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Brain Activity to Study Physical Pain: A Survey of Tools and Methods

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ABSTRACT Pain is a problem that has a significant effect on the quality of life, both personal and social, and in the knowledge of the authors. To date, there is no practical device or method that allows us to generate a quantitative pain index. In recent years, studies related to pain and its measurement have been reported, which have used brain activity as a biological marker of pain based on various methodologies. Therefore, the purpose of this survey article is to concentrate the tools and methods that use brain activity to study two types of physical pain: 1) chronic, as a result of a clinical condition; and, 2) acute physical induced by a painful stimulus. The survey analyzes the elements involved in evaluating these types of pain, considering the number of subjects, the EEG setting, the stimulus applied, the pain perception test used, the software for analysis and processing, and additional resources. The results present a systematic classification of the information; it contains the techniques and technologies that have been used for the study of pain. Finally, the article concludes identifying opportunity areas as quantitative pain measurement tools based on brain activity analysis to understand, adapt, or monitor the treatment responses.

INDEX TERMS EEG pain, pain measurement, brain activity, chronic pain, acute pain.

I. INTRODUCTION

Pain is an unpleasant sensory and emotional experience that protects the body. It appears every time the subject injures any tissue and causes the subject to react by eliminating (or trying to eliminate) the painful stimulus. Three characteristics define pain: time (acute and chronic), origin (nociceptive and neuropathic), and location (somatic and visceral). For this compilation, pain classification by time will be considered, that is, acute and chronic. According to the International Association for the Study of Pain (IASP), pain is associated with actual or potential tissue damage. It is described in terms of such damage but is considered a problem when it begins to present itself chronically, which means, it persists or repeatedly occurs in a period of three to six months with no apparent cause. Moreover, another problem inherent to chronic physical pain is the personal and social costs. One of these costs is related to the reduction of quality of life due to unsatisfied therapeutic needs [1]. Besides, there is evidence that people with chronic pain decreased their daily productivity because this condition generates depression and anxiety [2]. In this sense, the World Health Organization (WHO) recognizes chronic pain as a significant global public health problem. In Mexico only, it is estimated that 27% of the population suffers from chronic pain and in the United States, 17% of the patients cared for in primary care centers have chronic pain and, internationally, this health problem affects between 25 and 29% of the population [3].

Although pain is treated using pharmacological, non-pharmacological, behavioral, and interventional techniques, only 50% of patients in pain reported improvement. The most common barrier to effectively manage pain is the failure of health professionals to assess it and the effectiveness of the used relief measures [4]. The tools commonly used for the assessment of pain intensity (PI) are unidimensional pain scales, such as the Numerical Rating Scale (NRS), Verbal Rating Scale (VRS), or Visual Analogue Scale (VAS)[5]. However, these estimation methods are not sufficient because they only reflect on the subject's perception [6].

This worldwide problem encourages researchers to look for non-subjective options. According to literature, one of the physiological signal that offers adequate information is

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brain activity and it is considered a biomarker [1], [7], [8]. Recent studies report that chronic pain is related to the functioning and structural reorganization in the nervous system, so the activation of multiple areas on the brain generates a pain matrix [9]–[11]. Moreover, recent experiments presented evidence that brain function and behavior may be different in individuals with chronic pain compared to individuals who do not have any pain [8], [12], [13]. In response to painful physical stimuli, brain activity shows a significant effect in the electrocortical reaction [14]. Nowadays, the gold standard tool to measure the potentials produced by the brain is the electroencephalogram (EEG), which is defined as the non-invasive recording of the alternating electrical activity from the scalp's surface through metal electrodes and media conductive [15]. Electrodes position on the scalp must be based on the 10-20 system, which is a method to standardize the recordings and be able to compare results. The term "10-20" refers to the placement of electrodes in 10% or 20% of the total distance between specific skull locations [16], [17]. The EEG is widely used to study the functioning of the brain during rest, sensory stimulation, cognitive tasks, and even with the psychological pain suffered by people with depression [18]–[20].

