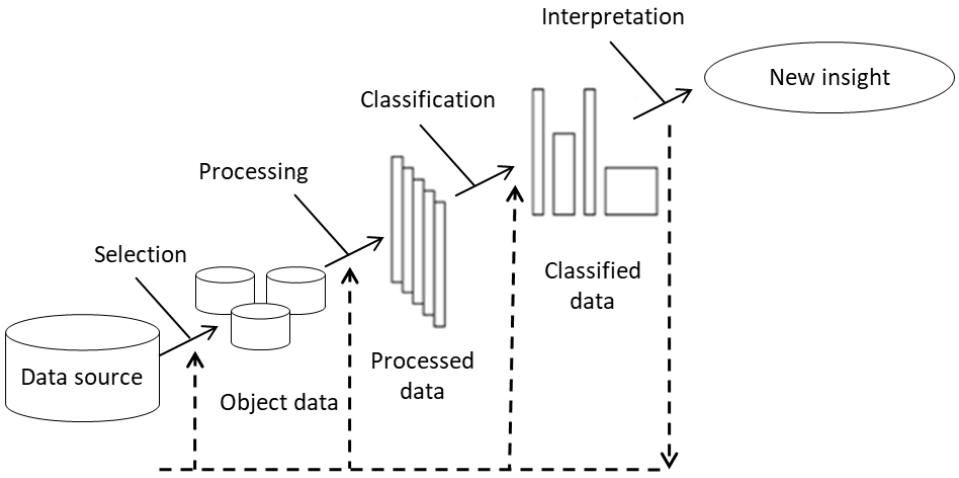

Figure 1. Flow diagram for the classification of patients with migraine.

define the selection of variables as an optimization process intended to identify the best subset of variables from a fixed variable set. The goal of selection is to reduce the size of the input data to facilitate processing and analysis, discarding data that does not further contribute to the subsequent classification process. This saves time in data processing without disregarding the generation of optimal results.

The selection of variables not only deals with the decrease in cardinality, i.e., setting a partial or predefined limit to the number of attributes that can be considered when creating a model, but also allows attributes to be properly discarded based on their utility for a good analysis process.

3. Classification: Classification involves searching patterns of interest that express dependency on the data and allows groups with similar features to be established. The process essentially consists of assigning each individual (entity or data) its own category or class, thereby creating sets of individuals sharing some feature that differentiate them from the rest. Classes can be binary, Yes or No, or multiclass, which include more than two categories. At this stage, machine learning, whose objective is to develop techniques that allow computers to learn, is used.

The past few years have seen the proliferation of different automatic classification techniques based in learning machine, including neural networks, decision trees, logistic regression, Bayesian classifiers, nearest neighbor, support vector machines (SVMs), and multiple discriminant analysis (Doupe *et al.*, 2019; Waring *et al.*, 2020).

In this article, because of the robustness of the data management technique, adaptability, and acknowledged generalization capacity, neural networks are used to classify patients with migraines.

Logistic regression models, SVMs, nearest neighbor, and decision trees are also implemented in order to compare data collected using other classification techniques.

4. Interpretation: In this phase, evaluation of the quality of the model is performed by analyzing and comparing the results from different metrics used for the classification based on the data obtained in the classification stage, which is aimed at understanding the main characteristics of the model.

For classification problems, common performance metrics are as follows:

- Accuracy: Proportion of correctly classified instances.

- Precision: Also called positive predictive value, it represents the fraction of correctly predicted positives among those classified as positive.

However, the need for tools aimed at enabling appropriate decision-making has led to an accelerated interest in the development of data classification models in recent decades, which is especially intended to overcome the theoretical, conceptual, and practical limitations of many of the techniques currently available. This has resulted in the emergence of a wide range of models, among which neural networks have demonstrated high potential given their adaptability, generalizability, and learning capabilities and because of the possibility of representing nonlinear relationships (Sánchez-Sánchez & García-González, 2017).

Some aspects that justify and favor the development of neural network models for data classification are as follows (Sánchez-Sánchez *et al.*, 2019a):

1. The data generating process is often unknown and difficult to identify, thereby limiting the capacity of parametric models to appropriately classify data. Neural networks are self-adaptive models that do not require *a priori* assumptions about the problem under study, a highly desirable feature in cases in which the data generating mechanism is unknown (Qi & Zhang, 2001).

