Fibromyalgia Detection and Diagnosis: A Systematic Review of Data-Driven Approaches and Clinical Implications

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TOPICAL REVIEW

Fibromyalgia Detection and Diagnosis: A Systematic Review of Data-Driven Approaches and Clinical Implications

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ABSTRACT Fibromyalgia syndrome (FMS) is a long-lasting medical condition that poses significant challenges for diagnosis and management because of its complex and poorly understood nature. It affects millions of people around the globe, predominantly women, causing widespread pain, fatigue, cognitive impairments, and mood disturbances. The lack of objective measures to address FMS complicates its assessment, often leading to delayed or misdiagnosed cases. By hindering daily activities and productivity, FMS negatively impacts the quality of the patient's life. Innovative approaches that use medical data, such as bio-signals and bioimaging, combined with machine learning techniques, hold the promise of deepening our knowledge of FMS, which might in turn lead to systems that offer efficient, precise, and personalized physician support. Furthermore, artificial intelligence-driven identification of biomarkers and patient subgroups could improve FMS management. In this systematic review, we explore the role of artificial intelligence in understanding FMS pathophysiology, discuss the present limitations, and shed light on future research avenues, aiming to translate findings into improved clinical outcomes.

INDEX TERMS Artificial intelligence, fibromyalgia, FMS detection, machine learning, pain assessment.

I. INTRODUCTION

Fibromyalgia syndrome (FMS) is a chronic medical condition which causes widespread muscle and joint pain (Fig. 1), cognitive impairment, tiredness, sleep issues, and mood disturbance, like depression and anxiety [1], [2]. It affects 2-4% of the global population, with most of them being women [3], [4]. FMS takes a toll on a person's mental well-being and quality of life. Many FMS patients suffer from sleeplessness, hypersensitivity, and find it difficult to perform their daily activities [5]. This functional limitation, decreased efficiency, and productivity affects both the

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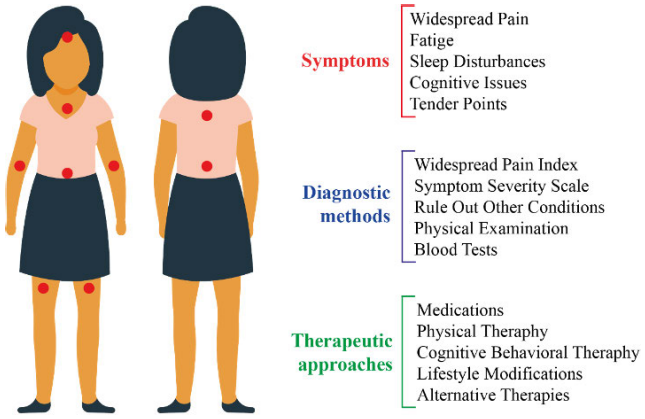

FIGURE 1. Clinical presentation, diagnosis and management of FMS. Red dots indicate the nine pain locations associated with FMS defined by the american pain society [13].

physical and emotional health [6]. Despite being prevalent and significantly affecting one's quality of life, the underlying biological and neurological mechanisms of FMS are still not well understood [7]. There is no definitive laboratory test or imaging study available to confirm FMS [8]. After excluding the possibility of other medical conditions, FMS is usually diagnosed based on patient-reported symptoms, which can be highly subjective [9], [10]. Additionally, the complex and variable nature of the disease, such as overlapping symptoms with other conditions and the absence objective biomarkers, makes it challenging for healthcare experts to provide an accurate diagnosis [11]. This often results in late or missed diagnoses [12]. More robust and accurate diagnostic approaches are the need of the hour to improve the outcomes in FMS, so that therapeutic interventions can be implemented at an early stage.

There is a lack of objective assessment measures for disease severity, progression, and treatment response in FMS. Hence, it is crucial to discover biomarkers beyond patient symptoms which are often subjective and variable [14]. Recent progress in the areas of artificial intelligence (AI) and machine learning (ML) [15], [16] enable efficient analysis of complex patient data with several parameters or features. They also allow the extraction of meaningful insights and patterns from the data that may not be obvious to humans [17]. These could be exploited not only for FMS diagnoses but also to facilitate personalized treatment selection and outcome monitoring. For example, multi-parametric data readouts of wearable devices (e.g., Fitbit, smartwatch) and medical imaging contain rich physiological and/or anatomical information that may associate with FMS and be useful for diagnostic classification [18], [19], [20]. ML-based models have the potential to identify biomarkers to discriminate and diagnose FMS [21] and standardize evaluation and clinical decision-making. Additionally, ML can detect clinically relevant subgroups within the FMS population based on shared feature patterns, which can enable targeted precision medicine strategies to address the individualized needs of patients with FMS [22]. Especially when gathered longitudinally from sizable FMS/control cohorts, the application of AI to medical data can offer clues to understanding the clinical behavior and trajectory of FMS, which may prove useful for clinical decision-making.

In this work, we comprehensively reviewed the literature in the past decade (2013-2023) on the diagnosis of FMS—with a focus on AI approaches—using various physiological signals and medical images as well as state-of-the-art disease understanding. In addition, we have identified gaps and provided researchers with a roadmap by highlighting areas that require further investigation. Past reviews mostly had a narrow focus with limited modality or lacked systematic analysis of ML applications. In this study, we performed a comprehensive synthesis of AI-driven diagnostic methods spanning multiple clinical endpoints and data types like EEG, MRI, and ultrasound. By highlighting robust patterns and emerging research gaps from 2013–2023, we bridge the gap between current FMS diagnostic challenges and the promise of next-generation AI solutions tailored for FMS detection and personalized treatment.

The rest of this paper is structured as follows: In Section II, we summarize related review articles and explain our literature search strategy. Section III details the results, focusing on studies that address FMS detection and diagnosis, pain assessment, and brain connectivity. Section IV provides an in-depth discussion of current challenges and opportunities for AI-driven FMS research, while Section V offers concluding remarks and outlines promising future directions.

II. METHODS

A. RELATED REVIEWS

In this section (Fig. 2), we discuss five recent reviews on FMS along with their focus and limitations.

Glombiewski et al. [23] reviewed the application of using electromyographic and electroencephalographic feedback, and their effect on the efficacy of biofeedback in FMS treatment. Adler-Neal and Zeidan [24] focused on mindfulness meditation and its effects on FMS outcomes. Once again, other treatment strategies were not considered in the review. Next, Jones et al. [25] examined the prevalence of FMS in axial spondyloarthritis (axSpA), but did not address broader topics like detection, diagnosis, and pain. Ricci et al. [26] and De Melo et al. [27] on the other hand, focused on one particular data modality. Ricci et al. [26] concentrated on imaging aspects, particularly molecular and neuroimaging techniques like fMRI and PET in clinical trials. De Melo et al. [27] examined studies that used EEG signals to assess FMS patients. However, neither of the studies covers a diverse list of data or imaging modalities and the use of AI for FMS detection and diagnosis. Notably, none of these studies also covered the use of ultrasound in FMS, which has gained popularity in recent years. Additionally, there is a

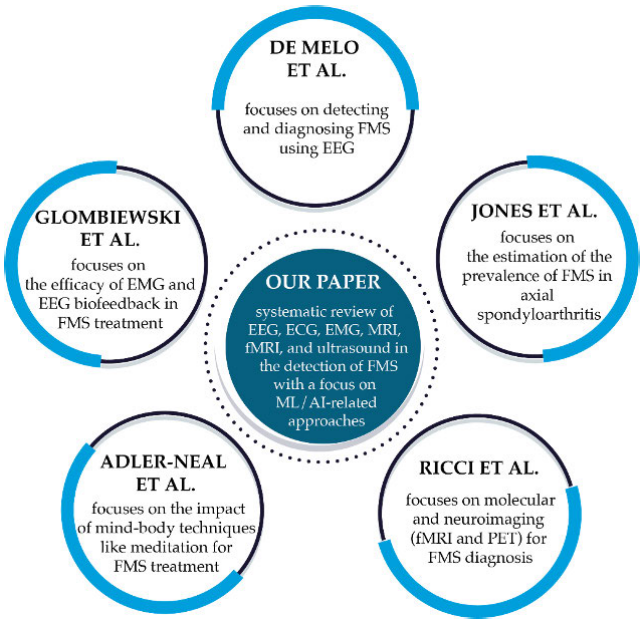

FIGURE 2. Comparison of the focus and coverage of our work with five recent FMS reviews.

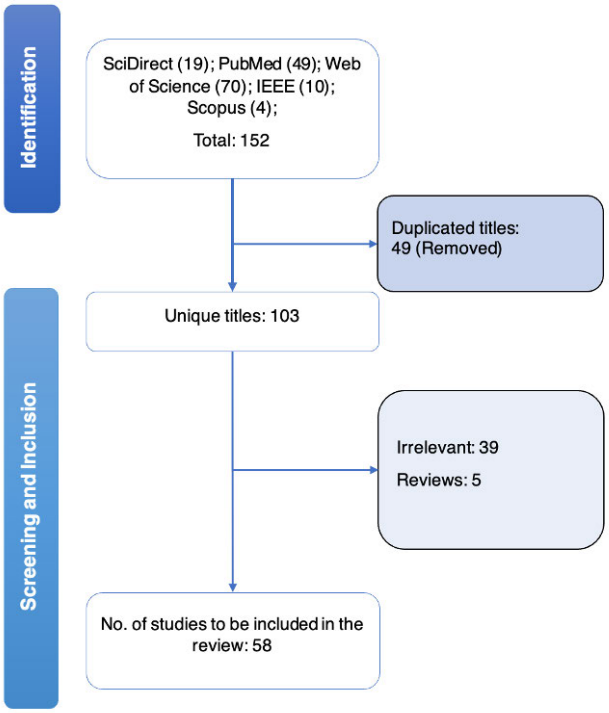

FIGURE 3. PRISMA guidelines for database search.

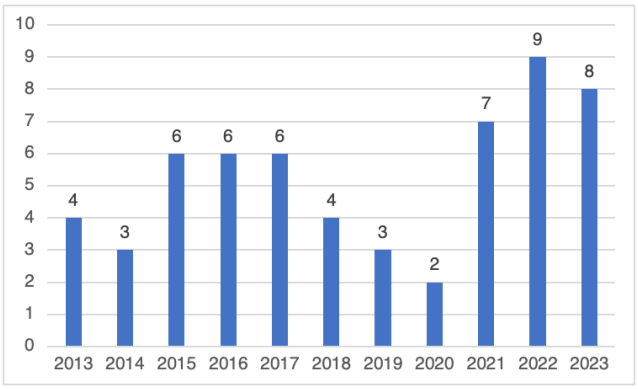

FIGURE 4. Distribution of articles by publication year.

lack of discussion on ML-related approaches in these review papers.

B. LITERATURE SEARCH STRATEGY

We conducted a literature survey across Scopus, PubMed, Web of Science, and the IEEE databases in January 2024 searching for full-text studies published in peer-reviewed conferences and journals between 2013 and 2023 (inclusive) using the following search term and their combinations: ''fibromyalgia'', ''detection'', ''identification'', ''classification'', ''diagnosis'', ''EEG'', ''ECG'', ''EMG'', ''ultrasound'', ''MRI'', ''fMRI'' (Fig. 3).

We excluded review studies, preprints, and unrelated articles (articles that didn't deal with FMS or its detection) along with papers that weren't written in English. The initial search returned 152 articles, which was reduced to a final set of 58 studies for analysis as per the PRISMA guidelines.

Of the 58 selected papers, 47 studies disclosed the location from which the data was collected, while 11 studies did not. Among these, 21 studies were based in Europe, 16 in North America, 8 in Asia, and 2 in South America. Within the Americas, 4 studies were from Canada, 2 from Brazil, and the rest from the USA. In Asia, the studies were distributed across India (2), China (1), Israel (2), Japan (1), Korea (1), and Taiwan (1). Among the European countries, Spain, Italy, and the UK accounted for 17 studies, while the remaining studies were from Denmark, Germany, Hungary, and Switzerland. This demographic distribution highlights a lack of representation from continents such as Africa and Australia. Additionally, the majority of studies rely on private datasets with fewer than 100 female participants, indicating the scarcity of large publicly available datasets.