The EEG is generated by a specific type of synchronous activity of neurons known as pyramidal neurons. The complex electrical output is thus reflected in the areas of the skin where the electrodes are located. The different patterns of electrical activity, known as brain waves, could be recognized by their amplitudes and frequencies. The frequency is measured by the number of waves per second (Hz), while the amplitude stands for the magnitude of these waves measured by microvolts (μV). The different frequency components are classified into delta (less than 4 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta (13-30 Hz), and gamma (30-100 Hz) [21].

Efforts have been made to consider evaluation methods, considering electroencephalography as a tool to determine how brain activity is related to pain and thus determine objective, reliable, and quantitative indicators [22]. Silva, Queirós, and Montoya [23] found that there is a general increase in the potential of lower EEG signal frequencies in patients with chronic pain at rest. Moreover, studies report that activity in gamma waves is closely related to pain compared to the response in other frequencies [14], [24], [33], [25]–[32].

Studies of physical pain through brain activity using EEG techniques have been developed from two perspectives. The first one, considering the chronic pain where the study included subjects presenting different types of physical pain like neuropathic [34], [35], back pain [36], [37], sickle cell disease [38], or pancreatitis [39]. The second one, considering the pain to be induced by a different type of stimulus, like tonic heat [25], [28], [29], or pressure application [24]. Regardless of the origin of the physical pain, the studies with brain activity had reported a relation. However, the difference in EEG acquisition devices, the number of electrodes, electrode placement positions on the scalp, number of subjects, type of stimulus, device to apply the stimuli or software to analyze the signal, made the comparison of the results difficult. In the quantification of pain through brain signals, not only the type and origin of pain intervene but also the tools to obtain these signals are also relevant. In this sense, this article's objective is to present a concentrate of information that allows researchers to shorten the path in the selection of techniques for the study of pain, based on the results obtained through the devices and techniques used by other researchers.

The rest of the paper is organized as follows: Section II describes materials and methods considering the search strategies and selection of studies, as well as the process of data extraction. Section III presents a summary of methodologies for the study of physical pain through brain activity considering chronic pain and acute pain approach. Section IV presents the common elements and methods in the study of pain through brain activity considering both approaches, identifying the devices to acquire EEG signals, stimulus application technology and technique, pain perception test, additional questionnaires to assess the perception of physical and mental health used besides the software to acquire and analyze the signals. Section V shows a discussion and Section VI includes the conclusions.

II. MATERIALS AND METHODS

A. SEARCH STRATEGIES AND SELECTION OF STUDIES

The papers collection for this survey was carried out between January 2018 and January 2020, managing a search approach from general to specific. The general search began with the use of the Google Academic tool; from which it was possible to identify the databases with relevant studies to meet the research objective. The keywords used in the general search were: Pain EEG and Pain quantification EEG. Based on the general search results, a more particular approach was given searching more specifically at IEEE Xplore, PubMed, and Science Direct. Based on the results of the specific search, the following keywords were added: tonic pain EEG, pain brain. The selection of studies was made considering the following eligibility criteria: a) articles in English language, b) articles published after 2010, c) brain activity is used to study pain. The considered exclusion criteria are a) the studies related to emotional pain, b) the study of pain associated with neurological diseases, such as stroke, schizophrenia, autism, or brain tumors. All studies examining physical pain through brain activity were considered in this survey, including the study of chronic pain and the ones in which pain was induced.

B. DATA EXTRACTION

Initially, the title and abstract data were extracted from 224 articles to assess its impact on the research purpose. From those, 115 articles were considered relevant and were examined in detail considering the context, problem, objective, justification, and results, thus allowing an analysis to be carried out considering the inclusion and exclusion, finishing with 31 articles selected for analysis.

TABLE 1. Elements to be considered in the study of pain with brain activity.

Classification	Subjects Information	EEG Montage	Stimuli	Pain Perception Tool Used	Acquisition and Analysis	Additional Tools
Chronic pain	Quantity	Device	Type	Scale	Software	Questionnaires
Acute pain (by stimuli)	Gender M/F (Male/Female)	Number of electrodes	Device to apply it		Models	Techniques
	Age range	Position of electrodes	Part of the body for application			
	Health conditions					

TABLE 2. Similarities and differences in the use of techniques for pain study through brain activity.