2. Real data often show unstable behavior. The ability of the neural network to learn and be generalized allows the model to learn complex behaviors directly from the data and correctly infer the unseen part of the data from the acquired knowledge (De Gooijer & Kumar, 1992).

3. The relationships between the data and the variables that explain its behavior are complex. The universal approximation characteristics of neural networks allow them to identify hidden dependencies, especially nonlinear dependencies (Cybenko, 1989; Franses & Van Dijk, 2000; Hornik, 1991; Hornik *et al.*, 1989), thereby favoring the representation of complex relationships.

4. Data units can be very large or very small. Neural networks are flexible in relation with the values they receive and deliver and do not require prior treatment.

5. Data are obtained from multiple fields of knowledge. Their functional flexibility and characteristics as universal approximators allow neural networks to represent complex behaviors regardless of the field of knowledge those data belong to.

Neural networks and their recent architectures, such as deep neural networks, have been used effectively in data classification tasks and display better results than other techniques, such as logistic regression, decision trees, Bayesian classifiers, etc.; their strength lies in their high capacity to dynamically create complex prediction functions and emulate human learning (Nikam, 2015; Sánchez-Sánchez & García-González, 2017; Sánchez-Sánchez & García-González, 2018).

A neural network is represented as a three-layer model: an input layer, one or more hidden layers, and an output layer (Figure 2) (Sánchez-Sánchez *et al.*, 2020b). An input layer represents the variables that influence the model, hidden layers perform the processing, and the output layer corresponds to the various migraine classes.

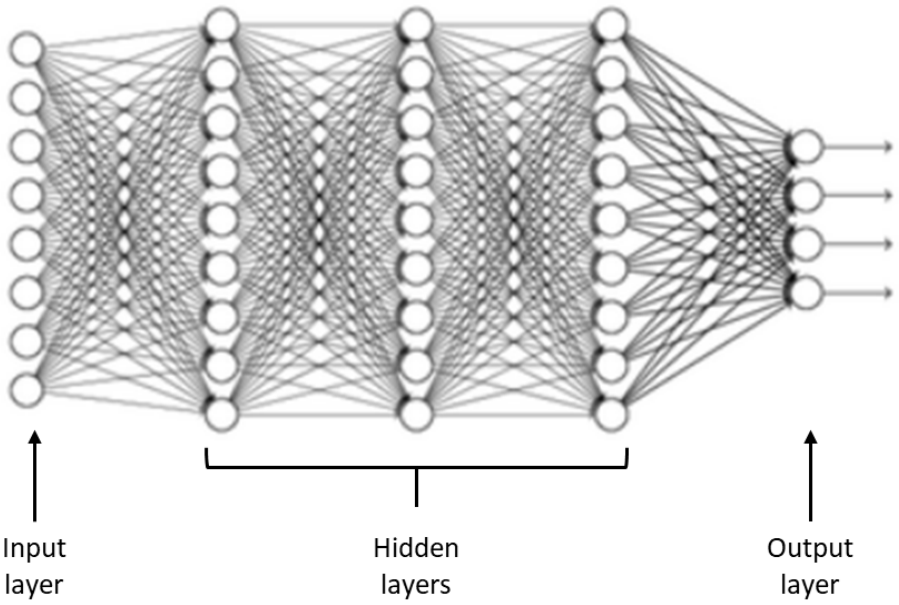

Figure 2. General scheme of an artificial neural network.

Migraine classification results

Method: We used the proposed methodology for the classification of migraines.

Population: This study used a database comprising 400 medical records of users diagnosed with various pathologies associated with migraines in the research of the master's thesis "Analysis of Artificial Neural Network Models, for a Migraine Diagnosis System with Aura and without Aura" (De la Hoz *et al.*, 2014). Data were recorded by trained medical personnel at the Hospital Materno Infantil de Soledad during the first quarter of 2013. The compiled database contains physician identification, symptoms, diagnosis, and treatment. No patient identifiable data was required. See underlying data (Sanchez-Sanchez *et al.*, 2020a).