III. RESULTS

Fig. 4 shows the publication trend of the 58 reviewed articles. Among them, 14 papers are AI-based studies, which have all been published after 2015 (Fig. 5). This suggests a growing trend in the use of AI methodologies in FMS diagnosis.

Among the 58 studies, most studies have concentrated on analyzing functional information through MRI/fMRI images ($n = 21$), with ultrasound surprisingly being the second most prevalent data type ($n = 18$). The most frequently utilized biosignal is EEG ($n = 13$), while studies utilizing ECG and EMG numbers 4 and 3, respectively. Fig. 6 illustrates the

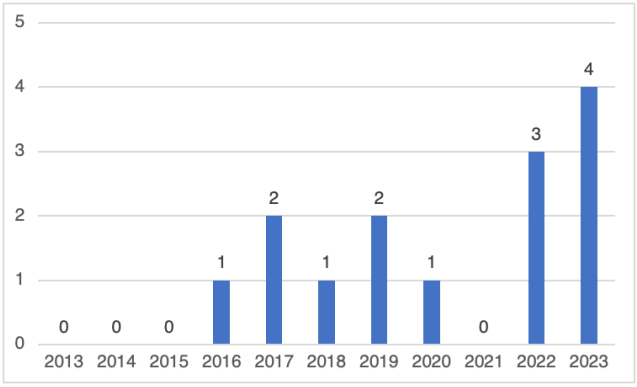

FIGURE 5. Distribution of AI-based articles by publication year.

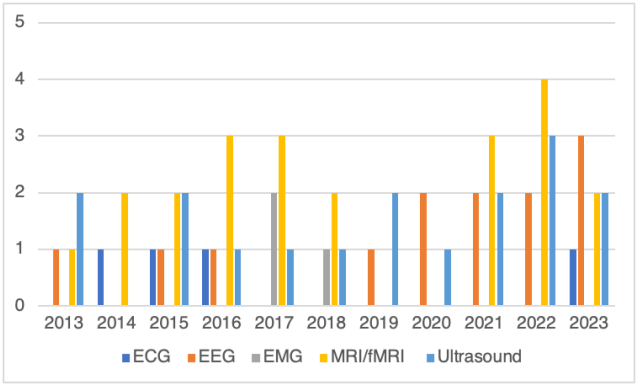

FIGURE 6. Distribution of articles by publication year and data modalities used.

usage of various data types in studies analyzing FMS during the examined period (2013-2023). It is evident that there has been a consistently high utilization of MRI/fMRI from the beginning. Notably, EMG was employed only between 2017 and 2018. Similarly, EEG has been used since 2013, but a noticeable upward trend is observed starting from 2020.

The 58 studies were categorized into four main groups based on their aims: (1) detection/diagnosis of FMS (n = 28); (2) brain connectivity (n = 7); (3) pain detection (n = 13); and (4) miscellaneous applications (n = 10). For each application, we also identified the most utilized data modality, which included bio-signals such as EEG, Electrocardiography (ECG), and Electromyography (EMG), and medical imaging modalities such as MRI, fMRI, and Ultrasound. Additionally, we examined whether ML techniques were employed in the studies. The detection/diagnosis category centered on studies aiming to identify and diagnose FMS. Various medical data modalities were utilized, with EEG being the predominant bio-signal modality, while MRI and fMRI were primary in medical imaging. ML techniques were frequently employed to enhance the accuracy of detection and diagnosis. The brain connectivity category encompassed studies investigating connectivity patterns and networks within the brains of individuals with FMS, predominantly using EEG and fMRI. In pain detection studies, the focus was on identifying markers of pain in individuals with FMS, and ultrasound imaging emerged as a widely used technique for pain detection and classification. Finally, in the miscellaneous applications category, studies explored various other applications related to FMS, such as examining the relationship between heart rate variability, anxiety stress, and FMS or studying sleep patterns in FMS-affected patients.

A. FMS DETECTION AND DIAGNOSIS

Table 1 summarizes the works reported in this section. Among the 28 papers considered in this section, 16 papers do not use any AI-based technique, while 12 papers use some AI-based technique, and a trend of more researchers using AI for their studies over the last few years can be seen in Fig. 5.

1) STUDIES THAT DO NOT USE AI-BASED METHODS

While the use of ECG and EMG signals has not been very common among researchers for the detection and diagnosis of FM, Elmas et al. [28] investigate potential diagnostic markers and physiological signals like protein levels, respiration rate, and temperature for FMS diagnosis along with ECG signals. Higher body temperature and platelet count in FMS patients compared to controls were observed, with ST height differences observed in ECGs. These findings suggest that these diagnostic markers could serve as predictive markers for FM, potentially shedding light on its underlying pathophysiology related to hormonal, circulatory, and inflammatory factors. EMG biofeedback in the context of FMS prediction was studied using a randomized controlled clinical trial by Baumueller et al. [30]. Thirty-six patients received either usual care, or 14 additional sessions of EMG biofeedback across 8 weeks. While EMG biofeedback failed to ameliorate the patients' health measured by the Fibromyalgia Impact Questionnaire, it significantly improved the threshold of pressure-pain in the trapezius muscles. Thus, the study concludes that EMG biofeedback does not improve health status in FMS patients, although it may have some localized pain-relieving effects. On the contrary, Losert-Bruggner et al. [31] conducted a study on 555 patients using EMG signals from patients with FMS and craniomandibular dysfunction or craniocervical dysfunction and highlighting, highlighting the importance of interdisciplinary treatment for patients with synchronous conditions. EEG datasets appear more popular for detecting FMS than ECG and EMG signals. Objective EEG indicators can be used to diagnose and assess FMS severity and their correlation with psychological and neuropsychiatric tests [33]. The paper highlights the potential of EEG indicators, particularly frequency ratios, in diagnosing and assessing FMS severity, warranting further validation and investigation. Similarly, cognitive-emotional dysregulation can also be used to study FMS and its severity. FMS patients showed a reduced ability to distinguish emotions and prolonged attention to negative distractors compared to healthy controls, along with decreased frontal-occipital EEG connectivity [36]. In chronic pain pathophysiology, the

TABLE 1. Summary of studies involving FMS detection and/or diagnosis stratified by signals used.

Publication	Study Aim	Signal Used	Findings/Results
Elmas et al. (2016) [28]	Evaluate ECG signals, protein levels, respiration rate, temperature, etc., for FMS diagnosis.	ECG/EMG	Platelet count, body temperature, and ST height have predictive capacities in FMS.
Barua et al. (2023) [29]	Diagnosis of FMS using ML from ECG data.	ECG/EMG	Accuracy = 93.87%.
Baumueller et al. (2017) [30]	Study the effectiveness of using EMG for FMS.	ECG/EMG	EMG biofeedback shows no improvement in health status in patients with FMS.
Losert-Bruggner et al. (2018) [31]	Use EMG to identify FMS in patients with craniocervical dysfunction (CCD)/ craniomandibular dysfunction (CMD).	ECG/EMG	FMS patients suffering from CCD/CMD simultaneously gain from an interdisciplinary treatment.
Navarro et al. (2013) [32]	Prognosis, classification of FMS.	EEG	N/A
Navarro López et al. (2015) [33]	Search for objective indicators on the diagnosis and severity assessment of FMS.	EEG	FMS patients exhibit significant quantitative EEG patterns that differ from controls, with decreased alpha power and increased theta and beta ratios. These patterns correlate with psychological test outcomes, suggesting central nervous system dysfunction.
Paul et al. (2019) [34]	Detect FMS from sleep patterns and signals.	EEG	Accuracy = 96.15% Sensitivity = 96.88% Specificity = 95.65%
Martín-Brufau et al. (2021) [35]	Detect FMS using EEG (brain activity) images and ROC curves, Fast Fourier Transforms.	EEG	Area Under Curve (AUC) values range between 91.3% and 100%.
Goldway et al. (2022) [36]	Study the correlation between cognitive and emotional processing and FMS and its severity.	EEG	Maladaptive affective attention modulation can help predict FMS.
Karabey Aksalli et al. (2023) [37]	Detection of FMS from sleep signals using Support Vector Machines (SVMs).	EEG	Accuracy = 91.83%
Rushbrooke et al. (2023) [38]	Classification of people with and without FMS.	EEG	Accuracy of 100% on BLINK Dataset.
Sundermann et al. (2014) [39]	Distinguish between FMS and Rheumatoid Arthritis (RA) using fMRI.	MRI/fMRI	You can't distinguish between FMS and RA using fMRI. Accuracy = 78.8%
Sevel et al. (2016) [40]	Distinguish between healthy controls and patients with FMS/chronic fatigue.	MRI/fMRI	Accuracy = 90.83%
Boissoneault et al. (2017) [21]	Classification of pain disorders into low back pain, osteoarthritis, FMS using ML.	MRI/fMRI	Accuracy = 92%
Jarrahi et al. (2017) [41]	Analyze changes in BOLD signal in FMS patients and healthy controls before and after a stressor.	MRI/fMRI	Significant difference in BOLD spectral power between FM, healthy controls ($p < 0.05$).
Sayılır et al. (2017) [42]	Study difference in odor identification ability between FMS and normal patients.	MRI/fMRI	Olfactory bulb volumes are significantly lower for FMS patients (all $p < 0.05$), especially women.
Tokumasu et al. (2021) [43]	Using growth hormone and adrenocorticotropin hormone levels to diagnose chronic fatigue syndrome (CFS) and FMS.	MRI/fMRI	Ask physicians to consider the possibility of adrenocorticotropin hormone deficiency while diagnosing patients with general fatigue.
Shan et al. (2022) [44]	Proposal paper - to use ML/deep learning to study neuropathophysiology.	MRI/fMRI	N/A.
Thanh Nhu et al. (2022) [45]	Use ML to distinguish between FMS and pain-free subjects.	MRI/fMRI	Accuracy = 95% AUC = 0.95.
Liang et al. (2023) [46]	CNNs for FMS diagnosis.	MRI/fMRI	Accuracy = 82.48% .
Ozkan et al. (2013) [47]	Identify how often enthesopathy occurs in FMS for further classification.	Ultrasound	No significant correlation between the Madrid Sonography Enthesitis Index (MASEI) score and the duration of FMS or the location of tender points.
Muro-Culebras et al. (2013) [48]	Compare the blood flow, stiffness, and morphology of tender points in normal and FMS-affected women.	Ultrasound	FMS patients showed larger amounts of hypoechoic area. Sono-myoelastography and sono-myography, cannot discrimate tender points effectively if used to identify myofascial trigger points.

TABLE 1. *(Continued.)* **Summary of studies involving FMS detection and/or diagnosis stratified by signals used.**

Ali et al. (2017) [49]	Distinguishing between RA and FMS.	Ultrasound	Develop a sensitive tool called Musculoskeletal ultrasound (MSKUS) to differentiate between FMS and inflammatory arthritis.
Behr et al. (2020) [19]	Use image texture to distinguish between patients with and without FMS.	Ultrasound	Accuracy = 84.1% (SVM), Accuracy = 66% (Logistic regression)
Polachek et al. (2021) [50]	Use ultrasound to assess PsA in patients with FMS.	Ultrasound	Among FMS patients, ultrasound is significantly more effective ($p<0.001$) than combined clinical scores in assessing disease activity in PsA.
Miladi et al. (2023) [51]	Compare ultrasounds of RA patients with FMS patients.	Ultrasound	A strong correlation ($r=0.95$) between the clinical and ultrasonographic scores for RA and FMS patients.

modulation of maladaptive affective attention predicts pain severity, while impaired frontal-occipital connectivity correlates with poor sleep quality, highlighting the significance of cognitive-emotional dysregulation. In another similar study, Navarro et al. [32] attempted to identify specific indicators that contributed to the diagnosis and severity assessment of FMS. They also studied the relationship of these indicators with psychological and neuropsychiatric tests. Patients with a higher clinical severity were seen to exhibit higher prefrontal cordances in the theta band. Meanwhile, a notable decrease in cordance was observed in the prefrontal regions after therapy. This indicates that cordance has the potential utility to diagnose FMS and other neuropsychiatric disorders. Next, Martí-Brufau et al. [35] used Fast Fourier Transforms on brain activity from EEG images to detect FMS. They compared the EEG recordings of 23 FMS patients 23 healthy control, and observed a significant difference in brain activity and connectivity. A high discriminative capacity (91.3–100%) between FMS patients and controls, suggested a distinct neurophysiological pattern associated with FMS.

