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Machine Learning in Pain Medicine: An Up-To-Date Systematic Review

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ABSTRACT

Introduction: Pain is the unpleasant sensation and emotional experience that leads to poor quality of life for millions of people worldwide. Considering the complexity in understanding the principles of pain and its significant impact on individuals and society, research focuses to deliver innovative pain relief methods and techniques. This review explores the clinical uses of machine learning (ML) for the diagnosis, classification, and management of pain.

Methods: A systematic review of the current literature was conducted using the PubMed database library.

Results: Twenty-six papers related to pain and ML research were included. Most of the studies used ML for effectively classifying the patients' level of pain, followed by use of ML for the prediction of manifestation of pain and for pain management. A less common reason for performing ML analysis was for the diagnosis of pain. The different approaches are thoroughly discussed.

Conclusion: ML is increasingly used in pain medicine and appears to be more effective compared to traditional statistical approaches in the diagnosis, classification, and management of pain.

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Key Summary Points
Machine learning techniques for classifying patients' levels of pain are effective.
Machine learning techniques can be used for the classification, manifestation, diagnosis, and management of pain.
Machine learning is increasingly used in pain medicine.

INTRODUCTION

Pain is a complex somatic and emotional phenomenon. Causes of pain are numerous and include traumas, medical diseases, and genetic disorders [1–4]. The universality of pain as a human experience and the high prevalence of pain underscore the significance of this symptom, while its complexity attracts significant attention from the research community to fully comprehend this experience.

A variety of pharmacological and non-pharmacological approaches have been used for the treatment of pain. Most pain management practices are put in place by medical and nursing staff. This highlights the imperative need to inform this community of professionals on innovative pain relief methods and techniques.

Machine learning (ML) is the use of data and algorithms to imitate the process of human thinking and learning. ML uses a set of methods to automatically detect patterns in big data to gradually inform and improve the algorithm's accuracy. Then the patterns are used to classify, predict, or extract information from future data from which the algorithm derives new knowledge. In particular, algorithms are trained to produce classifications or predictions, uncovering key insights in data mining projects through the use of statistical methods. Subsequently, these insights influence decision-making impacting key growth metrics. It is worth mentioning that these are accomplished utilizing supervised (i.e., labelled data), semi-supervised (i.e., within a large amount of unlabelled data, a small amount of data are labelled), unsupervised (i.e., unlabelled data), or reinforcement (i.e., develops patterns based on trials and errors) learning, which indicates the ability of the algorithm to independently discover, adapt, and respond to unscripted patterns and groups of data [5–7]. On the basis of the nature of the data, different techniques are used in ML analysis. The most common techniques are classification for supervised data (e.g., predict and categorize specific data, like the type of pain) or regression for semi-supervised and unsupervised data (e.g., predict a reaction that can cause pain, without having a prior

knowledge of that reaction). The most common ML algorithms discussed in this review are presented in Table 1.

With this systematic review, we are mostly interested in exploring the clinical uses of ML related to pain. For the purpose of this review, the following specific research questions were addressed:

1. Is ML an effective solution for classifying, predicting manifestation, and managing pain?
2. What are the ML techniques mostly used in pain medicine?
3. What are the future directions of ML?

METHODS

Protocol Registration

This review was registered in PROSPERO (registration number CRD42021248001), an international database of prospectively registered systematic reviews in the context of health and social care.

Compliance with Ethics Guidelines

This article is based on previously conducted research and does not contain any studies with human participants performed by any of the authors. Therefore, ethical approval was not required.

Literature Review Strategy

A systematic literature search of the PubMed database was performed on 15 July 2021 using three Medical Subject Heading (MeSH) terms that had to be present in the title. Term A was "Machine Learning" OR "Support Vector Machines" OR "Neural Networks" OR "Deep Learning" OR "Multi-Layer Perceptrons" and term B was "Pain" OR "Painful". No filter was applied. The reference lists of articles that met the eligibility criteria were further perused to identify additional studies that may fall within the scope of this review.

