A review of machine learning prediction methods for anxiety disorders

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ABSTRACT

Anxiety disorders are a type of mental disorders characterized by important feelings of fear and anxiety. Recently, the evolution of machine learning techniques has helped greatly to develop tools assisting doctors to predict mental disorders and support patient care. In this work, a comparative literature search was conducted on research for the prediction of specific types of anxiety disorders, using machine learning techniques. Sixteen (16) studies were selected and examined, revealing that machine learning techniques can be used for effectively predicting anxiety disorders. The accuracy of the results varies according to the type of anxiety disorder and the type of methods utilized for predicting the disorder. We can deduce that significant work has been done on the prediction of anxiety using machine learning techniques. However, in the future we may achieve higher accuracy scores and that could lead to a better treatment support for patients.

CCS CONCEPTS

• **Theory of computation** → **Machine learning theory**; • **Applied computing** → *Health care information systems*;

KEYWORDS

Machine learning, data mining, generalized anxiety disorder, panic disorder, agoraphobia, social anxiety disorder, posttraumatic stress disorder.

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1 INTRODUCTION

Anxiety disorders are the most common type of mental disorders. They constitute the largest group of mental disorders with a high societal and individual burden. Lots of patients with anxiety disorders experience physical symptoms related to anxiety and subsequently visit their primary care providers. In accordance with the Diagnostic and Statistical Manual of Mental Disorders, anxiety disorders include disorders that share features of excessive fear and related behavioral disturbances. The types of anxiety disorders are separated in Generalized Anxiety Disorder (GAD), Panic Disorder (PD), agoraphobia, Social Anxiety Disorder (SAD) and Post-traumatic stress disorder (PTSD) [28].

Anxiety is identified as an emotional integrity factor of the individual that is characterized by high complexity. A report conducted by the American Psychological Association [2], reveals that 18% of Americans are suffering anxiety disorders. In Europe, stress is the most frequent mental disorder affecting 16% of the total population [52]. Anxiety disorders cost the U.S. more than $42 billion a year, while in Europe the cost amounts to 74.4 billion Euros a year.

Furthermore, quality of life is closely related to emotional integrity factors of the individual that are characterized by high complexity. Stress is widely identified as one of these factors and vast research efforts have been made towards diagnosis and management. Since the evolution of computing technologies, these efforts are further supported by microelectronics and sensing devices, machine learning and data networks. Electroencephalogram [1] and electrocardiogram [50] signals acquisition, wearable body sensors [13] and data mining techniques [46] are only a few solutions proposed in the literature.

The diagnosis of anxiety disorders is a very complicated and challenging task. Therefore, one needs to be careful to diagnose them with high accuracy. Machine learning and data mining techniques can be utilized for analyzing patient's history to diagnose the problem, helping in copying the human reasoning or in making logical decisions. Some methods can even work upon uncertain or partial information using concepts of pattern matching, probability and other fields [3].

The rest of the paper is organized as follows. Section 2 introduces machine learning concepts and techniques in medical practice and prediction of mental health disorders while Section 3 presents the search strategy adopted in this review. Section 4 reviews the studies included in the review and Section 5 performs the analysis of the results. Finally, Section 6 concludes the paper discussing some issues for future research.

2 A REVIEW ON MACHINE LEARNING CONCEPTS AND TECHNIQUES

Supervised machine learning is the search for algorithms that reason from externally supplied instances to produce general hypotheses, which then make predictions about future instances [33]. More specifically, supervised classification techniques are a well-studied field of machine learning that makes use of structured (i.e. labeled) training data. The rest of this section describes in brief the major supervised learning algorithms and categories that are often met in the literature.

A Bayesian network is a probabilistic graphical model for representing a set of attributes or conditional dependencies among a set of attributes [22, 43].

Artificial Neural Networks (ANNs) are densely interconnected and adaptive processing units, with an inherent ability for learning from experience and discovering new knowledge [5].

Support Vector Machine (SVM) are supervised learning models appropriate for analyzing data used for classification and regression problems [51]. The learning procedure is based on a set of labeled training data and produces as output an optimal hyperplane which classifies new examples.