Initial studies that attempted to use MRI/fMRI to detect or distinguish FMS from other pain-related diseases were not very successful. Achieving an accuracy of around 78%, Sundermann et al. [39] conclude that fMRIs cannot be used to distinguish between FMS and RA successfully. However, this trend changed over the last few years with advancements in technology. In 2017, Jarrahi et al. [41] and Sayılır and Çullu [42] presented works on MRI images to successfully understand different aspects of FM. Jarrahi et al. [41] conducted a multivariate statistical analysis of fMRI data to investigate brain network connectivity and spectral power changes in response to stressors. They focused on areas related to pain processing. In contrast, [42] used structural MRI (sMRI) to measure olfactory bulb volumes in FMS patients. Their study offered insights into sensory dysfunction in FMS and indicated that impaired olfactory function could be a symptom of FMS. While [41] used network dynamics and functional connectivity alterations in the brain, [42] concentrated on structural abnormalities in specific regions related to sensory processing. Finally, Tokumasu et al. [43] presented one of the latest works to detect FMS using MRI images. They asked physicians to consider the possibility of adrenocorticotropin hormone deficiency while treating patients with tiredness and general fatigue. The case study indicated that growth hormone and adrenocorticotropin hormone levels could be used to diagnose chronic fatigue syndrome (CFS) and FMS.

Ultrasound has been widely used to detect FMS. One of the first studies involved the development of MASEI to identify FMS patients with ill-defined symptoms [47]. Such a setup would help prevent misdiagnosis and mistreatment. Compared to 48 healthy controls, 38 FMS patients showed significantly higher MASEI scores. An ultrasound score of 3.5 was identified as the optimal threshold for differentiation. Polachek et al. [50] and Marchesoni et al. [52] conducted similar studies to investigate the utility of ultrasound in distinguishing between psoriatic arthritis (PsA) and FMS in patients with overlapping symptoms. Polachek et al. [50] focused on evaluating disease activity by comparing clinical and ultrasound scores in PsA patients who may or may not have been affected by FMS. Ultrasound scores were significantly related to clinical indices in PsA patients without FMS alone. This meant that ultrasound is more useful to assess disease activity in PsA without FMS. On the other hand, Marchesoni et al. [52] concentrated on distinguishing between PsA enthesitis and FMS using ultrasound examination of entheseal sites. They found that PsA patients exhibited more ultrasound-detected entheseal changes compared to FMS patients in Achilles and proximal patellar tendon entheses. Hence, they concluded that ultrasound evaluation of entheses might help distinguish chronic widespread pain in PsA and FMS.

2) STUDIES THAT USE AI-BASED METHODS

The last five years saw the surge of AI-based techniques in FMS detection and diagnosis. Barua et al. [29] developed a lightweight ML algorithm for FMS diagnosis using single-lead ECG signals that were recorded when patients were asleep. Their cohort comprised FMS patients and healthy individuals. Achieving over 92% accuracy, their results suggested that measures across different sleep stages could have clinical applications in detecting FMS. Compared to ECG, a more commonly used data source was EEG signals [34], [37], [38]. These works also focused on studying different sleep stages and used different ML algorithms. First, Paul et al. [34] used a support vector machine (SVM) classifier to analyze various nonlinear parameters from sleep stage 2 EEG signals. Achieving accuracy, sensitivity, and specificity scores of over 95%, the paper suggested the

use of sleep abnormalities as a clinical feature to diagnose FMS. Karabey Aksalli et al. [37] introduced a novel, efficient feature extraction technique called GluPat and used it to train SVM and k-nearest neighbor classifiers. Their model achieved an accuracy of 91.83% in both tenfold cross-validation and leave-one-record-out strategies. Finally, Rushbrooke et al. [38] introduced multivariate time series classification to avoid dataset-specific feature selection. They found that theta and alpha EEG frequency bands were potentially discriminative. These results are believed to open up new avenues for FMS research.

MRIs and fMRIs have also been widely used to diagnose FMS and to distinguish it from different pain disorders [21], [40]. Boissoneault et al. [21] addressed the broader challenge of classifying various chronic pain conditions, emphasizing the weak correlation between clinical pain and tissue abnormalities. On the other hand, Sevel et al. [40] used sMRI data along with self-reports to distinguish healthy controls from FMS and CFS patients, and to differentiate between CFS and FMS patients. Their stacked ML model with LASSO-weighted features obtained an accuracy of over 90% in identifying unique neural mechanisms of FMS and CFS. These results also proved that sMRI performed better than self-report measures in distinguishing CFS and FMS. Finally, Thanh Nhu et al. [45] compared the effectiveness of resting-state functional connectivity (rs-FC) and brain structural features from MRI data to distinguish between FMS patients and healthy controls. A combined and structural ML model achieved the best diagnostic performance, yielding accuracy and area under the curve of 95%. The rs-FC-based ML model alone showed superior performance to the structural model and also revealed correlations with clinical symptoms of FMS. Finally, Liang et al. [46] introduced an innovative automatic diagnosis model for FMS that integrated low-rank Brain Functional Connectivity Networks (BFCNs) from resting state fMRI (rs-fMRI) with graph convolutional networks (GCNs). Using Pearson's correlation along with BFCN, they effectively constructed informative and less redundant networks, which were then enhanced with non-image patient data to build an attention-informed graph. This graph was processed through the GCN layer to diagnose FMS, achieving an accuracy of 82.48%.

Ali et al. [49], Behr et al. [19], and Marchesoni et al. [52] explored the application of ultrasound imaging to differentiate FMS from arthritis, including rheumatoid arthritis (RA) and PsA. While Ali et al. [49] and Marchesoni et al. [52] emphasized the diagnostic capability of ultrasound in differentiating FMS from specific types of arthritis through clinical and imaging features, Behr et al. [19] introduced a novel application of ML models for diagnosis based on quantitative image analysis. Ali et al. [49] conducted a case study where musculoskeletal ultrasound (MSKUS) effectively distinguished low-intensity and antibody-negative RA from FMS. Marchesoni et al. [52] attempted to differentiate FMS from pain caused by PsA enthesitis. To this end, they examined entheseal sites and found significant differences in enthesitis between PsA and FMS patients using gray-scale and power Doppler ultrasound. To diagnose FMS, Behr et al. [19] employed quantitative ultrasound techniques using image texture analysis from ultrasound videos of the trapezius muscle. They compared the performance of SVM with a logistic regression model and showed that SVMs achieved a higher accuracy (84.1%) in differentiating healthy controls from FMS patients.

3) COMPARISON BETWEEN MODELS THAT USE AI AND THOSE THAT DON'T

Research on diagnosing FMS without particularly using AI has explored a variety of methods. These include the use of ECG, EMG, and EEG signals, clinical trials on EMG biofeedback, studies on the effectiveness of MRI/fMRI, and the development of new ultrasound techniques like MASEI. Such methods have given us potential diagnostic markers, helped us understand the effectiveness of certain therapies, and aided the differentiation of FMS from other conditions. However, they have seen a varied range of success rates and diagnostic accuracy. AI approaches for detecting FMS have utilized advanced algorithms and diverse data types, including ECG signals, EEG signals, MRI/fMRI images, and ultrasound imaging. By developing previous works, researchers have come up with lightweight ML models for ECG analysis, complex algorithms for EEG signal processing, methods to exploit structural and functional MRI to distinguish FMS from other conditions, and ML models that work in conjunction with ultrasound imaging to differentiate FMS from arthritis. Such studies have generally achieved high accuracy, indicating the growing potential of AI in FMS diagnosis.

The shift from traditional diagnostic methods to ML-based techniques in FMS research indicates that these models are more accurate and faster in processing large amounts of data. While traditional methods have provided valuable insights and established a foundation for understanding FMS pathophysiology and prognosis, ML-based methods have shown their ability to handle complex data sets and reveal intricate patterns linked to FMS. Distinguishing FMS from conditions like arthritis is an example where AI models have outperformed traditional approaches. Ultrasound was traditionally used to distinguish between patients with FMS and arthritis. They were known for being able to identify physical markers. However, ML-based approaches have boosted their performance further. By analyzing ultrasound images, alongside ECG, EEG, and MRI/fMRI data, they extract and classify subtle features that may not be obvious to humans.

In summary, the application of AI in FMS promises excellent advances by using computational power to overcome the limitations of traditional diagnostic methods. Driven by advances in state-of-the-art ML models, the use AI to assist clinicians in medical diagnosis is expected to increase.

TABLE 2. Summary of studies on brain connectivity in FMS stratified by signals used.

Publication	Study Aim	Signal Used	Findings/Results
González-Villar et al. (2020) [53]	Study spontaneous brain oscillations in terms of functional connectivity or microstates in patients with FMS.	EEG	Six independent brain connectivity components explained 92.5% of the total variance. The independent sample t-score of the mean Phase Lag Indicators is t(92) = 3.76. No significant difference was found between FMS patients and their demographic information.
Cardoso et al. (2021) [54]	Study the correlation between attentional bias and FMS.	EEG	Significant differences between groups in depression (t(28)=5.50), impact of FMS (t(28)=13.3), and pain catastrophizing (t(28)=26.2), p<0.001, d=1.26. The FMS group has higher (but non-significant) scores across all self-reported measures.
Jensen et al. (2013) [55]	Investigate the relationship between the structure of the brain and its function in FMS patients.	MRI/fMRI	FMS patients show evident overlaps of reduced cortical thickness, smaller brain volumes, and lower functional regional coherence in the rostral anterior cingulate cortex.
Ichesco et al. (2016) [56]	Compare FMS patients and healthy controls with respect to state changes in resting brain connectivity following experimental pressure pain.	MRI/fMRI	There is a positive correlation (r = 0.610) between the difference in resting-state connectivity between the right thalamus and the posterior cingulate/precuneus in FMS and the difference in clinical pain scores. There is also a positive correlation between connectivity changes between the left thalamus and the superior frontal gyrus in FMS and anxiety (r = 0.561) and depression (r = 0.618).
Truini et al. (2016) [57]	Study correlation between changes in brainstem area and FMS during pain.	MRI/fMRI	A higher connectivity between PAG and areas like insula, anterior cingulate cortex, and anterior prefrontal cortex in FMS patients suggests dysfunction in the pain modulatory system. Studies suggest a potential link between altered PAG functioning and chronic pain experienced by FMS patients.
Cheng et al. (2021) [58]	Examine FMS patients for understanding dynamic changes in functional brain connectivity.	MRI/fMRI	FMS patients exhibit greater TSP than healthy controls.
Ioachim et al. (2022) [59]	Studies of the association between FMS and altered neural processes were conducted using the T-test.	MRI/fMRI	FMS patients have significantly higher pain scores and higher measures of depression BDI compared to healthy controls. No significant demographic difference observed.

B. BRAIN CONNECTIVITY

Understanding functional and structural brain connectivity are crucial to understand the pathophysiology of FMS (Table 1). While functional connectivity refers to time-based correlations between distant brain regions, structural connectivity refers to physical pathways that enable communication between these regions [60]. Alterations in connectivity between regions involved in affective processing may contribute to the emotional dysregulation commonly observed in FMS patients. Understanding these alterations in regions like the amygdala and prefrontal cortex could provide insights into the underlying neurobiology of FMS and might aid the development of targeted interventions. Further, studying and understanding intricate network dynamics within the brain plays a crucial role in identifying biomarkers and therapeutic targets for improving the management of FMS.

In one of the initial studies, Jensen et al. [55] compared brain connectivity and structure in FMS patients and healthy controls using MRI data. In the rostral anterior cingulate cortex, FMS patients exhibited lower levels of cortical thickness, brain volumes, as well as functional regional coherence. Moreover, patients with longer exposure to FMS pain showed higher levels of these changes. They also observed a correlation between structural and functional alterations in mesolimbic brain regions and the extent of depression in patients with FMS. This work created opportunities for early detection and prognosis of FMS, paving the way for future studies.