Table 1 Machine learning algorithms that have been used in pain medicine to date

Machine learning algorithm	Characteristics
Bayes [17, 19, 20, 22]	Estimates the probability of data patterns belonging to a specific class
Boosting: functional data boosting (FDboost) [13]; gradient boosting (GB) [24, 28]; extreme gradient boosting regression (XGBoost) [27, 31]	Merges weak classifiers into strong ones
Deep learning neural network (DLNN) [10, 11, 14, 16, 18, 34, 35]	Similarly to multiple linear regression it contains layers of interconnected nodes. A subclass of NN is the convolutional neural network (CNN)
Decision trees (DT) [14, 22, 29, 34]	Gradually reject classes assigned into multistage decision systems to accept a final class. In pain medicine, decision trees algorithms such as classification and regression trees have been used
k-means clustering [14]	Divides a number of data points into a number of clusters based on the nearest mean
k-nearest neighbors (kNN) [10, 22, 24, 27, 29, 32]	Assigns data patterns to a class on the basis of the distance to the training patterns of a certain class
Multilayer perceptron (MLP) [9, 22]	Trains on a set of input data patterns to predict/classify the output class
Random forest (RF) [14, 15, 28, 29, 31, 32]	Builds and merges multiple decision trees to provide a more accurate prediction
Regression: kernel ridge regression (KRR), [30]; elastic net (EN) [23, 28]; generalized linear mixed-models (GLMMs) based on repeated data points, Lasso [15, 24]; least square (LS) [28]; linear regression (LiR) [27, 33]; logistic regression (LoR) [10, 15, 29, 31, 32]; ridge regression (RR) [28]	Predicts the probability of agreement using continuous data points
Support vector machine (SVM) [9, 12, 15, 21, 22, 25–27, 29, 32, 34]	Creates a hyperplane to separate two classes. The hyperplane is found by optimizing a cost function
Multi-subject dictionary learning (MSDL) [16]	It is a feature learning method where a training example is represented as a linear combination of basic functions, and is assumed to be a sparse matrix

Inclusion and Exclusion Criteria

Studies eligible to be included in this review had to meet the following inclusion criteria: (1) human subjects were involved; (2) the full article was written in English; (3) papers studied ML in pain medicine.

The exclusion criteria were (1) publications where the study of pain was not the primary aim of the study; (2) publications that were not original studies (i.e., review articles, letters,

medical hypotheses, etc.); (3) publications where ML method was not used for pain assessment; (4) publications presented trials with fewer than ten patients per treatment arm; (5) publications presented trials studying subjects less than 18 years old; (6) duplicate publications or studies referring to the exact same population; (7) publications whose abstract was not accessible; (8) publications whose full text could not be obtained.

Data Collection Process

Following identification of the eligible publications, all relevant data were collected in a structured coding scheme using an Excel file. On the basis of the aim of each study, included papers publications that used ML for pain were grouped into the following categories: (1) pain classification; (2) pain diagnosis; (3) prediction of pain manifestation; (4) pain management. The data collected included demographics, the type of pain, the ML technique, the input data size, the instruments, the results, and the level of accuracy in each ML approach. When there was uncertainty regarding how the data should be interpreted or utilized, a cross reliability test between three authors was performed.

Data Synthesis

This study used aggregated data where possible, in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [8].

RESULTS

Search Results

This search strategy resulted in the identification of 100 articles. After the eligibility assessment, 78 articles were excluded. A further four

Term A
Machine Learning or Support Vector Machines or Neural Networks or Deep Learning or Multi-Layer Perceptrons

Term B
pain OR painful

100 publications identified by the systematic search through PubMed database

58 publications excluded at the abstract screening process

29 publications where pain was not the primary aim
21 publications were not original papers
1 publications where abstract was not available
4 publications studied underage population
3 publication not studying human subjects

42 full-text publications retrieved for full text eligibility assessment

20 publications excluded at the full-text screening process

7 publications where pain was not the primary aim
3 publications studied other types of methods (not ML)
2 publications studied underage population
1 publication with less that10 subjects
1 publication not studying human subjects
1 publication was not in English
2 publications was referring to the same population
3 publication where full text was not available