Procedure: Selection and processing: The compiled database contains information regarding patient identification, healthcare provider identification, treating physician identification, symptoms, diagnosis, and treatment. Based on these data, tasks related to noise elimination, error detection, and data translation into numerical variables were performed.

Finally, variables that influence the identification of the type of migraine were selected, focusing on symptoms and diagnosis and disregarding identification and treatment variables. This led to a selection of 23 variables associated with the symptoms or signs that a patient may present and 1 variable associated with the diagnosis that allows the identification of the type of migraine. Table 1 presents a list of the 24 identified variables and their description.

The type of variable states the different values that it can assume and can be either continuous, e.g., age, or binary, e.g., nausea. The variable "Type" indicates the diagnosis issued by the treating physician based on the symptoms and medical record of the patient, with the possibility of presenting of one of the following classifications:

1. Typical aura with migraine

2. Migraine without aura

3. Typical aura without migraine

4. Familial hemiplegic migraine

5. Sporadic hemiplegic migraine

6. Basilar-type aura

7. Other

Figure 3 presents the distribution of cases according to the classification of migraine types carried out in the study and which serves as a criterion for verifying accuracy and precision.

Tests are conducted with the complete dataset (23 variables), and variable reduction, recursive elimination of variables, and selection of the best number through cross-validation is applied, the latter in order to eliminate variables with redundant information. This produces a reduced set of 18 variables.

Classification: Preprocessed data are used as inputs to five different classification models: a multilayer perceptron-type neural network (MLP), which is validated using different network configurations that differ in the number of neurons and hidden layers; a logistic regression model; an SVM model; a nearest neighbor model; and an optimized classification and regression tree (CART).

Table 1. List of identified variables.

	Description	Name		Description	Name
1	Patient's age	Age	13	Lack of speech coordination	Dysphasia
2	duration of last episode in days	Duration	14	Disarticulated sounds and words	Dysarthria
3	Frequency of episodes per month	Frequency	15	Dizziness	Vertigo
4	Unilateral or bilateral pain location	Location	16	Ringing in the ears	Tinnitus
5	Throbbing or constant pain	Character	17	Hearing loss	Hypoacusis
6	Pain intensity, i.e., mild, medium, or severe	Intensity	18	Double vision	Diplopia
7	Nauseous feeling	Nausea	19	Simultaneous frontal eye field and nasal field defect and in both eyes	Visual defect
8	Vomiting	Vomit	20	Lack of muscle control	Ataxia
9	Noise sensitivity	Phonophobia	21	Jeopardized conscience	Conscience
10	Light sensitivity	Photophobia	22	Simultaneous bilateral paresthesia	Paresthesia
11	Reversible visual symptoms	Visual	23	Family background	Family
12	Reversible sensory symptoms	Sensory	24	Diagnosis of migraine type	Type