Ichesco et al. [56] and Truini et al. [57] used rs-fMRI to study alterations in brain connectivity related to chronic pain in FMS patients. First, Ichesco et al. [56] investigated the changes following acute pressure pain. Their results indicated an increase in the connectivity of the insula and anterior cingulate/hippocampus following pain as well as the thalamic connectivity to the precuneus/posterior cingulate cortex in patients. This positive correlation indicated that acute pain may influence the neural signature of chronic pain. Truini et al. [57] studied functional connectivity changes in the periaqueductal gray (PAG), a component of the endogenous pain modulatory system, in FMS patients compared to healthy controls. A higher connectivity between PAG and areas like insula, anterior cingulate cortex, and anterior prefrontal cortex in FMS patients, suggested dysfunction in the pain modulatory system. Additionally, correlations between PAG connectivity and clinical variables like the extent of pain, duration of the disease, and depressive personality behavior, indicated a potential link between altered PAG functioning and the chronic pain experienced by FMS patients. Cheng et al. [58] and González-Villar et al. [53] demonstrated changes in brain connectivity and organization in FMS patients compared to healthy controls, suggesting underlying neurobiological mechanisms contributing to pain perception. Cheng et al. [58] investigated dynamic changes in functional brain connectivity during temporal summation of pain (TSP) in FMS patients against healthy controls. Analyzing fMRI scans, they observed that FMS patients

exhibit greater TSP than healthy controls. They also noticed alterations in brain organization dynamics during pain processing, particularly in the primary somatosensory cortex and salience network regions. González-Villar et al. [53] explored variations in instantaneous brain oscillations in FMS patients using EEG recordings during the resting state. They showed a rise in beta band connectivity between various brain networks and changes in EEG microstates. This suggested the dominance of endogenous top-down influences and potential implications for cognitive control in FMS.

Attentional bias in FMS was first examined by Cardoso et al. [54] using a dot-probe task on EEG recordings. They studied 30 female participants including FMS patients and healthy controls. While behavioral differences were not observed, they found a complex interplay between attention and emotional processing in FMS patients. FMS patients exhibited reduced attentional resource allocation and larger late positive potentials, suggesting heightened emotional processing.

Trials involving predictable painful stimuli and no stimulus were used to investigate differences in pain processing between FMS patients and healthy controls [59]. Results from the t-test of the two cohorts indicated significant differences in the connectivity of the brainstem and spinal cord network, including regions, such as the hypothalamus, PAG, and PBN. These were regions that are primarily associated with autonomic regulation, and reveal an important link between sensory and autonomic systems in FMS. Additionally, FMS patients exhibited significantly higher pain scores and measures of depression when compared to healthy controls. There were no statistically significant differences between the groups demographically.

In summary, recent studies have highlighted the impact of chronic pain on the brain by studying distinctive brain connectivity and structural changes in FMS patients against healthy people. MRI and fMRI-based studies reveal decreased cortical thickness and altered functional connectivity in key brain regions that are related to pain processing. These include the rostral anterior cingulate cortex, insula, and periaqueductal gray, which correlate with clinical symptoms, including pain severity and depression. Dynamic changes in brain activity following acute pain and during pain processing tasks suggest a maladaptive neural signature in FM, highlighting alterations in the pain modulatory system and the potential for neurobiological mechanisms to contribute to the perception of pain. Furthermore, investigations into spontaneous brain oscillations, attentional biases, and pain processing reveal significant differences in the connectivity of the brainstem and spinal cord network and cognitive-emotional interplay in FMS patients. This suggests that FMS pain involves complex interactions between sensory, cognitive, and autonomic systems.

C. PAIN DETECTION

Pain detection plays an important role in the diagnosis and management of FMS. Detecting and quantifying pain in individuals with FMS is challenging due to its subjective nature and variable symptoms. However, recent advancements in medical imaging and digital health technologies have provided new avenues for objective pain assessment in FMS patients (Table 2).

Analyzing data from chronic FMS patients and healthy controls, Segning et al. [61] presented a proof-of-concept study establishing the feasibility of objectively identifying pain using EEG signals. They hypothesized that EEG-based signals could be used irrespective of pain intensity and task performance. coefficient of variation of the upper envelope (CVUE) of EEG signals from specific electrodes and frequency bands were used as the main measures for pain identification. In the beta frequency band, they observed a rise in CVUE during pain conditions, which supported their hypothesis. Rifbjerg-Madsen et al. [62] used the painDETECT questionnaire (PDQ) to assess the prognostic importance of pain classification in RA at treatment initiation. While patients with high PDQ scores showed greater improvement in DAS28-CRP, no independent association existed between PDQ pain classification and changes in DAS28-CRP, RAMRIS score, or VAS pain. However, they noticed that patients with high baseline PDQ scores tended to change pain classification groups. This suggested variability in pain mechanisms among RA patients. Using an electro-pneumatic circuit coupled with fMRI, Papuga et al. [63] introduced a novel method for objectively assessing pressure pain sensitivity in chronic lower back pain. They set up a test-retest experimental design [64] to demonstrate consistent and reliable results for pressure pain thresholds of the lumbar spine, with high interclass-correlation coefficients. Cankurtaran et al. [65] studied patients with chronic neck pain (NP) and myofascial pain syndrome to investigate if ultrasonography can detect trigger points successfully. They found that pain intensity, disability levels, and myofascial trigger points (MTPs) had significant correlations in various muscles. Within the muscles, they also observed hypoechoic variations along with decreased thickness in association with MTPs. This established the potential of ultrasound in assessing pain severity and disability in chronic NP.

To provide good FMS treatment, understanding what causes pain in specific body parts is very important. First, Andrade et al. [73] studied if baroreflex function is connected to pain in female FMS patients using blood pressure and ECG data. They discovered positive correlations between pressure pain threshold and coherence between systolic arterial pressure and RR interval variability. This implied that orthostatic posture was closely associated with the pressure required for FMS participants to perceive pain. Next, Cojocaru et al. [68] investigated the relationship between ultrasound results and thermal patterns of trigger points in muscle pain syndromes. Higher temperatures within trigger points surrounded by cooler areas in lower back thermography indicated potential blood flow deficits. These findings also suggest that infrared thermography could be a valuable

TABLE 3. Summary of studies on miscellaneous applications in FMS stratified by signals used.

Publication	Study Aim	Signal Used	Findings/Results
Papuga et al. (2015) [63]	Method to quantify pain based on stimulus.	EEG	The interclass and individual correlation coefficients for mild, moderate, and intense pain thresholds are 0.913, 0.652, 0.818, and 0.851, respectively.
Rifbjerg-Madsen et al. (2018) [62]	Pain classification.	EEG	Low, intermediate, and high PDQ groups showed statistically significant classification consistencies. The PDQ pain classification was not found to have significant predictive values regarding changes in DAS28-CRP, RAMRIS score, or VAS pain.
Deutsch et al. (2021) [66]	Study if FMS and interstitial cystitis/bladder pain are related.	MRI/fMRI	Compared to patients suffering from interstitial cystitis, healthy individuals showed considerable differences in the thalamus, amygdala, hippocampus, and right prefrontal cortex along with greater responsiveness to alterations in bladder fullness in the insula.
Tarnoki et al. (2021) [67]	Study if lumbar imaging could play a significant role in people struggling with lower back pain and sleep apnea.	MRI/fMRI	While backpain might cause increased sleep during the day, there is no significant difference in back pain between OSA patients and healthy individuals.
Cojocaru et al. (2015) [68]	Investigate relationships between ultrasound, localized pain manifestation points/trigger points.	Ultrasound	High temperature regions amidst cooler regions in infrared thermography represent trigger points that can help monitor the progression of neuromusculoskeletal ailments.
Ahmed et al. (2018) [69]	Distinguish between different gradients of pain using ultrasound.	Ultrasound	Determine 8 crucial components that explain 95% of the differences among the images.
Correa-Rodríguez et al. (2019) [70]	Study the impact of FMS on bone mass and find out if bone health and pressure pain thresholds are related.	Ultrasound	After adjusting for the body mass index (BMI), all pressure pain thresholds significantly relate to physical activity, menopause status, and BUA in female FMS patients.
Polat et al. (2023) [71]	Impact of synovial inflammation in RA patients diagnosed with FMS.	Ultrasound	Synovial inflammation is a common symptom among RA patients who also suffer from FMS.
Song et al. (2023) [72]	Study joint pain in Systemic Lupus Erythematosus.	Ultrasound	A significant association between clinically detected synovitis and ultrasound-detected inflammatory arthritis; weak association with erythrocyte sedimentation rate.
Cankurtaran et al., (2023) [65]	Use ultrasound to distinguish between demographic and disease characteristics of patients with myofascial pain syndrome.	Ultrasound	Detecting MTPs with ultrasonography is linked to pain and disability severity in people with chronic NP. Detecting MTP and lowered muscle thickness in the relevant muscles have significantly high correlations (between $p = 0.001$ and $p=0.034$).
Andrade et al. (2014) [73]	Study if baroreflex function extracted from ECG and pain in female FMS patients are related.	Other signals	A positive correlation between pressure pain threshold and the coherence between systolic arterial pressure and RR variability: $r = 0.67$; $p = 0.03$.
Segning et al. (2022) [61]	Use EEG signals for objective pain identification.	Other signals	Proof-of-concept for using EEG for objective pain identification.
Choi et al. (2017) [74]	Diagnosis of temporomandibular disorders using EMG.	Other signals	N/A (Proposal paper).

tool to monitor neuromusculoskeletal disorders and aid early treatment of conditions linked to changes in the temperature of tissues. Deutsch et al. [66] studied if FMS and interstitial cystitis/bladder pain are related. Subjects with both interstitial cystitis and FMS were found to be more hypersensitive in sensory measures compared to those without FMS and healthy controls. They responded better to any variations in bladder fullness in brain perfusion studies. The findings suggest distinct phenotypes of interstitial cystitis patients based on the presence of FMS, which could impact treatment responsiveness and support the need for stratification based on co-morbidities. Song et al. [72] studied joint pain in systemic lupus erythematosus (SLE) in the context of FMS. The study found that ultrasound-detected inflammatory and co-existing FMS diagnosis had no significant relationship. In fact, ultrasound-guided intra-articular steroid injection was found to be crucial in predicting reduced joint pain at follow-up visits. This verifies its ability in pain relief treatment for SLE patients irrespective of whether they're affected by FMS.

Tarnoki et al. [67] conducted experiments to understand the relationship between obstructive sleep apnea (OSA) and lumbar disc degeneration. OSA patients exhibited higher numbers of disc bulges, anterior spondylophytes, increased disc degeneration, and vertebral fatty degeneration compared to non-OSA controls. Oxygen desaturation index and plasma levels of klotho were used as measures of OSA severity. These scores correlated with disc bulges and anterior spondylophytes, suggesting a potential link between OSA and lumbar spondylosis.

Polat et al. [71] compared musculoskeletal ultrasonography findings in RA patients with concomitant FMS based on the 1990 American College of Rheumatology (ACR) FMS classification or the 2016 ACR FMS diagnostic criteria.

Compared to the former, the latter showed a higher prevalence of concomitant FMS in RA patients. While musculoskeletal US findings were similar between RA patients with FMS, those meeting only the 2016 criteria exhibited higher synovitis scores, suggesting a prominent role of synovial inflammation in FMS diagnosis based on the 2016 criteria. While none of the above papers use ML-related techniques, Ahmed et al. [69] and Correa-Rodríguez et al. [70] use ML-based methods for pain detection. They also achieved superior results compared to previous papers, as seen in Tables 2. Ahmed et al. [69] assessed whether ultrasound texture features could distinguish chronic pain patients with different degrees of central sensitization (CS). Thirty people suffering from chronic pain were evaluated using the CS inventory and B-mode ultrasound imaging of the upper trapezius muscle. Results indicated that texture features could differentiate between patients with mild, moderate, severe, or extreme CS, suggesting the potential of texture analysis as a diagnostic marker for chronic widespread pain severity and progression. Correa-Rodríguez et al. [70] studied if FMS impacted bone mass and determined if the bone mass status was associated with thresholds of pressure pain. Results showed significantly lower sound speed and broadband ultrasound attenuation (BUA) in FMS patients compared to controls. Lower pain thresholds and a higher number of tender points were linked to lower calcaneal BUA values in FMS women. This suggests that low pain thresholds may independently predict low bone mass in this population.