4 articles were identified through screening the reference lists of included papers

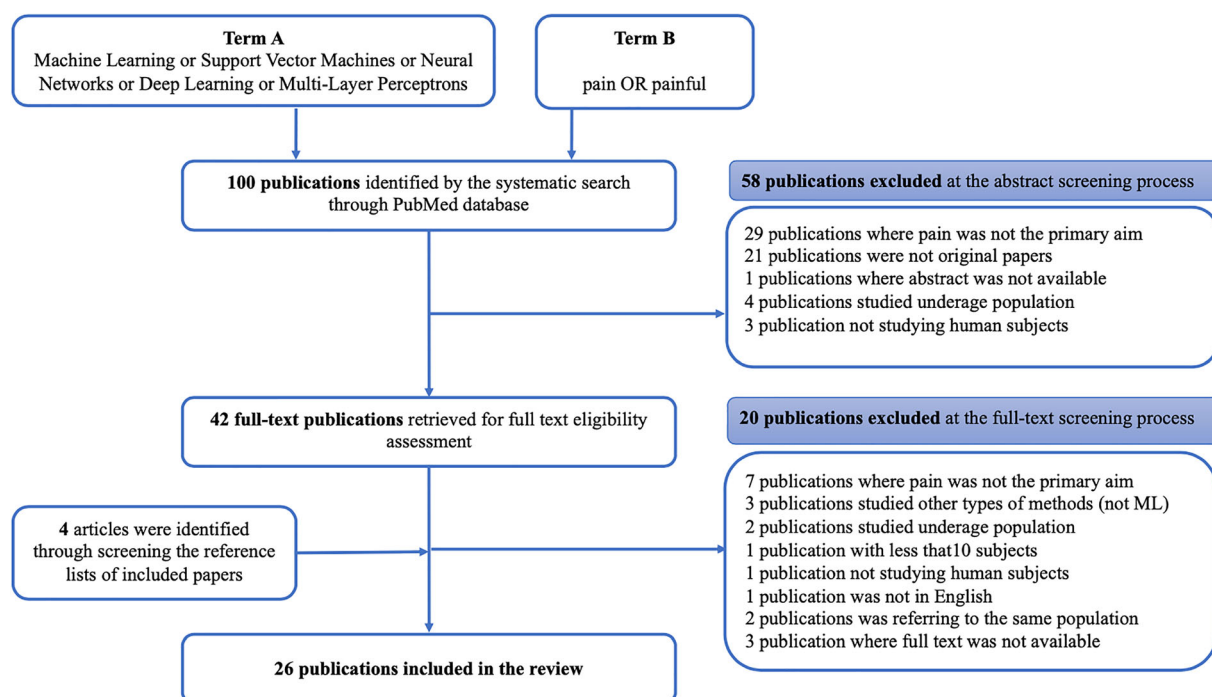**26 publications included** in the review

Fig. 1 PRISMA chart

articles were identified through manually perusing the reference lists of the included articles. In total, 26 papers met the inclusion criteria and were used for this review [9–34]. These studies were published between 2015 and 2021. Figure 1 (PRISMA chart) illustrates the study selection process.

Effectiveness of ML in Pain Classification, Diagnosis, Manifestation, and Management

Table 2 presents the characteristics of the studies, including the ML method that was applied and the respective results.

ML techniques for classifying the intensity of pain were found to be effective in patients with low back pain (LBP) [9, 12, 13, 16], osteoarthritis [21], ankylosing spondylitis [30], spinal cord injury [26], thoracic pain[29], sickle cell disease (SCD) [32], evoked heat pain [25, 27], and other types of pain [15]. In their case-controlled study, Abdollahi et al. classified pain based on quantitative kinematic data. In their case-controlled study, Liew et al. collected electromyographic and kinematic data which were used to classify pain [13]. Brain functional imaging and autonomic activity (i.e., heart rate variability) data were collected by Lee et al. after back pain exacerbation maneuvers to measure pain intensity with the aid of support vector machine (SVM) [12]. In their case controlled study, Santana et al. used functional magnetic resonance imaging (fMRI) data in 60 patients with chronic pain (36 subjects with fibromyalgia and 24 subjects with low back pain) and 98 pain-free controls in order to compare the performance of different ML models in pain classification and found that CNN, which assessed data using the MSDL probabilistic atlas, was the most efficient with balanced accuracy ranging from 69% to 86% [16]. In two studies, EEG data have been used for pain classification in patients with osteoarthritis [21] and in patients with pain due to spinal cord injury [26]. Overall, the results of these studies suggested that supervised ML algorithms can accurately classify the intensity of pain regardless of its type. For more accurate results, it was suggested to