Decision trees are one of the most popular supervised learning algorithms able to predict the values of responses through decision rules derived from features. They are recursive and create models based on tree structures utilizing a set of training data and attempt to separate instances belonging to separate categories [32].

Linear regression (LR) is the most common method used for predictive analysis and explains the linear relationship between a dependent-outcome variable and one or more risk factors or confounding variables. The LR models are often preferred to more complicated statistical models because you can fit them relatively easily in contrast to other methods, such as nonlinear or nonparametric models which become computationally complicated and fail as the number of variables increase.

Neuro-Fuzzy Systems (NFSs) combine neural networks and fuzzy logic and can be trained to develop fuzzy rules and determine membership functions for input and output variables of the system. Kar et al. [23] presented an excellent survey about NFS development and applications in real-world problems.

The ensemble procedure improves the performance of single classifiers by combining the predictions of various learners. The most popular ensemble methods found in the literature are: voting [31], bagging [6] and stacking [53]. Random Forest (RF) is an ensemble algorithm which combines a group of random decision trees in a bagging ensemble [7].

Over the last years, hybrid machine learning methods, have gained the attention of the scientific community. Multiple learning techniques have been proposed that provide significantly better performance than single weak learners, especially while dealing with high dimensional, complex regression and classification problems [26]. The construction of a hybrid model is usually a two stage process [36]. The first stage applies classification techniques for data preprocessing (e.g. feature selection and dimensionality reduction techniques) [8, 40] while the second stage, uses the processed data as input on the second stage classifier.

2.1 Machine learning in medical practice and in prognosis of mental health disorders

Machine learning techniques have been extensively applied as a decision making support tool in the complex environment of health data analysis. Research efforts in healthcare informatics domain have proposed such systems that span from classifying electrocardiography (ECG) signals and regulation of glucose levels of diabetic patients to cancer diagnosis, home rehabilitation, diagnosis of Alzheimer's disease and mental health disorders [34]. Disease prediction is a newly studied research field mainly for two reasons. The first lies in the fact that health data analytics is a newly introduced field of study. The second one rests on the evolution of sensing and monitoring devices that are able to produce real (or near real) time, voluminous and high quality data for further processing. However, preliminary efforts in the field of data mining and machine learning techniques in health domain depict some promising results. In [42] the authors attempt a comparison of three prediction models of diabetes in terms of accuracy, sensitivity and specificity. The decision tree model exhibited the best accuracy that reached 77.87% based on 12 common risk factors. It is worth mentioning that diabetes is one of the most challenging chronic diseases in the 21st century and has attracted vast research efforts. Recent research on predicting stroke incidents, heart failure or different types of cancer prognosis can be found in [34].

The prevalence of mental health disorders is constantly increasing especially in children and youth population [44]. The same applies to stress disorders which are identified as the most commonly diagnosed mental disease regardless of age. However, to our knowledge mental health prediction mechanisms based on machine learning and data mining techniques have attracted little attention from the research community. Preliminary efforts have been devoted on the prognosis of dementia [14] through neurophysiological test and demographic data, bipolar disorders [15], panic disorder [19], social psychosis [18] based on neuroimaging data and sleep quality [48] from wearable medical sensors.

3 REVIEW METHODOLOGY

The main objective of this work is to study the efforts reported in the literature aiming to reduce the prevalence of anxiety disorders through effective early prediction, thus improving the quality of life of such patients, minimizing significant hospitalization and decreasing related health care costs. Accordingly, we pose three (3) research questions that drive our research process. More specifically, the outcomes of this work should develop our understanding on:

- Which prediction method managed to achieve the best classification accuracy, depending on the type of anxiety disorder?
- What is the most frequently utilized prediction method?
- What type of anxiety had gained the greatest interest?