Similarities	Differences
• There is no standard number of subjects. • There is no standard for the EEG device. • 67% of the studies mention the use of the 10-20 position protocol for EEG montage in different adaptations. • The 64% of the studies mention the use of a pain perception scale such as the NRS and/or VAS mainly. • The software and models considered for the signal analysis are mainly MATLAB using the toolbox EEGLAB and software from the company Brain Products.	• The studies of chronic pain commonly consider a group of patients with some disease and a control group of healthy subjects. • The studies of pain caused by stimulus consider commonly only healthy subjects. • The studies of chronic pain do not consider the application of a stimulus. • The studies of chronic pain commonly consider the application of additional questionnaires to identify general information about the physical and mental health of subjects.

It was possible to identify a group of elements that every researcher uses but proposing different methods to carry out the study of pain considering brain activity. Table 1 presents the group of elements identified in the studies.

Once the analysis of studies began, it was possible to identify two types of pain, chronic pain caused by different types of diseases and pain caused by stimuli, in which the researcher must select the type and conditions of the stimuli. After the analysis of conditions and variables presented in Table 1, it was possible to identify some similarities and differences in the use of techniques and technology between these two perspectives of studies presented in Table 2.

III. METHODOLOGIES USED TO STUDY PAIN THROUGH BRAIN ACTIVITY

A. STUDY OF CHRONIC PAIN USING A BRAIN ACTIVITY APPROACH

The study of chronic pain through brain activity considers different variables to establish a correlation between pain, brain activity, and other types of physical and mental health indicators. Tables 3a, 3b, 3c, and 3d summarize a group of studies selected in chronological order, identifying the technology and techniques implemented based on the data extraction criteria presented in Table 1. The studies consider chronic pain as a result of diseases like sickle cell disease, fibromyalgia, back pain, pancreatitis, postoperative patients, and one case considered for depressive disorder. Likewise, according to the criteria defined in Table 1, ten reported studies were found in which it is observed that, subjects of both genders were studied with an age range between 18 and 85 years.

B. STUDY OF ACUTE PAIN USING BRAIN ACTIVITY APPROACH

Considering the study of pain is significant to contemplate that pain and nociception are not the same phenomenon. Nociception refers to the peripheral and central nervous system processes triggered by the activation of nociceptors and pain is a subjective experience; one of the possible outcomes of nociceptors activation [40]. Commonly, nociception and the perception of pain are evoked only at pressures and temperatures extreme enough to injure tissues potentially and by toxic molecules and inflammatory mediators. These high threshold physical and noxious chemical stimuli are detected by specialized peripheral sensory neurons called nociceptors. A nociceptor is a peripherally localized neuron preferentially sensitive to a noxious stimulus or to a stimulus that would become noxious if prolonged, capable of encoding stimulus intensities within the noxious range. It may have a wide dynamic range of thresholds from innocuous to noxious but there is a stimulus- peaks response relationship in the noxious range. These also include responses that are not activated immediately but the body becomes responsive upon prolonged stimulation, such as heat and mechanical stimulation [41]. Nociceptive stimuli

TABLE 3. Summary of methodologies for the study of chronic pain.