compare patients' responses with responses collected by healthy individuals [26]. In a case series study, Rojas-Mendizabal et al. performed an analysis of 27 variables, which included demographic and clinical parameters, in order to evaluate the origin of thoracic pain and determine a possible correlation between these parameters and the presence of cardiac pain, managing to obtain a mean accuracy of 96% [29]. Rogachov et al. acquired resting-state functional MRI and quantified frequency-specific regional low-frequency oscillations (LFOs) in patients with chronic pain and ankylosing spondylitis and, using an ML approach, found that higher frequencies can be used to make generalizable inferences about patients' average pain ratings (trait-like pain) but not current (i.e., state-like) pain levels [30]. These results were also validated with healthy individuals, revealing higher brain signal variability in the dynamic pain connectome [30]. Pouromran et al. evaluated electrophysiological data of evoked heat pain from healthy subjects via different ML methods in order to predict the pain intensity and found that electrodermal activity using a support vector regression (SVR) model gave the best performance with an accuracy of 83% [27]. In their study, Gruss et al. using biopotential data and an SVR model estimated the evoked heat pain intensity and characterized the pain patterns with an accuracy of over 90% [25]. Yang et al. used physiological measurements for 40 patients with SCD to predict their pain intensity by applying different ML methods [32]. Multinomial logistic regression (MLR) illustrated the best performance on pain prediction with a mean accuracy of 0.578 at the intra-individual level and a mean accuracy of 0.429 at the inter-individual level. Finally, a study suggested that to increase the positive outcomes of ML on pain, the predictive models of pain should consider other variables like sleep patterns which can be associated with the experience of pain, offering an accuracy of 81% [14].

Grauhan et al. used CNN for the effective diagnosis of the cause of shoulder pain on 2700 plain radiographs (X-rays) with the best accuracy to be for osteoarthritis (87%), even when presented with poor image quality [30]. Santra

Table 2 Summary characteristics of pain studies included in this review

Study	Type of pain	Study population	Use of ML	Main findings
Abdollahi 2020 [9]	Low back	94 patients, age 20–50 years	Classification	ML can effectively classify pain intensity based on quantitative kinematic data
Lee 2019 [12]	Low back	53 patients, age 18–60 years	Classification	ML can effectively classify intensity of evoked pain
Liew 2020 [13]	Low back	33 patients and 16 controls, age 18–55 years	Classification	ML can effectively classify pain intensity using electromyographic and kinematic data
Rahman 2018 [15]	Various causes	782 patients	Manifestation	ML can effectively measure and predict pain volatility
Santana 2019 [16]	Low back fibromyalgia	60 patients and 98 controls, age 18–55 years	Classification	ML can effectively classify pain intensity using fMRI data
Snyder 2021 [18]	Low back	10 subjects	Manifestation	ML can classify the relative risk of low back pain due to lifting activities, using gyroscope and accelerometer data
Kimura 2021 [21]	Osteoarthritis	23 patients, age 44–80 years	Classification	ML can effectively classify pain using EEG data
Levitt 2020 [26]	Spinal cord injury	37 patients and 20 controls, age ≥ 25 years	Classification	ML can effectively classify pain using EEG data
Rojas-Mendizabal 2021 [29]	Thoracic	256 patients	Classification	ML can effectively classify pain using demographic and clinical data
Gruss 2015 [25]	Evoked heat pain	85 subjects, age 18–65 years	Classification	ML can effectively classify evoked pain using biopotential data
Santra 2020 [17]	Low back	30 patients	Diagnosis	ML can effectively diagnose the cause of low back pain
Rogachov 2018 [30]	Ankylosing spondylitis	71 patients and 62 controls, age 18–61 years	Classification	ML can effectively classify pain using fMRI data
Grauhan 2021[11]	Shoulder	2442 patients	Diagnosis	ML can effectively diagnose the cause of shoulder pain analysig plain X-rays
Darvishi 2017 [10]	Low back	92 patients and 68 controls, age 29–50 years	Manifestation	ML can predict development of work-related low back pain
Miettinen 2021 [14]	Various causes	277 patients, age 18–77 years	Classification	ML can effectively predict pain based on sleep patterns