D. MISCELLANEOUS APPLICATIONS

Several miscellaneous studies related to FMS were reviewed (Table 3). Although the discussed papers do not directly address the detection or diagnosis of FM, they are deemed pertinent to our study due to their relevance to the condition. Many of their insights could be interpreted as potential indicators or symptoms of FM. One study examined the correlation between FMS and arachnoiditis, while another investigated if heart rate variability (HRV) and anxiety levels are related to FMS. Additionally, it was found that sleep disorders are prevalent in FMS patients, although periodic leg movement disorder and bad sleeping patterns had no significant association. Another study compared hippocampal volume levels in FMS patients with those without FMS, revealing potential differences. Moreover, RA patients with FM-like symptoms were found to have less synovitis as detected by power Doppler ultrasound, highlighting potential distinctions between RA and FMS. Furthermore, the role of MSKUS in PsA was explored, along with its potential to enhance the performance of Classification Criteria for Psoriatic Arthritis (CASPAR). Sleep patterns in FMS patients were also studied. At the same time, another investigation demonstrated how classification results could be inadvertently inflated by treating longitudinal or contemporaneous scans as independent data points, showcasing the importance of rigorous methodology in FMS research.

Adhesive arachnoiditis is a serious illness that leads to severe pain and neurological issues. Idris et al. [75] conducted a case study of a 47-year-old woman to discuss adhesive arachnoiditis in the context of FMS. Their study highlights the importance of recognizing the relationship of adhesive arachnoiditis with the immune and nervous systems for interdisciplinary management and treatment involving neurosurgery, pain specialists, and neuropsychologists.

McGonagle et al. [76] investigated the discrepancy between subjective and objective data in FMS patients, focusing on sleep patterns compared to healthy controls. Results reveal differences in sleep parameters such as BMI, sleep quality, and microstructure, with FMP showing decreased microarousals but higher percentages of alpha delta sleep and NREM myoclonia. Rosenfeld et al. [77] also presented a study on finding the relationship between sleep patterns and FMS and concluded that sleep apnea was prevalent in 45% of FMS patients. Notably, a low ratio between qEEG delta and alpha during non-rapid eye movement sleep proved specific for FM, with potential diagnostic value, especially when considering benzodiazepine use.

Lee [78] studied the role of MSKUS in the early detection of PsA, while Mian et al. [79] and Basu et al [80] compared FMS and RA. Using ultrasound, Mian et al. [79] studied if RA patients who met the clinical criteria for FMS showed lower levels of joint inflammation. In fact, RA patients meeting FMS criteria showed higher disease activity, and mental illness like depression, disability, and tiredness scores. Further, individuals meeting both FMS and joint count criteria showed significantly lower synovial inflammation in ultrasound scans. This suggests that identifying and treating such patients might require researchers to come up with different treatment strategies. Next, Basu et al [80] investigated whether RA patients with higher fibromyalgianess scores exhibit similar brain functional connectivity abnormalities as seen in FMS patients. Using fMRI, they found a significant positive correlation between connectivity of the default mode network to the left mid/posterior insula and fibromyalgianess scores in RA patients. These results indicate that RA patients showing an increased fibromyalgianess share neurobiological features observed in FM. From this, one could infer a potential central nervous system involvement in pain symptoms beyond classic inflammatory mechanisms.

Bilgin et al. [81] studied if anxiety in FMS patients was related to their HRV frequency subbands. By creating multilayer perceptron neural networks that take ECG signals as the input, they discovered correlations between specific HRV high-frequency subbands and scores from the Beck Anxiety Inventory and Hamilton Anxiety Inventory. By complementing anxiety tests in clinical evaluation, they concluded that HRV parameters could potentially serve as an adjunct diagnostic method for FMS. Finally, in the context of mental health and anxiety, McCrae et al. [82]

studied if FMS patients exhibit smaller hippocampal volume compared to healthy controls. They examined 40 female FMS patients and 22 healthy controls by taking T1-weighted sMRI scans. The FMS patients in their study demonstrated significantly smaller hippocampi volumes in both hemispheres, independent of depression levels. This suggests that neurobiological mechanisms could contribute to cognitive complaints in FMS, such as abnormal neurotransmission and glucocorticoid dysfunction.

IV. DISCUSSION

Secular trends of publications stratified by data modality and use of AI have been presented in Fig. 5. Nearly half of the reviewed papers (n = 28) focused on detecting and diagnosing FMS, with several using modalities like EEG and ECG. Specifically, EEG signals were explored for the prognosis, classification, and severity assessment of FMS and the detection of abnormal patterns and sleep-related features. Physiological parameters, including protein levels, respiration rate, and temperature, showed potential for FMS diagnosis using ECG signals. Of note, many articles (n = 13) focused on pain detection in FMS. These studies used a range of medical data, including EMG and US. EMG indicators had been developed to diagnose temporomandibular disorders, providing a protocol for assessing and diagnosing pain-related conditions in the jaw. Ultrasound studies focused on trigger points and their correlation with pain manifestation. Eight studies focused on brain connectivity and brain changes in FMS. The relationship between the function and structure of the brain in FMS patients was explored using fMRI to identify overlapping changes in the brain's structural and functional aspects. EEG was used to study brain activity to analyze physical and chronic pain. The studies reviewed in this work are summarized in Fig. 7.

While we reviewed different methodologies used in FMS research in the previous section along with their advantages, it is also crucial to recognize and discuss their limitations and disadvantages. Although traditional clinical and questionnaire-based methods for diagnosing FMS remain valuable, they exhibit several limitations that drive researchers to explore novel approaches. First, self-reported questionnaires depend heavily on patient perception, which can vary widely and introduce subjectivity into the diagnostic process [9]. As a result, clinicians often encounter delayed or missed diagnoses, particularly when FMS symptoms overlap with other chronic pain disorders [11].

Methods involving EMG or EEG provide objective physiological markers but can be challenging to integrate into routine clinical use because of noise sensitivity, the need for specialized equipment, and complex signal processing protocols [23], [27]. Furthermore, while EEG-based techniques capture neural correlates of pain, they may not always reflect the full clinical complexity of FMS, whose pathophysiology often extends beyond single-marker observations [7]. Similarly, MRI and fMRI offer detailed structural and functional insights but can be expensive, time-consuming, and logistically difficult for routine assessments [26]. Additionally, conventional MRI/fMRI analyses may overlook subtle variations in brain connectivity patterns linked to FMS due to limited temporal resolution, further complicating attempts to standardize imaging-based biomarkers [17].

In recent years, ultrasound-based approaches have been studied for muscle stiffness and tissue abnormalities in FMS [19]. However, variations in operator skill, patient anatomy, and scanning conditions can influence the acquired images, reducing inter-operator reliability. In turn, wearable device data (e.g., from fitness trackers) is inherently high-dimensional and unstructured; although it captures longitudinal trends, it is prone to artifacts, missing values, and dependence on user compliance [20].

These limitations have motivated researchers to formulate more robust, data-driven problem statements that aim to unify diverse clinical, physiological, and imaging modalities. By using ML and AI algorithms, researchers seek to address common issues—such as subjective biases in questionnaires, complex multisystem presentations of FMS, and variable data quality—through automated feature extraction and classification [18], [21]. These AI-driven approaches aspire to provide clinicians with reliable, scalable, and reproducible methods for FMS detection and diagnosis, ultimately improving patient outcomes and facilitating personalized treatment strategies.

In the remainder of this section, we focus specifically on the use of AI for FMS assessment, discuss their relative advantages and disadvantages, and propose future directions in FMS research.

A. USE OF AI FOR FMS ASSESSMENT

Since 2016, there has been a growing trend in the use of AI methodologies (Fig. 5), predominantly in the areas of ML, deep learning, and neural networks, to address the multifaceted challenges posed by FMS. Specifically, the last couple of years have seen a surge in the number of research papers leveraging AI methodologies for the detection/diagnosis of FMS. This trend underscores the growing recognition and application of advanced technologies to enhance the understanding and management of FMS.

Using AI to detect, classify, and diagnose FMS presents several advantages. Our review found numerous studies that illustrate these approaches' qualitative and quantitative benefits. First, using AI-based approaches increases diagnostic accuracy since AI algorithms can process complex, high-dimensional data, identifying patterns that may not be visible to human observers. AI and ML-based algorithms can efficiently handle large amounts of data coming from diverse sources (e.g., EEG, ECG, MRI, fMRI), saving time and resources in research and clinical settings. By analyzing subtle patterns in patient data, AI models can potentially

TABLE 4. Summary of studies involving pain detection in FMS stratified by signals used.

Publication	Study Aim	Signal Used	Findings/Results
Idris et al. (2014) [75]	Study the relationship between FMS and arachnoiditis.	MRI/fMRI	Adhesive arachnoiditis syndrome is a chronic condition affecting multiple body systems (nervous, immune, and visceromusculoskeletal systems), often resembling an acute spinal disorder, highlighting the need for neurosurgeons to conduct detailed assessments and careful interpretation of neuroinvestigations.
McCrae et al. (2015) [82]	Compare hippocampal volume levels in patients with and without FM.	MRI/fMRI	FMS patients have significantly smaller hippocampi in both the left and right hemispheres. No statistically significant impact of depression in hippocampal volume (p-values of 0.811 and 0.813).
Basu et al. (2018) [80]	Study the similarities between RA and FMS.	MRI/fMRI	RA patients with increased levels of FMness share neurobiologic features that are consistently observed in FMS patients.
Haibel and Sieper (2015) [83]	Explore the diagnostic challenges and treatment options for enthesitis in spondyloarthritis and PsA, emphasizing the role of imaging techniques and the efficacy of various therapies.	Ultrasound	Tumor necrosis factor-alpha (TNF-alpha) blockers are extremely useful in randomized controlled trials for spondyloarthritis/PsA. However, they are not yet approved for enthesis.
Mian et al. (2016) [79]	Use Doppler Ultrasound to study the level of synovitis in RA patients with fibromyalgic clinical features.	Ultrasound	RA patients with concomitant FMS scores have higher disease activity scores but may have lower levels of synovial inflammation.
Lee (2019) [78]	Study the role of MSKUS in PsA.	Ultrasound	N/A.
Geng et al. (2022) [84]	Ultrasound can be used to improve the performance of CASPAR.	Ultrasound	Specificity 91.40% Sensitivity 95.70% Accuracy = 93.60%
Bilgin et al. (2015) [81]	Examine if heart rate variability, anxiety tests, and FMS are related using ECG signals.	EEG/ECG	Accuracy = 91.11%
Rosenfeld et al. (2015) [77]	Study the relationship between sleep disorder and periodic leg movement with FMS using EEG signals.	EEG/ECG	Sleep apnea is highly prevalent in FMS patients. However, periodic leg movement disorder and bad sleep efficiency are not.
McGonagle et al. (2023) [76]	Study sleep patterns in patients with FMS using EEG signals.	EEG/ECG	FMS patients exhibit specific differences in sleep microstructure compared to healthy controls, including decreased microarousals, higher periodic limb movements, and more dissociated states.