A literature search was performed for studies published from 2010 till November 2017 and was accomplished in three stages. During the first stage, studies related to mental disorders and machine learning were included by reviewing their abstracts and titles. At the second stage, articles that were directly related to prediction of anxiety disorders using machine learning techniques were included by reviewing their full-text. Their reference lists were also checked, for extra related studies. The third stage, involved the thorough examination of the final included studies, in order to acquire essential information as for, the input data and measurements methods, the prediction methods and tools used for the experiments, the accuracy achieved and the conclusions drawn.

Additionally, we defined a set of strict inclusion criteria to minimize the risk of considering studies being out of scope of our review. More specifically:

- The review methodology was restricted to full papers written in English.
- The survey period covered a period of eight years spanning from 2010 till November 2017.
- The literature survey was conducted over the following databases: PubMed and Scopus.
- Only studies addressing the prediction of anxiety disorders applying machine learning techniques were eligible for consideration.

The database search yielded 155 studies (with duplicates removed). Initially 83 articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment. Of the 72 remaining articles 56 were excluded based on full text content leaving us with 16 studies which met the inclusion criteria.

Table 1 (where NoS implies Number of Studies and NoM implies Number of used Methods) aggregates the major characteristics of the articles included in the review. The majority of the articles considered in our review coped with PTSD (35.29%) and GAD (29.41%). The most applied methods are the Hybrid one and SVM. Despite that our search strategy included articles being published since 2010, the vast majority of the articles was published after 2014 (93.75%). Most of the studies enrolled less than 100 participants, while overall the number of participants is spanning from 5 to 89840.

Notice that although the studies included were sixteen (16), one of them [47], copes with the prediction of both SAD and PD & agoraphobia disorder types. Consequently, the subtotal of studies of anxiety disorder type characteristic is seventeen (17). Furthermore, in Table 1 we cannot provide any comparable prediction scores since the studies included employ two different methods on measuring the algorithms' prediction performance (see Section 5 Results Analysis), namely Accuracy and Area Under the Curve (AUC) score, which are not equivalent.

Studies characteristics		
Anxiety Disorder Type	**NoS**	**%**
GAD	5	29.41%
PD	1	5.88%
PD & Agoraphobia	1	5.88%
PTSD	6	35.29%
SAD	4	23.53%
Publication Year	**NoS**	**%**
2011	1	6.25%
2014	5	31.25%
2015	8	50.00%
2017	2	12.5%
Sample size	**NoS**	**%**
<100	9	56.25%
100-1000	5	31.25%
>1000	2	12.5%
Classification and prediction method	**NoM**	**%**
Bayesian networks	2	10%
Regression	1	5%
Hybrid methods	6	30%
SVM	5	25%
ANN	1	5%
Ensemble method	3	15%
Fuzzy systems	1	5%
Decision tree	1	5%

Table 1: Characteristics of studies included in review

4 PREDICTION MODELS OF ANXIETY DISORDERS

As mentioned in the introduction, the main types of anxiety disorders are classified in generalized anxiety disorder, panic disorder, agoraphobia, social anxiety disorder and Posttraumatic stress disorder [30]. The rest of this section summarizes the findings the studies classified by anxiety types.

4.1 Prediction of generalized anxiety disorders

Generalized anxiety disorder (GAD) is a condition where people suffer from excessive and inappropriate worrying that is persistent and not restricted to particular circumstances [35].

In [9], Chatterjee et al. propose a method of automatic anxiety prediction based on visually inferred heart-rate measurements. Multiple heart-rate variability descriptors were investigated along with the available information in the heart-rate variability. Also, they applied a probabilistic machine learning based approach to evaluate the descriptors with a categorization of a population from those suffering from anxiety disorders. The classifiers utilized in their study were Logistic Regression, Naive Bayes and a Bayesian Network. Their findings revealed that the Bayesian Network Model exhibit the highest accuracy, depicting 73.33% of successful classification.

Chen et al. [10] used self-esteem data measured at mean ages 13, 16 and 22, and anxiety disorder diagnosis at mean age of 33 to examine the impact of development of self-esteem on onset of adult anxiety disorder. The analysis was based on a Bayesian joint model with: a linear mixed effects model for the longitudinal measurements, and a generalized linear model for the binary primary endpoint. The comparison showed that the joint model has better predictive accuracy than a two-step model with area under ROC curve (AUC) 0.75 and 0.60, respectively.