Table 2 continued

Study	Type of pain	Study population	Use of ML	Main findings
Fernandes 2017 [20]	Osteoarthritis	1822 subjects, age 40–79 years	Manifestation	ML can effectively predict pain manifestation in community-based population using clinical data
Lotsch 2020 [22]	Rheumatoid arthritis	288 patients, age 18–70 years	Manifestation	ML can effectively predict pain manifestation using demographic and clinical data
Tighe 2020 [24]	Post-surgery	8071 subjects, age > 21 years	Manifestation	ML can effectively predict acute pain manifestation using clinical data
Tan 2020 [31]	Labor	20,716 subjects	Manifestation	ML can effectively predict pain manifestation during labor using clinical data
Juwara 2020 [28]	Cancer	195 subjects, mean age 56 years	Manifestation	ML can effectively predict manifestation of neuropathic pain using clinical data
Goldstein 2020 [33]	Low back pain	65 patients, age 21–70	Manifestation	ML can effectively predict pain manifestation based on clinical data
Yang 2018 [32]	Sickle cell disease	40 patients	Classification	ML can predict pain intensity using physiological parameters
Pouromran 2021 [27]	Evoked heat pain	87 subjects, age 18–65 years	Classification	ML can predict pain intensity using electrophysiological parameters
Parthipan 2019 [23]	Post-surgery	4306 subjects, mean age 58 years	Management	ML can effectively predict the required opioids dose for pain management
Ahn 2018 [19]	Osteoarthritis	40 patients, age 50–70 years	Management	ML demonstrated the effect of transcranial direct current stimulation (tDCS) in the management of pain
Wang 2021 [34]	Cancer	746 subjects	Management	ML can effectively predict whether patients should receive local treatment for pain due to bone metastases

et al. used Bayesian networks to resolve diagnostic conflicts for the cause of LBP [17].

Prediction of manifestation of pain was also one of the commonest reasons for performing ML analysis. In a case control study, Darvishi et al. compared the neural network model approach with the logistic regression model approach in 92 workers with LBP and 68 healthy workers and showed that the former can predict more effectively the development of LBP [10]. Goldstein et al. built a mobile platform to predict patients' pain levels after a period of 2 weeks based on self-reported pain ratings and emotional state and found that a previous history of pain and fatigue are good predictors of pain [33]. In an open-label trial, Snyder et al. used a deep CNN model with which they used gyroscope and accelerometer data and classified the relative risk that lifting activities have for the development of back pain and injury, achieving an accuracy of 91% compared to an alternative CNN and multilayer perceptron (MLP) [18]. ML techniques were found to be effective in predicting even in real-time pain occurrence in a large cohort of postoperative patients, using numerous clinical variables retrieved through surgical records [24], which accurately helped the clinicians to provide the

patient with appropriate pharmacological analgesics [24, 31]. This was done via self-reported data such as pain intensity scales, emotional responses, quality of life, and an indication of the pain areas. Fernades et al., using a Bayesian modelling approach, developed a risk prediction model based on clinical parameters for the development of knee pain, regardless of underlying structural changes of knee osteoarthritis, which appeared to work well in a community-based population [20]. Lötsch et al. analyzed demographic, patient-rated, and objective clinical factors and using ML identified early parameters that provided information about a future development of persistent pain in rheumatoid arthritis [22]. Juwara et al. identified baseline clinical data as predictive factors for neuropathic pain after breast cancer surgery using machine learning [28]. Finally, one study focused on measuring and predicting pain volatility, which was defined as the mean of absolute changes between two consecutive self-reported pain severity scores recorded via a mobile application [15].