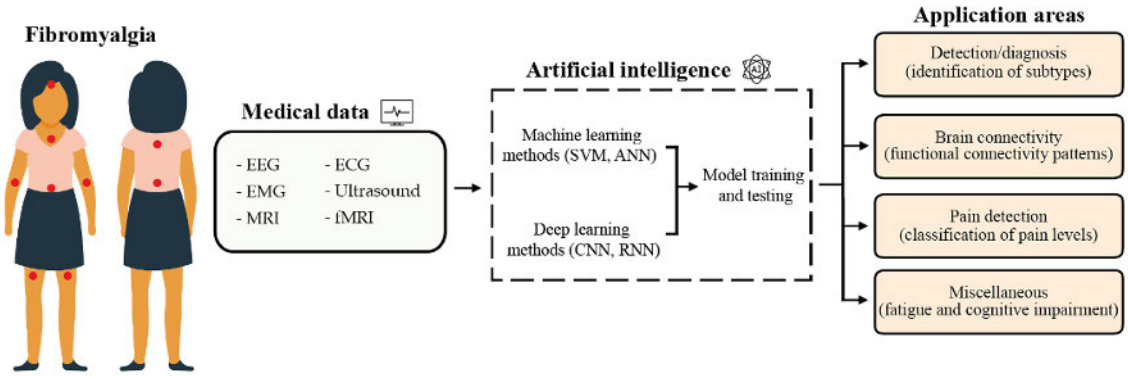

FIGURE 7. Pictorial summary of our review.

identify FMS at earlier stages, even before the full spectrum of symptoms has emerged. Early detection is crucial for timely intervention, which can improve patient outcomes. They can also help identify subgroups within the FMS population based on shared characteristics and predict individual responses to treatments, enabling personalized medicine approaches. Finally, through the analysis of extensive datasets, AI models can aid in discovering biomarkers for FMS, providing objective measures for disease severity, progression, and treatment response, thus moving beyond the reliance on subjective patient reports. An analysis of the different metrics presented in the reviewed studies reveals a significant variance in the accuracy, sensitivity, and specificity of different models. This indicates the current trend of optimization and adaptation of AI models to the nuanced characteristics of FMS. For example, the ability of EEG signals to capture unique features associated with FMS is evident from EEG-based studies that use SVM

and K-nearest neighbors to achieve accuracies ranging from 91.83% to 96.15%. Similarly, the application of ML algorithms in MRI/fMRI studies has achieved accuracies of up to 95%. This showcases the ability of AI to understand complex patterns within imaging data and to map them with FMS pathology.

Barua et al. [29]developed a lightweight ML algorithm for FMS diagnosis using single-lead ECG signals that were recorded when patients were asleep. Their cohort comprised FMS patients and healthy individuals. Achieving over 92% accuracy, their results suggested that measures across different sleep stages could have clinical applications in detecting FMS. While they used ECG signals, several others used EEG signals to detect FMS [34], [37], [38]. They too achieved high accuracies (up to 96.15%) with different ML techniques, highlighting EEG as yet another feasible signal to detect FMS. The adoption of MRI and fMRI for FMS detection along with ML algorithms has also started gaining popularity. They have been found to achieve great results in differentiating FMS from other conditions. Boissoneault et al. [21] used sMRI and fMRI to classify healthy controls and patients with FMS and CFS accurately. Behr et al. [19] also used SVM on ultrasound images to differentiate FMS from healthy individuals, achieving an accuracy of 84.1%. Finally, Liang et al. [46] came up with a novel, automatic diagnosis model for FMS. They integrated BFCNs derived from rs-fMRI with GCN and achieved an accuracy of 82.48%. With accuracies ranging from 82.48% to over 95%, these studies quantitatively highlight the efficacy of ML in improving diagnostic accuracy for FMS. Qualitatively, they indicate that ML algorithms can detect FMS patients with high accuracy irrespective of the image signal – be it ECG, EEG, MRI, or ultrasound. Such state-of-the-art models promise enhanced diagnostic capabilities and pave the way for timely, tailored, and effective treatment strategies for FMS patients.

B. CURRENT CHALLENGES IN FMS RESEARCH

While AI-based approaches in FMS research show several promising avenues, it is also important to recognize its limitations and address them carefully.

One of the biggest challenges in exploring AI methods for FMS research is the lack of publicly available, comprehensive datasets specifically curated for FMS research. Our review indicates that AI models that can effectively handle vast amounts of data already exist. However, they need to be tested to understand their performance on multimodal data. While integrating diverse data types (e.g., clinical records, imaging, and sensor data) can offer a more holistic view of FMS, the effect of doing so on the performance of existing ML models remains unclear. Some potential challenges in using multimodal data include class imbalance and data heterogeneity. Class imbalance can skew model training and affect the accuracy of predictions. It could also increase the number of false positive or true negative results. On the other hand, data heterogeneity and variability arise from the diverse nature of FMS symptoms and the wide range of data types used in research. Diverse data requires the implementation of clever strategies for data integration. This includes multi-modal data fusion techniques to ensure robustness and generalizability across different patient populations and study designs. Additionally, most of the reviewed studies rely on small datasets, making it difficult to train robust and generalizable AI models. As a result, the algorithms risk overfitting the data, showing high performance only within their narrow study parameters but failing to scale to real-world clinical settings. Potential solutions include adopting transfer learning and data augmentation techniques along with synthetic data generation to expand sample size.

Explainable AI (XAI) can help overcome skepticism among clinicians about using AI to diagnose FMS by providing understandable and interpretable model outputs that clinicians can trust. Validating the developed AI models is very important. Since FMS data can be highly heterogeneous, AI models have to be tested across various setups before being deployed clinically. This validation should be performed across different data modalities as well as patient cohorts from diverse demographic and clinical settings. Performing such a validation would help improve trust among clinicians by mitigating any bias and ensuring generalizability.

Finally, there is a pressing need to collect and analyze longitudinal data and highlight the temporal evolution of FMS. Such data would not only help track disease progression, but would also be invaluable to identify early predictive biomarkers, and study the long-term effectiveness of various treatments. Longitudinal studies, when conducted parallelly with ML analysis, hold the potential to interpret intricate mechanisms underpinning FMS, facilitating early detection and intervention strategies. Also, no studies in the ''Brain Connectivity'' section employed AI techniques for data analysis or pattern recognition. This highlights a potential gap in the literature and opens up an opportunity for future research to leverage the power of AI in examining complex neurobiological mechanisms underlying brain connectivity in FMS patients.

C. FUTURE DIRECTIONS IN FMS RESEARCH

AI algorithms offer considerable strengths in FMS research, primarily due to their ability to uncover complex patterns within vast datasets that may elude traditional analysis techniques. One of the significant advantages is the application of transfer learning and domain adaptation techniques. These approaches enable researchers to leverage pre-trained models from related fields, significantly reducing the need for extensive labeled datasets specific to FMS. Such methodologies are invaluable in contexts where data collection is challenging or when aiming to accelerate the development of diagnostic and prognostic models. ML's capability to handle and analyze multi-dimensional data allows for integrating various data types (e.g., clinical, biochemical, imaging data), thereby

enriching the analysis and offering a better understanding of the syndrome. The adaptability of ML models to learn from new data continually means they can evolve and improve as more information becomes available, making them increasingly effective over time in diagnosing and understanding FMS.

With AI research in FMS gaining popularity, this field is well set for major progress and breakthroughs in the near future. Application of deep learning models that are the state-of-the-art (Transformers, Graph CNN models, and Semi-supervised learning algorithms, for example) on multimodal data could lead to the creation of new baselines and benchmarks. Transformers and Graph CNNs in particular have shown great promise and results in other fields that involve processing of unstructured data. This makes them potentially well-suited for understanding the intricacies of FMS detection and management. Implementing these models by parallelly adopting XAI and uncertainty quantification (UQ) could be the next big breakthrough in FMS research. By ensuring models not only yield accurate predictions but also provide interpretable explanations, researchers and clinicians can gain insights into the decision-making process of algorithms. This would build trust and help translate AI findings into practical clinical applications, leading to a faster and more timely diagnosis. This is extremely crucial for a condition like FMS because of its complexity and lack of clear understanding. To efficiently scale up the application of AI in FMS research, implementing cloud-based systems is very important. Cloud computing can provide the necessary infrastructure to support the large-scale analysis of multimodal data. This would allow researchers to exploit the full potential of AI without being limited by local hardware constraints.

Integration of wearable devices and mobile health technologies provide another promising research direction. These devices are an excellent source of real-time, continuous data that can be obtained through activity trackers, biosensors, and other wearable technologies. They would allow for a more nuanced understanding of the condition, facilitate the collection of extensive data, and support the development of precise and timely treatment strategies tailored specifically to the patient's symptoms and lifestyle. However, because of privacy and ethical reasons, sharing data from mobile and wearable devices could be dangerous and hard to implement. In such a setup, encouraging collaborations across disciplines and creating open-source datasets could accelerate advancements in FMS research. Data sharing enables researchers to reproduce existing results and study them in diverse settings. They create a platform for conducting validation studies across diverse populations and settings. Furthermore, integrating genomic, proteomic, and metabolomic data with clinical and physiological data could provide a comprehensive, multimodal approach to understanding FMS. This would lead to breakthroughs in FMS diagnosis, management, and treatment, thereby improving the quality of the patients' lives significantly. Finally, real-world clinical adoption of AI-based diagnostics requires addressing practical challenges, such as ensuring cost-effectiveness and providing adequate training for clinicians and technicians who implement these methods in daily practice. High-end equipment and software maintenance can be expensive. Targeted training programs for frontline clinical staff, coupled with user-friendly software interfaces, could help mitigate these challenges. By reducing the operational burden and cost barriers, AI-based diagnostic tools can be seamlessly integrated into conventional methodologies, enabling broader adoption and, ultimately, timely FMS detection.

V. CONCLUSION

In this work, we conduct a systematic review highlighting the importance of AI-based techniques in FMS detection. The complex and poorly understood nature of FMS poses significant challenges in diagnosis and prognosis. The absence of clear methods for measuring disease severity, diagnosis, and progression creates an urgent need for innovative research approaches to address these issues. AI holds significant potential for enhancing understanding of FMS and improving patient care. By analyzing vast datasets and identifying patterns, AI can help in early detection of FMS along with precise diagnosis, and personalized treatment. Despite its strengths, using AI in FMS research faces challenges like interpretability, data variability, and the lack of publicly available open-source datasets. Future research directions should focus on incorporating XAI and UQ techniques, integrating wearable devices for real-time data collection, and conducting longitudinal studies to track disease progression. Collaboration, data sharing, and using multimodal data are crucial to getting a better understanding of FMS and enhancing patient outcomes.

REFERENCES

[1] C. M. Galvez-Sánchez and C. I. Montoro, "Psychoeducation for fibromyalgia syndrome: A systematic review of emotional, clinical and functional related-outcomes," *Behav. Sci.*, vol. 13, no. 5, p. 415, May 2023.

[2] J. M. Glass, "Cognitive dysfunction in fibromyalgia syndrome," *J. Musculoskeletal Pain*, vol. 18, no. 4, pp. 367–372, Oct. 2010.

[3] A. P. Marques, A. D. S. D. E. Santo, A. A. Berssaneti, L. A. Matsutani, and S. L. K. Yuan, "A prevalência de fibromialgia: Atualização da revisão de literaturaPrevalence of fibromyalgia: Literature," *Rev. Bras. Reumatol.*, vol. 57, pp. 356–363, Jul. 2017.

[4] R. Siracusa, R. D. Paola, S. Cuzzocrea, and D. Impellizzeri, "Fibromyalgia: Pathogenesis, mechanisms, diagnosis and treatment options update," *Int. J. Mol. Sci.*, vol. 22, no. 8, p. 3891, Apr. 2021.

[5] D. S. Molnar, G. L. Flett, S. W. Sadava, and J. Colautti, "Perfectionism and health functioning in women with fibromyalgia," *J. Psychosomatic Res.*, vol. 73, no. 4, pp. 295–300, Oct. 2012.

[6] L. M. Arnold, L. J. Crofford, P. J. Mease, S. M. Burgess, S. C. Palmer, L. Abetz, and S. A. Martin, "Patient perspectives on the impact of fibromyalgia," *Patient Educ. Counseling*, vol. 73, no. 1, pp. 114–120, Oct. 2008.

[7] D. J. Clauw, "Fibromyalgia: A clinical review," *Jama*, vol. 311, no. 15, pp. 1547–1555, 2014.

[8] C. Boomershine, "Fibromyalgia: The prototypical central sensitivity syndrome," *Current Rheumatology Rev.*, vol. 11, no. 2, pp. 131–145, Jul. 2015.

[9] F. Wolfe, D. J. Clauw, M.-A. Fitzcharles, D. L. Goldenberg, W. Häuser, R. L. Katz, P. J. Mease, A. S. Russell, I. J. Russell, and B. Walitt, "2016 revisions to the 2010/2011 fibromyalgia diagnostic criteria," *Seminars Arthritis Rheumatism*, vol. 46, no. 3, pp. 319–329, Dec. 2016.