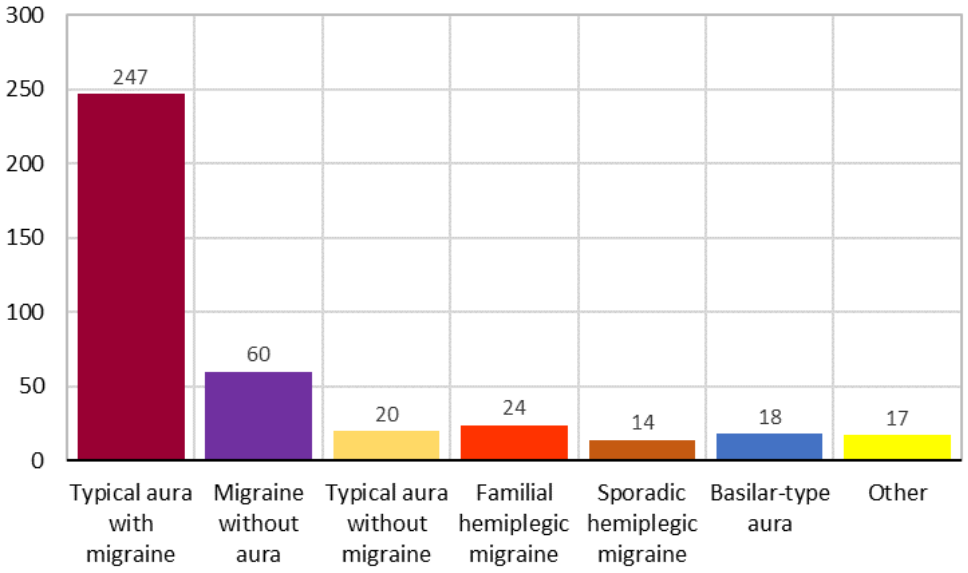

Figure 3. Number of cases by type of migraine.

Python 3 script is used with Scikit-learn 0.23.1[1] and pandas' 1.0.4 libraries (Sanchez-Sanchez *et al.*, 2020a).

The neural network model used is equivalent to an MLP trained using backpropagation. The configuration parameters used for the neural network models are as follows:

[1]Scikit-learn (formerly scikits.learn and also known as sklearn) is a free software machine learning library for the Python programming language. https://scikit-learn.org

• Input neurons: 23 variables corresponding to the first 23 variables presented in Table 1 for the complete model and 18 variables for the reduced model.

• Hidden neurons: An iterative optimization process is performed on each hidden layer, varying from 1 to 25. The number of neurons per layer is based on the best accuracy obtained.

• Hidden layers: An incremental construction process of 1 to 4 layers is conducted. The best number of neurons from

the previous hidden layer is taken and is iteratively increased from 1 to 25 in the new hidden layer.

• Output neurons: Seven neurons that correspond to each class of migraine

• Transfer function: Logistics

• Performance metrics: Accuracy and precision

• Learning algorithm: Adam[2]

• Number of epochs: 2000

Logistic regression uses logistic regression regularization with built-in cross-validation, which automatically selects the best hyperparameters for model fit. A 10-fold and random restart model was used[3].

The SVM model uses the SVC function for classification, in which the fit time quadratically scales with the number of samples[4].

In the nearest neighbor model, the optimal number of neighbors is estimated based on the accuracy, and the Euclidean function with uniform weights is used as a distance measure.

The decision tree model included in the Scikit-learn library corresponds to an optimized version of CART (Classification and Regression Trees) that uses discrete numerical variables and where an iterative process is used to fit the number of levels based on accuracy.

In all cases, the dataset is divided into two sets: training and testing, the first corresponding to 80% of the data (320) and the second to 20% (80).

Results and discussion

Results were validated based on the type of migraine diagnosed by the treating physician and using the respective measurement made during the classification process provided by the neural network.

Table 2 presents the results of the performance measures for various neural network configurations and classification models. Precision, a metric calculated independently for each of the classes, is taken as the weighted average of the seven migraine classes.

The results presented in Table 2 indicate the following results:

• The maximum accuracy for both 23 and 18 variables is obtained by using a neural network model with 10 hidden neurons, which results in an accuracy of 97.5%. This means that the classification of migraines by the neural network coincides with that issued by the treating physician in 97% of the 80 cases comprising the test set.

• The neural network models show accuracies and precisions >90%, highlighting values obtained with the neural network model with 10 hidden neurons and a hidden layer for 23 variables and 20 hidden neurons for 18 variables, which reaches values >97% in both metrics, thereby indicating adequate classification.

• Those models with all variables have accuracies >80%, with the exception of the nearest neighbor model, which strongly demonstrates that the predicted values coincide with the real values, allowing for the correct classification of the different types of migraine in percentages >80%.

• The maximum average weighted precision was obtained with the neural network model with a layer of 20 hidden neurons that was reduced to 18 variables, which obtained a value of 98%; this indicates that there is a 98% probability that the model classifies the migraine within a certain type and that the treating physician has also classified it as such.

• The precisions obtained using logistic regression and SVM models do not differ greatly from the value obtained using neural networks, even exceeding them in complex neural network configurations with three and four hidden layers.

• Logistic regression, nearest neighbor, and decision tree models show better accuracy values when using models reduced to 18 variables.