Hilbert et al. [20] used machine learning on multimodal biobehavioral data from a sample of GAD (19 subjects), major depression (14 subjects) and healthy persons (14 subjects) to separate problematic subjects from healthy ones and discriminate GAD from major depression (without GAD). As input data, they used clinical questionnaires, cortisol release, gray matter, and white matter volumes. Binary SVM was applied within a nested leave-one-out cross-validation framework. The results indicated that the prediction of GAD was difficult using clinical questionnaire data alone whereas the inclusion of cortisol and gray matter volume data obtained 90.10% accuracy for case-classification and 67.46% accuracy for disorder-classification.

A neural network model was used by Dabek et al. [11] for the analysis of a dataset of 89840 patients. The reported classification was ranging from 73% to 95%, with an overall accuracy of 82.35%. Katsis et al. [25], proposed an integrated system based on physiological signals for the assessment of affective states in patients with anxiety disorders . This system objective is to predict an individual's affective state based on 5 predefined classes (neutral, relaxed, startled, apprehensive and very apprehensive). The classification algorithms used for this task were ANNs, RF, NFS and SVM and the best overall classification accuracy was achieved by NFS with a score of 84.3%. ANNs, RF, and SVM achieved a score of 77.33%, 80.83%, and 78.5%, respectively.

4.2 Prediction of PTSD

Posttraumatic stress disorder (PTSD) is recognized as a common anxiety disorder that often lasts for years and is associated with exposure to traumas [27].

Prediction in acutely traumatized children was attempted by Saxe et al. [49]. They employed machine learning techniques and the data were collected from 163 children hospitalized with an injury and PTSD was determined three months after hospital discharge. During hospitalization, the authors collected biopsychosocial risk factor variables and applied feature selection techniques to identify specific variables with putative causal relations to PTSD. They performed a comparative analysis of SVM, RF, Lasso, Logistic regression and Linear Regression as predictive classification models. The maximum AUC score achieved was 0.79 and 0.78 by SVM and RF, respectively.

Galatzer-Levy et al. [17] made an attempt to improve prediction of PTSD course using machine learning forecasting. The data was collected from 957 trauma survivors within 10 days of a traumatic event. The maximum AUC score achieved was 0.78 by SVM. Likewise, Karstoft et al. [24] identified group-level risk-indicators about portions of survivors. More specifically, the authors evaluated the potential of machine learning feature selection techniques to identify and integrate a panel of unique predictive characteristics and determine their accuracy in forecasting nonremitting PTSD from information collected within 10 days of a traumatic event. They pointed out that the existence of interchangeable sets of risk indicators can increase the efficiency of risk assessment and the use of machine learning can be efficiently applied for the prediction of PTSD.

An alternative approach for predicting PTSD was followed by Omurca and Ekinci [45]. The authors proposed a hybrid system of standard machine learning techniques such as MLP, NB and SMO to classify PTSD individuals but also allowed three popular feature selection methods such as chi-square, principal component analysis and correlation based-feature selection to determine important indications of patients' trauma. The accuracy achieved varied from 74% to 79%.

In study [29], Kessler et al. used a large sample based on the World Health Organization (WHO)'s World Mental Health Surveys, including 47466 traumatic experiences collected from24 countries. Machine learning methods (penalized regression, RF, super learner) were used to build a model for PTSD prediction. The results revealed that, RF and Super learner methods achieved the highest AUC score with 0.96 and 0.98 at full sample, whereas at subsample with no prior PTSD achieved 0.97 and 0.96 respectively. Liu et al. in [38] applied fMRI on 20 PTSD patients and 20 demographically matched healthy controls for their experiment. The results showed that the features of each level could successfully distinguish PTSD patients from healthy controls. Moreover, the combination of multi-level features using multi-kernel learning can lead to an improvement of the classification performance with SVM achieving a score of 92.5%.