[10] D. Russell, I. C. Álvarez Gallardo, I. Wilson, C. M. Hughes, G. W. Davison, B. Sañudo, and J. G. McVeigh, "'Exercise to me is a scary word': Perceptions of fatigue, sleep dysfunction, and exercise in people with fibromyalgia syndrome—A focus group study," *Rheumatology Int.*, vol. 38, no. 3, pp. 507–515, Mar. 2018.

[11] L. M. Arnold, E. Choy, D. J. Clauw, D. L. Goldenberg, R. E. Harris, M. Helfenstein, T. S. Jensen, K. Noguchi, S. L. Silverman, T. Ushida, and G. Wang, "Fibromyalgia and chronic pain syndromes: A white paper detailing current challenges in the field," *Clin. J. Pain*, vol. 32, no. 9, pp. 737–746, 2016.

[12] F. Wolfe, D. J. Clauw, M. Fitzcharles, D. L. Goldenberg, R. S. Katz, P. Mease, A. S. Russell, I. J. Russell, J. B. Winfield, and M. B. Yunus, "The American college of rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity," *Arthritis Care Res.*, vol. 62, no. 5, pp. 600–610, May 2010.

[13] W. Häuser, E. Brähler, J. Ablin, and F. Wolfe, "Modified 2016 American college of rheumatology fibromyalgia criteria, the analgesic, anesthetic, and addiction clinical trial translations innovations opportunities and networks–American pain society pain taxonomy, and the prevalence of fibromyalgia," *Arthritis Care Res.*, vol. 73, no. 5, pp. 617–625, May 2021.

[14] A. M. Finucane, J. Lugton, C. Kennedy, and J. A. Spiller, "The experiences of caregivers of patients with delirium, and their role in its management in palliative care settings: An integrative literature review," *Psycho-Oncology*, vol. 26, no. 3, pp. 291–300, Mar. 2017.

[15] M. I. Jordan and T. M. Mitchell, "Machine learning: Trends, perspectives, and prospects," *Science*, vol. 349, no. 6245, pp. 255–260, Jul. 2015.

[16] J. Schmidhuber, "Deep learning in neural networks: An overview," *Neural Netw.*, vol. 61, pp. 85–117, Jan. 2015.

[17] M. E. Robinson, A. M. O'Shea, J. G. Craggs, D. D. Price, J. E. Letzen, and R. Staud, "Comparison of machine classification algorithms for fibromyalgia: Neuroimages versus self-report," *J. Pain*, vol. 16, no. 5, pp. 472–477, May 2015.

[18] E. Docampo, A. Collado, G. Escaramís, J. Carbonell, J. Rivera, J. Vidal, J. Alegre, R. Rabionet, and X. Estivill, "Cluster analysis of clinical data identifies fibromyalgia subgroups," *PLoS ONE*, vol. 8, no. 9, Sep. 2013, Art. no. e74873.

[19] M. Behr, S. Saiel, V. Evans, and D. Kumbhare, "Machine learning diagnostic modeling for classifying fibromyalgia using B-mode ultrasound images," *Ultrason. Imag.*, vol. 42, no. 3, pp. 135–147, May 2020.

[20] A. Leroux, R. Rzasa-Lynn, C. Crainiceanu, and T. Sharma, "Wearable devices: Current status and opportunities in pain assessment and management," *Digit. Biomarkers*, vol. 5, no. 1, pp. 89–102, Apr. 2021.

[21] J. Boissoneault, L. Sevel, J. Letzen, M. Robinson, and R. Staud, "Biomarkers for musculoskeletal pain conditions: Use of brain imaging and machine learning," *Current Rheumatology Rep.*, vol. 19, no. 1, pp. 1–9, Jan. 2017.

[22] D. Dadabhoy, L. J. Crofford, M. Spaeth, I. J. Russell, and D. J. Clauw, "Biology and therapy of fibromyalgia. evidence-based biomarkers for fibromyalgia syndrome," *Arthritis Res. Therapy*, vol. 10, no. 4, p. 211, 2008.

[23] J. A. Glombiewski, K. Bernardy, and W. Häuser, "Efficacy of EMG- and EEG-biofeedback in fibromyalgia syndrome: A meta-analysis and a systematic review of randomized controlled trials," *J. Evidence-Based Complementary Altern. Med.*, vol. 2013, no. 1, 2013, Art. no. 962741.

[24] A. L. Adler-Neal and F. Zeidan, "Mindfulness meditation for fibromyalgia: Mechanistic and clinical considerations," *Current Rheumatol. Rep.*, vol. 19, no. 9, pp. 1–9, Sep. 2017.

[25] G. T. Jones, B. Mallawaarachchi, J. Shim, J. Lock, and G. J. Macfarlane, "The prevalence of fibromyalgia in axial spondyloarthritis," *Rheumatol. Int.*, vol. 40, no. 10, pp. 1581–1591, Oct. 2020.

[26] M. Ricci, A. Cimini, M. R. Grivet Fojaja, M. Ullo, B. Carabellese, V. Frantellizzi, and E. Lubrano, "Novel approaches in molecular imaging and neuroimaging of fibromyalgia," *Int. J. Mol. Sci.*, vol. 23, no. 24, p. 15519, Dec. 2022.

[27] G. A. de Melo, M. L. L. H. Madruga, and N. Torro, "Electroencephalographic evaluation in fibromyalgia: A systematic review," *Clin. EEG Neurosci.*, vol. 55, no. 1, pp. 76–87, Jan. 2024.

[28] O. Elmas, S. Yildiz, S. Bilgin, S. Demirci, S. Comlekci, H. R. Koyuncuoglu, S. Akkus, O. H. Colak, E. Koklukaya, E. Arslan, O. Ozkan, and G. Bilgin, "Physiological parameters as a tool in the diagnosis of fibromyalgia syndrome in females: A preliminary study," *Life Sci.*, vol. 145, pp. 51–56, Jan. 2016.

[29] P. D. Barua, M. Kobayashi, M. Tanabe, M. Baygin, J. K. Paul, T. Iype, S. Dogan, T. Tuncer, R.-S. Tan, and U. R. Acharya, "Innovative fibromyalgia detection approach based on quantum-inspired 3LBP feature extractor using ECG signal," *IEEE Access*, vol. 11, pp. 101359–101372, 2023.

[30] E. Baumueller, A. Winkelmann, D. Irnich, and M. Weigl, "Electromyogram biofeedback in patients with fibromyalgia: A randomized controlled trial," *Complementary Med. Res.*, vol. 24, no. 1, pp. 33–39, 2017.

[31] B. Losert-Bruggner, M. Hülse, and R. Hülse, "Fibromyalgia in patients with chronic CCD and CMD–A retrospective study of 555 patients," *Cranio*, vol. 36, no. 5, pp. 318–326, 2018.

[32] J. Navarro, R. Del Moral, Y. L. del Hoyo, T. Vergara, R. Magallon, J. Garcia-Campayo, and P. Marijuan, "Validation of electroencephalic cordance for evaluation, prognosis and classification of fibromyalgia," *Trauma-Spain*, vol. 24, no. 2, pp. 93–100, 2013.

[33] J. Navarro López, R. D. Moral Bergós, and P. C. Marijuán, "Significant new quantitative EGG patterns in fibromyalgia," *Eur. J. Psychiatry*, vol. 29, no. 4, pp. 277–292, Dec. 2015.

[34] J. K. Paul, T. Iype, R. Dileep, Y. Hagiwara, J. W. Koh, and U. R. Acharya, "Characterization of fibromyalgia using sleep EEG signals with non-linear dynamical features," *Comput. Biol. Med.*, vol. 111, Aug. 2019, Art. no. 103331.

[35] R. Martín-Brufau, M. N. Gómez, L. S.-Sanchez-Rojas, and C. Nombela, "Fibromyalgia detection based on EEG connectivity patterns," *J. Clin. Med.*, vol. 10, no. 15, p. 3277, Jul. 2021.

[36] N. Goldway, N. M. Petro, J. Ablin, A. Keil, E. Ben Simon, Y. Zamir, L. Weizman, A. Greental, T. Hendler, and H. Sharon, "Abnormal visual evoked responses to emotional cues correspond to diagnosis and disease severity in fibromyalgia," *Frontiers Behav. Neurosci.*, vol. 16, May 2022, Art. no. 852133.

[37] I. Karabey Aksalli, N. Baygin, Y. Hagiwara, J. K. Paul, T. Iype, P. D. Barua, J. E. W. Koh, M. Baygin, S. Dogan, T. Tuncer, and U. R. Acharya, "Automated characterization and detection of fibromyalgia using slow wave sleep EEG signals with glucose pattern and D'hondt pooling technique," *Cognit. Neurodynamics*, vol. 18, no. 2, pp. 383–404, Apr. 2024.

[38] A. Rushbrooke, J. Tsigarides, S. Sami, and A. Bagnall, "Time series classification of electroencephalography data," in *Proc. Int. Work-Conf. Artif. Neural Netw.* Cham, Switzerland: Springer, Jan. 2023, pp. 601–613.

[39] B. Sundermann, M. Burgmer, E. Pogatzki-Zahn, M. Gaubitz, C. Stüber, E. Wessolleck, G. Heuft, and B. Pfleiderer, "Diagnostic classification based on functional connectivity in chronic pain: Model optimization in fibromyalgia and rheumatoid arthritis," *Acad. Radiol.*, vol. 21, no. 3, pp. 369–377, 2014.

[40] L. Sevel, J. Letzen, J. Boissoneault, A. O'Shea, M. Robinson, and R. Staud, "(337) MRI based classification of chronic fatigue, fibromyalgia patients and healthy controls using machine learning algorithms: A comparison study," *J. Pain*, vol. 17, no. 4, p. S60, Apr. 2016.

[41] B. Jarrahi, K. T. Martucci, A. S. Nilakantan, and S. Mackey, "Investigating the BOLD spectral power of the intrinsic connectivity networks in fibromyalgia patients: A resting-state fMRI study," in *Proc. 39th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc. (EMBC)*, Jul. 2017, pp. 497–500.

[42] S. Sayılır and N. Çullu, "Decreased olfactory bulb volumes in patients with fibromyalgia syndrome," *Clin. Rheumatology*, vol. 36, no. 12, pp. 2821–2824, Dec. 2017.

[43] K. Tokumasu, K. Ochi, and F. Otsuka, "Idiopathic combined adrenocorticotropin and growth hormone deficiency mimicking chronic fatigue syndrome," *BMJ Case Rep.*, vol. 14, no. 10, Oct. 2021, Art. no. e244861.

[44] Z. Y. Shan, A. Z. Mohamed, T. Andersen, S. Rendall, R. A. Kwiatek, P. D. Fante, V. D. Calhoun, S. Bhuta, and J. Lagopoulos, "Multimodal MRI of myalgic encephalomyelitis/chronic fatigue syndrome: A cross-sectional neuroimaging study toward its neuropathophysiology and diagnosis," *Frontiers Neurol.*, vol. 13, Sep. 2022, Art. no. 954142.

[45] N. Thanh Nhu, D. Y.-T. Chen, and J.-H. Kang, "Identification of resting-state network functional connectivity and brain structural signatures in fibromyalgia using a machine learning approach," *Biomedicines*, vol. 10, no. 12, p. 3002, Nov. 2022.

[46] Y. Liang, M. Long, P. Yang, T. Wang, J. Jiao, and B. Lei, "Fused brain functional connectivity network and edge-attention graph convolution network for fibromyalgia syndrome diagnosis," in *Proc. 45th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc. (EMBC)*, Jul. 2023, pp. 1–5.

[47] F. Ozkan, B. Bakan, M. F. Inci, F. Kocturk, G. Y. Cetin, M. Yuksel, and M. Sayarlioglu, "Assessment of enthesopathy in patients with fibromyalgia by using new sonographic enthesitis index," *Revista Brasileira de Reumatologia*, vol. 53, no. 4, pp. 335–340, Jul. 2013.

[48] A. Muro-Culebras and A. I. Cuesta-Vargas, "Sono-myography and sono-myoelastography of the tender points of women with fibromyalgia," *Ultrasound Med. Biol.*, vol. 39, no. 11, pp. 1951–1957, Nov. 2013.