• The values of accuracy and precision obtained using neural network models do not favor the increase of hidden layers, leading to reduction phenomena in both metrics as the number of hidden layers and neurons increases, which is representative of overlearning processes.

Comparison with previous studies

To assess the performance of the classification obtained by the best model proposed here, the performance was compared with that from previous studies. Table 3 presents the migraine classification results from previous studies using precision as a performance measure. The proposed neural network model with 10 neurons presents better values than those obtained from the previous studies, with a precision of 97% with all variables and 98% with reduction to 18 variables.

Conclusions

This study presents the development of a methodology for migraine classification using artificial neural network models. The results show that neural networks can achieve higher precision and accuracy than other classification models commonly used in machine learning, which is consistent with the results found when compared with various models proposed in the literature. The first experiments included 24 variables involved in migraine diagnosis, achieving a 97% precision

[2]arXiv:1412.6980

[3]https://scikit-learn.org/stable/modules/linear_model.html#logistic-regression

[4]https://scikit-learn.org/stable/modules/generated/sklearn.svm.SVC.html#sklearn.svm.SVC

Table 2. Results of the performance metrics of various neural network configurations and classification models.

Complete model with 23 variables			
Hidden Layers	**Internal configuration (number of hidden neurons)**	**Accuracy**	**Precision**
1	10	**0.975**	**0.97**
2	(10, 15)	0.9625	0.97
3	(10, 15, 15)	0.9375	0.95
4	(10, 15, 15, 25)	0.9375	0.94
Logistic regression		0,875	0.9563
Support vector machines		0.8625	0.9531
Nearest neighbor		0.7875	0.8719
Decision trees		0.8125	0.8100
Model reduced to 18 variables			
Hidden Layers	**Internal configuration (number of hidden neurons)**	**Accuracy**	**Precision**
1	20	**0.975**	**0.98**
2	(20, 25)	0.95	0.95
3	(20, 25, 25)	0.9375	0.92
4	(20, 25, 25, 20)	0.85	0.79
Logistic regression		0,925	0.9467
Support vector machines		0.85	0.8844
Nearest neighbor		0,825	0.8594
Decision trees		0.8578	0.8650

level for the neural network model. However, a second testing phase reduced the set of variables to 18, reaching a precision of 98%. This not only proves that the neural network model is effective for the proper classification of the different types of migraine but shows that it can also be improved by considering a reduced set of variables that significantly affect the classification.

The implementation of migraine classification through neural networks is a powerful tool whose potential has only incipiently been developed and which constitutes a valuable preliminary progress on the broad problem that automatic detection of migraines can encompass. The significance of this work lies in proposing an accurate and timely method of migraine classification that may support the diagnosis established by the treating physician based on an appropriate reading and identification of the primary and secondary symptoms that the patient presents and that results in the appropriate choice of treatment.

The main novelties are as follows:

• The development of a holistic methodology for migraine classification that encompasses selection of correct data and interpretation of the results obtained.

• The successful use of artificial neural network models for the classification of different types of migraines based on patients' symptoms, which use a database with data from patients who have experienced migraines and have been diagnosed by their treating physicians, resulting in a model that allows for the near-perfect distinction among the different types of migraine.

Table 3. Comparison of precision for migraine classifications reported in previous studies.

Reference study	Classification model	Precision
Migraine diagnosis support system based on classifier ensemble (Jackowski *et al.*, 2014)	LAD Tree	75.9%
Automatic diagnosis of primary headaches by machine learning methods (Krawczyk *et al.*, 2013)	Random Forest	81%
Analysis of repetitive flash stimulation frequencies and record periods to detect migraine using artificial neural network (Akben *et al.*, 2012)	ANN	83.3%
Classification of multi-channel EEG signals for migraine detection (Akben *et al.*, 2016)	SVM	85%
Effect of photic stimulation for migraine detection using random forest and discrete wavelet transform (Subasi *et al.*, 2019)	Random Forest	85.95%
Analysis of Artificial Neural Networks Models, for a System of Diagnoses of Migraines with Aura and without Aura (De la Hoz *et al.*, 2014)	ANN	91.04%
A clinical decision support system for the diagnosis of probable migraine and probable tension-type headache based on case-based reasoning (Yin *et al.*, 2015)	CBR	93.14%
This study	ANN (complete)	97%
This study	ANN (reduced)	98%

LAD - least absolute deviations, ANN – artificial neural network, SVM – support vector machine, CBR – case-based reasoning

In addition, increasing the number of patient records in the database can lead to more accurate results in migraine classification because it enhances learning.