4.3 Prediction of SAD

SAD is a chronic and disabling disorder associated with low quality of life, serious malfunction and psychiatric comorbidity [12] and the standard treatments are Cognitive Behavioral Therapy (CBT) and pharmacotherapy.

Liu et al. [37] investigated the potential of the functional connectivity to be used for SAD diagnosis. They recruited twenty patients with SAD and twenty healthy controls who were scanned using resting-state fMRI. Subsequently, multivariate pattern analysis was used to classify patients from healthy controls. The pattern classifier was designed using linear SVM. The experimental results revealed a classification rate of 82.5%. In a similar study, Frick et al. [16] tried to study the possibility to discriminate SAD patients using SVM, fMRI and regional gray matter volume. SVM capitalizes on brain activation and structural patterns to classify individuals. The results revealed a significant balanced accuracy of 72.6% proving that SVM may be useful for identifying imaging biomarkers of SAD. Linear SVM was used by Zhang et al. [54] to predict SAD. Forty 40 patients with SAD and 40 healthy controls were recruited in this classification study and the prediction accuracy achieved was 76.25%. Pantazatos et al [47] made a combined fMRI and SVM approach to predict SAD on sixteen subjects with SAD and nineteen healthy controls. The maximum AUC score achieved was 0.89. Moreover, a discrimination between PD and SAD patients was attempted with a AUC score of 0.82.

Authors	Measurements - Input data	Classification and prediction methods	Main findings
Chatterjee et al. [9]	Visually inferred heart-rate measurements.	Logistic Regression, Naive Bayes and a Bayesian Network	The highest achievable prediction accuracy was 73.33% with the Bayesian Network model.
Chen et al. [10]	Self-esteem data measured at mean ages 13, 16 and 22, and anxiety disorder diagnosis at mean age of 33.	Bayesian joint model with a linear mixed effects model and a generalized linear model.	The comparison showed that the joint model has better prediction accuracy than a two-step model with 75% and 60% respectively.
Dabek et al. [11]	Dataset of 89.840 patients.	ANN	Achievable overall prediction accuracy was 82.35%.
Katsis et al. [25]	N/A	ANN, RF, NFS and SVM.	The best overall prediction accuracy achieved was for NFS reaching 84.3%, whereas ANN, RF, and SVM achieved 77.33%, 80.83%, and 78.5%, respectively.
Hilbert et al. [20]	Clinical questionnaires, cortisol release, gray matter and white matter volumes.	SVM within a nested leave-one-out cross-validation framework.	Classification of GAD was difficult using clinical questionnaire data alone whereas particularly cortisol and gray matter volume data managed to improve the classification of GAD. With all data combined SVM achieved 90.10% accuracy to differentiate subjects with a disorder from healthy subjects and 67.46% to differentiate GAD from major depression.

Table 2: Studies characteristics of the GAD disorder type

Authors	Measurements - Input data	Classification and prediction methods	Main findings
Saxe et al. [49]	163	Hybrid method (Feature selection with SVM, RF, Lasso, LR)	The prediction accuracy achieved was 79%.
Galatzer-Levy et al. [17]	957 trauma survivors within 10 days of a traumatic event	Hybrid method (Feature selection + SVM, RF, Adaboost, RBF)	The maximum score achieved was 78.
Karstoft et al. [24]	A portion of trauma survivors	Hybrid method (Feature selection + SVM)	Target Information Equivalence Algorithm maximized the prediction of PTSD when incorporated in a support vector machine. The mean AUC was 0.75.
Omurca and Ekinci [45]	391 subjects	Hybrid method (Feature selection + SVM, ANN, NB)	The prediction accuracy achieved was 74%-79%.
Kessler et al. [29]	47466 traumatic experiences exposures in 24 countries	Penalized regression, RF, ensemble method (super learner)	RF and super learner methods achieved the highest AUC score with 0.96 and 0.98 at full sample, whereas at sub-sample with no prior PTSD achieved 0.97 and 0.96 respectively.
Liu et al. [38]	fMRI on 20 PTSD patients and 20 demographically matched healthy controls	Hybrid method (Feature selection + SVM)	The combination of multi-level features using multi-kernel learning can lead to an improvement of the classification performance. The prediction accuracy achieved was 92.5%.