Reference	Subjects				EEG Montage			Pain Perception Tool Used	Acquisition and Analysis		Additional	
	Quantity	Sex M/F	Age Range M, Sd	Health Conditions	Device	# of Electrodes	Electrodes position	Scale	Software	Method	Questionnaires	Techniques
(Case et al., 2018) [38]	34	19/15	23±7	20 sickle cell disease patients and 14 healthy controls	EEG system BrainAmp MR-64 plus, Brain Products	64	NI	NRS	EEGLAB toolbox, RStudio, Fieldtrip toolbox, SPM12	Independent Component Analysis (ICA), Power Spectral Density (PSD), Welch's method, Hamming window, Center of Gravity Method (COG), Wilcoxon tests, Wilcoxon rank, non-Gaussian distribution, Magnetic Resonance Imaging (MRI) of Colin27, EEG cross-spectra, exact low resolution brain electromagnetic tomography (eLORETA)	NI	NI
(Fallon, Chiu, Nurmikko & Stancak, 2018) [42]	37	0/37	Fibromyalgia: 40.0 ± 8.0 years. Healthy: age 39.2 ± 8.0 years	Fibromyalgia syndrome patients and healthy controls	Biosemi Ag-Cl active-two electrode system	64	Extended 10–20 system	NI	MATLAB v.8.10, EEGLAB toolbox, SPSS v.21	Analysis of variance (ANOVA), Student's independent samples t-tests, Bootstrapping method, Spearman's correlation analysis, standardized low resolution brain electromagnetic tomography (sLORETA)	Activation-Deactivation Adjective Check list (AD-ACL), clinical MTPS examination, Beck Depression Inventory, Pain Catastrophising Scale, Fibromyalgia Impact Questionnaire (FIQ)	NI
(Vanneste, Ost, Van Havenbergh, & De Ridder, 2017) [43]	88	8/80	Fibromyalgia subjects: (M= 46.33; Sd =9.56), Healthy controls (M= 46.33; Sd = 9.56)	44 fibromyalgia condition, 44 healthy	Mitsar-201 EEG amplifiers (Nova-Tech)	19	Fp1, Fp2, F7, F3, Fz, F4, F8, T7, C3, Cz, C4, T8, P7, P3, Pz, P4, P8, O1, O2	NI	LORETA-Key software	Average Fourier cross-spectral matrices, sLORETA algorithm, boundary element method	Fibromyalgia Impact Questionnaire (FIQ), Pain Vigilance and Awareness Questionnaire (PVAQ), Modified Fatigue Impact Scale (FIS), Beck Depression Inventory (BDI-II)	Standardized low resolution brain electromagnetic tomography (sLORETA)
(Xiangjun et al., 2017) [37]	26	NI	NI	Specific low back pain (SLBP)	Emotiv software development kit (SDK), Emotiv Systems Company	14	Adopted 10/20 international standard system	NI	SPSS19.0 package	Approximate entropy (ApEn), Hilbert-Huang Transform Marginal spectrum entropy (HHTMSEn), Wavelet packet decomposition, Visual inspection and Fast Fourier Transform (FFT), Paired-samples t tests	NI	SLBP patients received massage therapy for 25 minutes
(An, Wang, Cope, & Williams, 2017) [12]	211	101/110	18–85 years	111 pain patients postherpetic neuralgia, spinal cord injury, femoral head necrosis, lumbar disc herniation, trigeminal neuralgia, complex regional pain syndrome. 100 healthy group	HXD-I EEG Monitor (Heilongjiang Huaxiang Technology Co., Ltd)	5	FZ, left FP1, right FP2); reference electrodes were placed on bilateral earlobe (left A1, right A2)	Pain Index (PI), NRS1, VAS2	EEG analysis software package (Beijing Easymonitor Technology Co), SPSS 13.0 (SPSS Inc)	Wavelet algorithm, continuous and discrete wavelet transform, Fast Fourier transform (FFT), mean ± (SD) for normally distributed continuous variables, the Pearson correlation	NI	NI
(González-Roldán, Cifre, Sitges, & Montoya, 2016) [11]	40	0/40	Fibromyalgia: 34 – 67, age=53.3; SD=8.1. Pain free: 29 – 67 mean age=52.6; SD=10.3	Fibromyalgia syndrome patients and pain-free controls	QuickAmp amplifier	64	International 10/20 system	NI	Brain Vision Analyzer software (Version 1.05), SPSS (version 21.0)	Gratton & Coles algorithm, cross-correlation in the frequency domain, FFT, region of interest (ROI), two-sample t-tests, Statistical nonparametric mapping, sLORETA, analysis of covariance (ANCOVA), Pearson's correlations Greenhouse-Geisser epsilon corrections, Bonferroni correction	West Haven–Yale Multidimensional Pain Inventory, the Beck Depression Inventory (BDI), the Spielberger State Anxiety Inventory (STAI), the Positive and Negative Affect Schedule (PANAS) and the Edinburgh Handedness Inventory	Electroculogram signals were recorded
(Meerwijk, Ford, & Weiss, 2015) [20]	35	8/27	35.0 years (SD 11.8)	Depressive disorder	Biosemi ActiveTwo system	34	NI	Psychache Scale	GNU Octave 3.2.3, PASW Statistics 18.0	Cronbach's α, Hann window, Fast Fourier transformation (FFT), Fractal Dimension, Intraclass Correlation Coefficient (ICC)	Beck depression inventory (BDI) II, Beck hopelessness scale (BHS), and the Beck scale for suicide ideation (BSS), Psychache Scale (PS), Orbach & Mikulincer mental pain (OMMP)	Rest state with Sound attenuated room (constant 50 dB ambient sound level, mostly from air conditioning)
(Kumar, Kumar, Trikha, & Anand, 2015) [22]	31	14/17	18 and 65 years (37.61 ± 12.58)	Preoperative conditions	Standard EEG recorder, Recorders & Medicare Systems	7	Fp1, Fp2, C3, C4, P3, P4, CZ	VAS and NRS	NI	Simple variance analysis, prediction probability (PK), Kim's measure, Hjorth Activity and Spectral Entropy, fuzzy logic	NI	Anesthesia, Session 1: During normal awake state in pre anaesthetic room for 30 min to obtain baseline EEG. Session 2: Pain EEG data when the patient was shifted to PACU after surgery till the patients were shifted back to ward