Lastly, it was also demonstrated that ML for pain management has also been a key sector since it is empowering the reduction of negative body sensations and pain. Parthipan et al. studied the treatment of pain via prediction and prescription of the required opioid dose for managing pain due to osteoarthritis or post-surgery [23]. In their study, Ahn et al. used ML to demonstrate the effect of transcranial direct current stimulation (tDCS) in the management of pain [19]. In their study, Wang et al. developed and tested ML models to predict which patients with lung cancer and pain due to bone metastases should receive local treatment and found that a decision tree (DT) model was the most effective and accurate method for that aim [34].

ML Techniques

In the studies evaluated, a wide variety of ML algorithms were used. Most of these algorithms were supervised classification or regression techniques to address issues related to pain. The selected studies used mostly classical ML

algorithms, such as SVM [9, 12, 15, 21, 22, 25–27], and random forest (RF) [14, 15, 28, 29, 31, 32] followed by Bayes [17, 19, 20, 22] techniques to classify tasks by assigning a predefined class label to an observation.

Numerous types of regression ML algorithms were also used by the reviewed studies [10, 15, 23, 27, 28, 30, 32]. This type of ML algorithm outputs continuous numerical values, rather than assigning a predefined class label to a data pattern.

Most of the reviewed studies used this ML technique to classify the patient's intensity of pain [9, 12, 14, 15, 21, 22, 28]. On the other hand, most of the reviewed studies which used the regression ML algorithms mostly predicted pain occurrence, probability, volatility, and management response, via a continuous set of data [10, 15, 23, 27, 28, 30, 32].

The best performing ML algorithms were a boosting (i.e., FDboost), a regression (i.e., Elastic Net), and a neural network (NN), all three of which achieved a classification accuracy of more than 90% [10, 13, 23]. The worst performing ML algorithm was a k-nearest neighbors (kNN), which achieved a 52% accuracy [32]. Table 3 presents the data sources and size along with the ML methods and their accuracy.

DISCUSSION

More than half of the studies included in this review were published since 2020, which indicated that the use of ML for pain has increased over time. ML has been shown to be successful in learning how to map complex features to a known class.

The large number of papers in this literature review shows that the use of ML in research on pain has been of great importance and is considered to be highly beneficial for classifying, predicting, diagnosing, and managing pain This is because the amount of health-related data is rapidly expanding and large amounts of data are stored in clinical systems (i.e., a result of the advances in health technologies deployed in the medical sector) and personal consumer

Table 3 Data sources and size, ML methods, and percentage accuracy

Study	Data input	Data sources/instruments	ML methods	ML methods' accuracy (%)	Sensitivity	Specificity	Validation	Number of classes
Abdollahi 2020 [9]	4	Kinematics, inertial measurement units—range of movement, balance, self-reported data	SVM, MLP	SVM = 75%, MLP = 60%	SVM = 59%, MLP = 51%	SVM = 52%, MLP = 54%	Leave-one-participant-out cross-validation	3 classes classification of pain risk groups: low, medium, and high
Darvishi 2017 [10]	4	Self-reported data	kNN, LoR, NN	kNN = 81%, LoR = 83%, NN = 92%	Not reported	Not reported	Training/testing	2 classes of "healthy individuals" and "individuals with LBP"
Grauhan 2021 [11]	6	Radiography data	CNN	CNN = 81%	CNN = 80%	CNN = 82%	Training/testing	4 classes of shoulder pain: osteoarthritis; calcification; dislocation; fracture
Lee 2019 [12]	7	Functional magnetic resonance imaging (fMRI)	SVM	SVM = 81%	SVM = 50%	SVM = 50%	Leave-one-patient-out cross-validation	2 classes of relatively lower pain and higher pain
Liew 2020 [13]	10	Electromyographic (EMG), kinematics	FD Boost	FDBoost = 92%	Not reported	Not reported	Cross-validation	Numerical rating scale (NRS) (0 no pain, 10 being maximal pain)