Data availability

Underlying data

Code Ocean: Migraine Classification Model. https://doi.org/10.24433/CO.2826453.v1 (Sanchez-Sanchez *et al.*, 2020a)

This project contains the following underlying data:

- Migraine.cvs (Dataset contain medical records of patient with migraines)
- Migraine Dataset Description.txt (Description of data.)

Reporting guidelines

Zenodo: STARD checklist for 'Automatic Migraine Classification Using Artificial Neural Networks' http://doi.org/10.5281/zenodo.3872279 (Sanchez-Sanchez, 2020)

Software availability

Code for the model is available from Code Ocean: https://doi.org/10.24433/CO.2826453.v1 (code.ipynb)

License: GNU General Public License (GPL)

Ethical considerations

Ethical approvals

Data used in the recent study are the result of the master's thesis work of the author Juan Manuel Rúa Áscar, who had authorization for their academic use by the Hospital Materno Infantil de Soledad, in accordance with Colombian Law 1581 of 2012 and Decree 1377 of 2013 art. 10, which regulates the treatment of personal information and allows the use for scientific purposes, and that authorization is it extends for the current study.

Ethics approval for the use of the original data in the current study was obtained from Universidad Simón Bolívar Research Ethics Committee on 12 May 2020 (reference PRO-CEI-USB-CE-0328-00)

Consent

This research is not a clinical trial, and doesn't involve any direct patient contact. Anonymized retrospective data collected as part of routine clinical care are included. As a retrospective patient records study, consent was not requested from individual patients. In such cases the ICO code of practice states that explicit consent is not generally required.

Acknowledgments

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Reviewer Report 06 July 2020

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?

Shengyuan Yu
Medical School of Chinese PLA, Beijing, China

I have carefully read and thoroughly considered your manuscript, "Automatic migraine classification using artificial neural networks".

Our comments:

This is a meaningful idea to study the migraine classification by artificial neural networks. There are several significant problems with the description of the study and interpretation of the results.

First, the preface of the article is too wordy. We need not to describe the details of migraine as a reviews, including the epidemiology, diagnosis,differential diagnosis and treatment. In the preface, we should include the brief introduction of migraine and artificial neural networks,the current status of research on this subject, the problem in this field, why we do this study.

Second, the methods of study should include the Inclusion and exclusion criteria of the study. the reviews of classification progression of migraine should not included in this part,you can put it partial to the discussion.

Third, the discussion is too simple, we advice to discuss the present methods that using in the migraine classification and where is our comparative advantage, potential mechanism of the artificial neural networks using in the migraine classification. By the way, you can points out the direction of future research.

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Headache

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 10 Jul 2020

Paola Sanchez-Sanchez, Universidad Simón Bolívar, Barranquilla, Colombia

We appreciate the evaluation, which is very timely and pertinent. In response, and following the recommendations, a new version of the manuscript will be made

Competing Interests: No competing interests were disclosed.

Author Response 13 Jul 2020

Paola Sanchez-Sanchez, Universidad Simón Bolívar, Barranquilla, Colombia

We sincerely appreciate the reviewer feedback on this work and have improved the article based on your recommendations.
We have addressed each comment as follows in the article:
1. We rewrite the preface focusing the content on aspects relevant to research such as a short introduction to migraine, the current state of research in the area, the problems surrounding the classification of different types of migraine, how artificial neural networks help to solve the problems and why of this study.
2. The methods section is rewritten for better clarity in the writing. Clarifications are made regarding the inclusion and exclusion criteria, which are described in the results.
3. The discussion section was expanded to include the validation of the results with the different models applied, the significance of the results obtained, an account of some aspects that justify the development of classification models with artificial neural networks and the comparison with some studies previous. Likewise, the conclusions was expanded to include future research fields.

Competing Interests: No competing interests were disclosed.