Table 3: Studies characteristics of the PTSD disorder type

Authors	Measurements - Input data	Classification and prediction methods	Main findings
Liu et al. [39]	Twenty patients with SAD and 20 healthy controls were scanned using resting-state fMRI	Hybrid method (Feature selection + SVM)	The experimental results revealed a prediction accuracy of 82.5%.
Frick et al. [16]	fMRI and regional gray matter volume	SVM	A significant balanced prediction accuracy of 72.6% was achieved proving that SVM may be useful for identifying imaging biomarkers of SAD.
Zhang et al. [54]	40	SVM The prediction accuracy achieved was 76.25%.	
Pantazatos et al. [47]	35	SVM	The prediction accuracy achieved was 89%.

Table 4: Studies characteristics of the SAD disorder type

Authors	Measurements - Input data	Classification and prediction methods	Main findings
Pantazatos et al. [47]	32	SVM The prediction accuracy achieved was 82%.	
Lueken et al. [41]	fMRI	Random under sampling tree ensemble in a leave-one-out cross-validation framework	Comorbid depression was successfully predicted in 79% of patients and the prediction accuracy was 73%.

Table 5: Studies characteristics of the PD & Agoraphobia disorder type

4.4 Prediction of PD and agoraphobia

Panic Disorder (PD), is characterized by unexpected periods of intense fear and patients who suffer from PD is very probable (about one-third to one-half) to also suffer from agoraphobia, which is associated with the avoidance of certain places or situations [4].

In [41] Lueken et al. adopted a combined fMRI and machine learning approach to separate depressive comorbidity from PD (comorbid depression is frequent in panic disorder with agoraphobia). They investigated the impact of comorbid depression in PD with agoraphobia on the neural correlates of fear conditioning and the ability of machine learning to predict comorbidity status. The method they used was to predict comorbidity status with a random under sampling tree ensemble in a leave-one-out cross-validation framework. The study resulted in successfully predicting 79% of the patients and the relevant accuracy was 73%.

5 RESULT ANALYSIS

Tables 2-5 summarize all sixteen (16) included studies for prediction of anxiety disorders. The reviewed studies employ two different metrics for measuring the algorithms' prediction performance, namely Accuracy and Area Under the Curve (AUC) score. These two metrics are not directly comparable while Huang and Ling [21] justified that AUC is a more concrete optimization measure compared to accuracy.

Tables 2-5 designate that, ANNs managed to achieve the highest prediction score compared to the other methods used for the prediction of GAD. Additionally, super learner method achieved the highest score for the prediction of PTSD. Moreover, we noticed that Hybrid methods and support vector machine were the most frequently used methods for PTSD and SAD. Lastly, the fMRI tool was exclusively used for the creation of input data in SAD, PD and agoraphobia.

6 CONCLUSIONS

In summary, we deduce that significant work has been done on the prediction of anxiety disorders using artificial intelligence and data mining. Several machine learning techniques have been utilized to develop accurate prediction models in order to assist in providing better medical services.

We observed that Hybrid methods and SVM was the most highly used methods especially for the prediction of PTSD and SAD respectively. Moreover, ANNs and ensemble methods performed very well, managing to achieve the highest prediction scores. RF and NFS had some good scores too. Furthermore, we saw that the combination of multi-level features using multi-kernel learning can lead to an improvement of the classification performance for predicting PSTD. However, in all those cases where the dataset size is too small, not available (N/A), or not explicitly mentioned in the respective article, one cannot verify with any degree of certainty the classification accuracy reported as achieved by the authors of the article. In future work, an improvement regarding to which method is better to use depending on the type of anxiety disorder and how each type affects each method, is worth investigating. Also, by experimenting with other methods and approaches, we may achieve even higher scores for the prediction of anxiety and that could lead in a better treatment support for patients.

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