Table 3 continued

Study	Data input	Data sources/ instruments	ML methods	ML methods' accuracy (%)	Sensitivity	Specificity	Validation	Number of classes
Miettinen 2021 [14]	6	Self-reported data	CART, PART, RF	CART = 80%, PART = 80%, RF = 81%	CART = 63% PART = 56% RF = 66%	CART = 83% PART = 92% RF = 85%	Cross validation	3 pain phenotype classes: lowest pain intensity and pain interference; moderate pain intensity and pain interference; high pain intensity and pain interference
Rahman 2018 [15]	13	Self-reported data	LASSO, LoR, RF, SVM	LASSO = 72%, LoR = 69%, RF = 70%, SVM = 63%	Not reported	Not reported	Fivefold cross-validation	2 classes of low and high pain volatility
Santana 2019 [16]	21	fMRI data	CNN	CNN = 87%	Not reported	Not reported	k-fold cross-validation	2 classes of yes or no chronic pain

Table 3 continued

Study	Data input	Data sources/instruments	ML methods	ML methods' accuracy (%)	Sensitivity	Specificity	Validation	Number of classes
Santra 2020 [17]	15	Self-reported data	Bayes	Bayes = 71%	Not reported	Not reported	Training/testing	5 classes of different LBP: SIJA (pain from sacroiliac joint); FJA (pain from lumbar facet joints); DP (pain from the disc); PIVD (pain from the nerve roots adjacent to vertebral body); PS (myofascial pain from piriformis muscle)
Snyder 2021 [18]	6	Inertial measurement unit sensors	CNN	CNN = 91%	Not reported	Not reported	Cross-validation	3 classes of low, medium and high risk of back injury

Table 3 continued

Study	Data input	Data sources/instruments	ML methods	ML methods' accuracy (%)	Sensitivity	Specificity	Validation	Number of classes
Ahn 2018 [19]	4	NeuroSensory analyzer, pressure algometer	Bayes	Bayes = 75%	Not reported	Not reported	Training/testing	2 classes of higher experimental pain sensitivity and lower experimental pain sensitivity
Fernandes 2017 [20]	6	Self-reported data	Bayes	Bayes = 70%	Bayes = 95%	Bayes = 32%	Testing	2 classes of knee pain and no knee pain
Kimura 2021 [21]	9	Electroencephalography (EEG), self-reported data	SVM	SVM = 80%	Not reported	Not reported	Testing	2 classes of hip pain and no hip pain
Lotsch 2020 [22]	12	Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), swollen joint count (SJC), tender joint count (TJC), self-reported data	Bayes, CART, kNN, MLP, SVM,	Bayes = 70%, CART = 71%, kNN = 72%, MLP = 70%, SVM = 70%	Bayes = 36%, CART = 43%, kNN = 45%, MLP = 31%, SVM = 39%	Bayes = 78%, CART = 73%, kNN = 70%, MLP = 87%, SVM = 77%	Nested cross-validation analysis	3 classes of low, moderate, and high pain score
Parthipan 2019 [23]	6	Self-reported data	EN	EN = 92%	Not reported	Not reported	Tenfold cross-validation	Numerical rating scale (NRS) (0 no pain, 10 being maximal pain)

Table 3 continued

Study	Data input	Data sources/instruments	ML methods	ML methods' accuracy (%)	Sensitivity	Specificity	Validation	Number of classes
Tighe 2015 [24]	14	Self-reported data	GB, LASSO, kNN	GB = 67%, LASSO = 71%, kNN = 64%	LASSO = 68%,	LASSO = 61%	Training/testing	2 classes of moderate and severe postoperative pain
Gruss 2015 [25]	42	EMG, skin conductance level (SCL), EEG	SVM	SVM = 85%	SVM = 83%	SVM = 85%	Threefold cross-validation	2 classes of pain and no pain
Levitt 2020 [26]	39	EEG	SVM	SVM = 83%	Not reported	Not reported	Tenfold cross-validation	2 classes of healthy participants and participants with pain
Pouromran 2021 [27]	4	Electrodermal activity (EDA), ECG, EMG	kNN, LiR, NN, SVM, XGBoost	kNN = 81%, LiR = 81%, NN = 79%, SVM = 83%, XGBoost = 81%	Not reported	Not reported	Testing	Numeric scale from 0 to 4 for pain intensity
Juwara 2020 [28]	8	Self-reported data	EN, GB, LS, RF, RR	EN = 74%, GB = 78%, LS = 72%, RF = 73%, RR = 75%	Not reported	Not reported	Tenfold cross-validation	2 classes of acute pain and not acute pain