[49] M. A. Ali, M. Rehman, and M. Saeed, "Rheumatoid arthritis masquerading as fibromyalgia," *J. College Physicians Surgeons–Pakistan (JCPSP)*, vol. 27, no. 9, pp. S134–S136, Sep. 2017.

[50] A. Polachek et al., "Role of ultrasound for assessment of psoriatic arthritis patients with fibromyalgia," *Ann. Rheumatic Diseases*, vol. 80, no. 12, pp. 1553–1558, Dec. 2021.

[51] S. Miladi, H. Ben Ayed, A. Fazaa, H. Boussaa, Y. Makhlouf, L. Souabni, K. Ouenniche, S. Kassab, S. Chekili, K. B. Abdelghani, and A. Laatar, "Rheumatoid arthritis with concomitant fibromyalgia: The role of ultrasound in assessing disease activity," *Musculoskeletal Care*, vol. 21, no. 4, pp. 1011–1019, Dec. 2023.

[52] A. Marchesoni, P. Macchioni, S. Gasparini, C. Perricone, F. M. Perrotta, R. D. Grembiale, E. Silvagni, R. Ramonda, L. Costa, A. Zabotti, G. Curradi, G. Gualberti, F. Marando, and C. Salvarani, "Use of ultrasonography to discriminate psoriatic arthritis from fibromyalgia: A post-hoc analysis of the ULISSE study," *J. Clin. Med.*, vol. 11, no. 1, p. 180, Dec. 2021.

[53] A. J. González-Villar, Y. Triñanes, C. Gómez-Perretta, and M. T. Carrillo-De-La-Peña, "Patients with fibromyalgia show increased beta connectivity across distant networks and microstates alterations in resting-state electroencephalogram," *NeuroImage*, vol. 223, Dec. 2020, Art. no. 117266.

[54] S. Cardoso, C. Fernandes, and F. Barbosa, "Emotional and attentional bias in fibromyalgia: A pilot ERP study of the dot-probe task," *Neurol. Therapy*, vol. 10, no. 2, pp. 1079–1093, Dec. 2021.

[55] K. B. Jensen, P. Srinivasan, R. Spaeth, Y. Tan, E. Kosek, F. Petzke, S. Carville, P. Fransson, H. Marcus, S. C. R. Williams, E. Choy, O. Vitton, R. Gracely, M. Ingvar, and J. Kong, "Overlapping structural and functional brain changes in patients with long-term exposure to fibromyalgia pain," *Arthritis Rheumatism*, vol. 65, no. 12, pp. 3293–3303, Dec. 2013.

[56] E. Ichesco, T. Puiu, J. P. Hampson, A. E. Kairys, D. J. Clauw, S. E. Harte, S. J. Peltier, R. E. Harris, and T. Schmidt-Wilcke, "Altered fMRI resting-state connectivity in individuals with fibromyalgia on acute pain stimulation," *Eur. J. Pain*, vol. 20, no. 7, pp. 1079–1089, Aug. 2016.

[57] A. Truini, E. Tinelli, M. C. Gerardi, V. Calistri, C. Iannuccelli, S. L. Cesa, L. Tarsitani, C. Mainero, P. Sarzi-Puttini, G. Cruccu, F. Caramia, and M. D. Franco, "Abnormal resting state functional connectivity of the periaqueductal grey in patients with fibromyalgia," *Clin. Exp. Rheumatol.*, vol. 34, no. 2, pp. 129–133, May 2016.

[58] J. C. Cheng, A. Anzolin, M. Berry, H. Honari, M. Paschali, A. Lazaridou, J. Lee, A. Grahl, M. Lindquist, R. R. Edwards, and V. Napadow, "Dynamic functional connectivity underlying temporal summation of pain in fibromyalgia," *J. Pain*, vol. 22, no. 5, pp. 603–604, May 2021.

[59] G. Ioachim, H. J. M. Warren, J. M. Powers, R. Staud, C. F. Pukall, and P. W. Stroman, "Altered pain in the brainstem and spinal cord of fibromyalgia patients during the anticipation and experience of experimental pain," *Frontiers Neurol.*, vol. 13, May 2022, Art. no. 862976.

[60] V. Napadow, L. LaCount, K. Park, S. As-Sanie, D. J. Clauw, and R. E. Harris, "Intrinsic brain connectivity in fibromyalgia is associated with chronic pain intensity," *Arthritis Rheumatism*, vol. 62, no. 8, pp. 2545–2555, Aug. 2010.

[61] C. M. Segning, J. Harvey, H. Ezzaidi, K. B. P. Fernandes, R. A. da Silva, and S. Ngomo, "Towards the objective identification of the presence of pain based on electroencephalography signals' analysis: A proof-of-concept," *Sensors*, vol. 22, no. 16, p. 6272, Aug. 2022.

[62] S. Rifbjerg-Madsen, A. W. Christensen, M. Boesen, R. Christensen, B. Danneskiold-Samsøe, H. Bliddal, L. Dreyer, H. Locht, and K. Amris, "The course of pain hypersensitivity according to painDETECT in patients with rheumatoid arthritis initiating treatment: Results from the prospective FRAME-cohort study," *Arthritis Res. Therapy*, vol. 20, no. 1, pp. 1–11, Dec. 2018.

[63] M. O. Papuga, J. R. Burke, and P. E. Dougherty, "The reliability of a novel magnetic resonance compatible electro-pneumatic device for delivering a painful pressure stimulus over the lumbar spine," *Somatosensory Motor Res.*, vol. 32, no. 1, pp. 51–60, Jan. 2015.

[64] G. J. Matheson, "We need to talk about reliability: Making better use of test-retest studies for study design and interpretation," *PeerJ*, vol. 7, p. e6918, May 2019.

[65] D. Cankurtaran, Z. A. Yığman, Ş. Güzel, and E. Umay, "The importance of myofascial trigger points in chronic neck pain: An ultrasonography preliminary study," *PM R*, vol. 15, no. 8, pp. 954–964, Aug. 2023.

[66] G. Deutsch, H. Deshpande, H. H. Lai, J. J. Kutch, and T. J. Ness, "Cerebral perfusion and sensory testing results differ in interstitial cystitis/bladder pain syndrome patients with and without fibromyalgia: A site-specific MAPP network study," *J. Pain Res.*, pp. 3887–3895, Dec. 2021.

[67] A. D. Tarnoki, D. L. Tarnoki, C. Oláh, M. Szily, D. T. Kovacs, A. Dienes, M. Piroska, B. Forgo, M. Pinheiro, P. Ferreira, L. Kostyál, M. Meszaros, J. Pako, L. Kunos, and A. Bikov, "Lumbar spine abnormalities in patients with obstructive sleep apnoea," *Sci. Rep.*, vol. 11, no. 1, p. 16233, Aug. 2021.

[68] M. C. Cojocaru, I. M. Cojocaru, V. M. Voiculescu, N. A. Cojan-Carlea, V. Dumitru, and M. Berteanu, "Trigger points-ultrasound and thermal findings," *J. Med. Life*, vol. 8, no. 3, p. 315, Sep. 2015.

[69] S. Ahmed, M. Behr, and D. Kumbhare, "Differentiating varying degrees of central sensitization in chronic widespread pain using quantitative ultrasound," *Ann. Phys. Rehabil. Med.*, vol. 61, p. e430, Jul. 2018.

[70] M. Correa-Rodríguez, J. El Mansouri-Yachou, R. M. Tapia-Haro, F. Molina, B. Rueda-Medina, and M. E. Aguilar-Ferrandiz, "Associations between bone mass in women with fibromyalgia and widespread pressure pain hypersensitivity, tenderness, perceived pain level, and disability," *Biol. Res. Nursing*, vol. 21, no. 3, pp. 272–278, May 2019.

[71] M. Polat, A. Kahveci, D. Tecer, Z. Günendi, and F. Gögüş, "The role of ultrasonographic synovial assessment in rheumatoid arthritis patients with concomitant fibromyalgia," *Arch. Rheumatol.*, vol. 38, no. 2, pp. 174–182, Jun. 2023.

[72] Y. Song, G. Kirsch, and W. Jarjour, "The utility of ultrasound in evaluating joint pain in systemic lupus erythematosus: Looking beyond fibromyalgia," *J. Personalized Med.*, vol. 13, no. 5, p. 763, Apr. 2023. [Online]. Available: https://www.mdpi.com/2075-4426/13/5/763

[73] C. P. Andrade, A. R. Zamunér, M. Forti, A. M. Catai, P. Driusso, and E. da Silva, "Association between baroreflex function and pressure pain threshold in women with fibromyalgia," in *Proc. 8th Conf. Eur. Study Group Cardiovascular Oscillations (ESGCO)*, May 2014, pp. 211–212.

[74] K.-H. Choi, O. S. Kwon, U. M. Jerng, S. M. Lee, L.-H. Kim, and J. Jung, "Development of electromyographic indicators for the diagnosis of temporomandibular disorders: A protocol for an assessor-blinded cross-sectional study," *Integrative Med. Res.*, vol. 6, no. 1, pp. 97–104, Mar. 2017.

[75] Z. Idris, F. Ghazali, and J. Abdullah, "Fibromyalgia and arachnoiditis presented as an acute spinal disorder," *Surgical Neurol. Int.*, vol. 5, no. 1, p. 151, 2014.

[76] D. McGonagle, R. Ramonda, L. Scagnellato, S. Scriffignano, J. Weddell, and E. Lubrano, "A strategy towards disentangling treatment refractory from misdiagnosed axial spondyloarthritis," *Autoimmunity Rev.*, vol. 23, no. 1, Jan. 2024, Art. no. 103405.

[77] V. W. Rosenfeld, D. N. Rutledge, and J. M. Stern, "Polysomnography with quantitative EEG in patients with and without fibromyalgia," *J. Clin. Neurophysiol.*, vol. 32, no. 2, pp. 164–170, 2015.

[78] A. Lee, "The role of musculoskeletal ultrasound in psoriatic arthritis," *Ultrasound Med. Biol.*, vol. 45, pp. S63–S64, 2019.

[79] A. N. Mian, K. Chaabo, J. Wajed, S. Subesinghe, N. J. Gullick, B. Kirkham, and T. Garrood, "Rheumatoid arthritis patients with fibromyalgic clinical features have significantly less synovitis as defined by power Doppler ultrasound," *BMC Musculoskeletal Disorders*, vol. 17, no. 1, pp. 1–5, Dec. 2016.

[80] N. Basu, C. M. Kaplan, E. Ichesco, T. Larkin, R. E. Harris, A. Murray, G. Waiter, and D. J. Clauw, "Neurobiologic features of fibromyalgia are also present among rheumatoid arthritis patients," *Arthritis Rheumatol.*, vol. 70, no. 7, pp. 1000–1007, Jul. 2018.

[81] S. Bilgin, E. Arslan, O. Elmas, S. Yildiz, O. H. Colak, G. Bilgin, H. R. Koyuncuoglu, S. Akkus, S. Comlekci, and E. Koklukaya, "Investigation of the relationship between anxiety and heart rate variability in fibromyalgia: A new quantitative approach to evaluate anxiety level in fibromyalgia syndrome," *Comput. Biol. Med.*, vol. 67, pp. 126–135, Dec. 2015.
[82] C. McCrae, A. O'Shea, J. Boissoneault, K. Vatthauer, M. Robinson, R. Staud, W. Perlstein, and J. Craggs, "Fibromyalgia patients have reduced hippocampal volume compared with healthy controls," *J. Pain Res.*, vol. 8, p. 47, Jan. 2015.
[83] H. Haibel and J. Sieper, "Enthesitis in the context of spondyloarthritides," *Z. Rheumatol.*, vol. 74, pp. 39–50, Jan. 2015.
[84] Y. Geng, Z. Song, X. Zhang, X. Deng, Y. Wang, and Z. Zhang, "Improved diagnostic performance of CASPAR criteria with integration of ultrasound," *Frontiers Immunol.*, vol. 13, Oct. 2022, Art. no. 935132.

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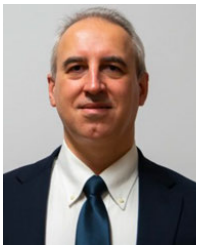

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