Table 3 continued

Study	Data input	Data sources/instruments	ML methods	ML methods' accuracy (%)	Sensitivity	Specificity	Validation	Number of classes
Rojas-Mendizabal 2021[29]	27	Self-reported data	DTs, kNN, LoR, RF, SVM,	DTs = 79%, kNN = 71%, LoR = 96% RF = 81%, SVM = 81%	Not reported	Not reported	Tenfold cross-validation	2 classes of cardiac pain and non-cardiac pain
Rogachov 2018 [30]	4	fMRI	KRR	Not reported	Not reported	Not reported	Cross-validation	Numerical rating scale (NRS) (0 no pain, 10 being maximal pain)
Tan 2020 [31]	15	Electronic health record	LoR, RF, XGBoost,	LoR = 77%, RF = 76%, XGBoost = 76%	LoR = 69%, RF = 69%, XGBoost = 76%	LoR = 73%, RF = 71%, XGBoost = 76%	Fivefold cross-validation	2 classes of pain and no pain
Yang 2018 [32]	11	Electronic health records	kNN, LoR, RF, SVM	kNN = 52%, LoR = 58%, RF = 52%, SVM = 58%,	Not reported	Not reported	Tenfold cross-validation	Numerical rating scale (NRS) (0 no pain, 10 being maximal pain)
Wang et al. 2021 [34]	7	Self-reported data	DTs, SVM, CNN	DTs = 90%	Not reported	Not reported	Tenfold cross-validation	Numerical rating scale (NRS) (0 no pain, 10 being maximal pain)

Table 3 continued

Study	Data input	Data sources/ instruments	ML methods	ML methods' accuracy (%)	Sensitivity	Specificity	Validation	Number of classes
Goldstein et al. 2020 [33]	12	Mobile platform	LiR	LiR = 72%	Not reported	Not reported	k-fold cross-validation	Numerical rating scale (NRS) (0 no pain, 10 being maximal pain)

SVM support vector machine, *MLP* multilayer perceptron, *kNN* k-nearest neighbors, *LoR* logistic regression, *NN* neural network, *CNN* convolutional neural network, *FD Boost* functional data boost, *CART* classification and regression trees, *RF* random forest, *LASSO* least absolute shrinkage and selection operator, *GB* gradient boosting, *LiR* linear regression, *XGBoost* extreme gradient boost, *EN* elastic net, *LS* least square, *RR* ridge regression, *DTs* decision trees, *KRR* kernel ridge regression

health devices such as mobile applications and wearables.

To improve the management and treatment of pain it is essential to be able to identify personalized healthcare treatment patterns. ML is considered to be beneficial because it succeeds at recognizing and predicting patterns, links, and relationships throughout big and complex datasets, independently of human supervision. As a result, ML was found to predict, classify, and suggest potential treatments of pain.

This review revealed that a wide variety of ML techniques have been employed in pain medicine. Most of these methods involve supervised classification or regression algorithms and contributed to the management of pain.

Our results should be interpreted with some caution given the limitations of our design. First, there was a great deal of heterogeneity between the studies, involving different interventions and different populations. Second, we only searched for publications in PubMed—albeit the largest medical database—and we therefore might have missed a few more papers that are indexed only in other databases.

CONCLUSION

Our review highlights the need for further use on ML in pain research in order to develop more algorithms that will be able to accurately predict and assist medical personnel in efficient diagnosis, successful decision-making, and effective treatment of pain. Furthermore, it is expected that explainable artificial intelligence systems will be developed to support decision-making [35] so that the medical personnel can better handle pain management.

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Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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