have been seen to provoke high-frequency oscillation activity of the human primary somatosensory cortex and gamma oscillations [24].

Taking into account the principles of nociception, many researchers began to study pain associated with the application of harmful stimuli to generate pain and thus analyze brain

TABLE 3. ***(Continued.)*** **Summary of methodologies for the study of chronic pain.**

(De Vries, 2013) [39]	32	20/12	Chronic pancreatitis (CP) subjects: 24-72 years. Healthy subjects: 48 (11.6) years mean	16 with Abdominal pain resulting from chronic pancreatitis and 16 healthy controls	Quickcap NuAmps, (Compumedics Neuroscan)	26	Fp1, Fp2, F7, F3, Fz, F4, F8, FC3, FCz, FC4, T3, C3, Cz, C4, T4, CP3, CPz, CP4, T5, P3, Pz, P4, T6, O1, Oz, O2	NI	Brain Vision Analyzer 2.0 software, Brain Products GmbH, Gilching. SPSS software for Windows version 16.0 from IBM Corporation	FFT, Hanning window (10%), ROIs, center of gravity, Kolmogorov–Smirnoff Test, t-test, non-parametric Mann–Whitney U test. General Linear Model, repeated measures - ANOVA, Mauchly's test, Greenhouse–Geisser estimation	Neuropsychological/ neurophysiological testing	Electrooculogram were recorded and additional physiological signals were obtained from the orbicularis oculus and the masseter muscles
(Schmidt et al., 2012) [36]	74	NI	NI	37 Chronic back pain condition and 37 Healthy controls	ActiCAP System, Quickamp, MES	72	Internation al 10–20 system	VAS	Brain Vision Analyzer 2.0, MATLAB, SPSS for Windows 15.0	Gratton & Coles algorithm, FFT, Source Density Distribution (CSD), Power spectral density (PSD), Kolmogorv Smirnoff Test, Mann-Whitney U-Test, non-parametric Spearman's rho, Cohen's D	EuroQol Quality of Life EQ-5D, Brief Symptom Inventory BSI, Hospital Anxiety and Depression Scale HADS, Pain Perception Scale PPS, Chronic Pain Grade CPG, Questions on Life Satisfaction QLS, Interdisciplinary Pain Unit CONSORT checklist	Diagonal EOG was recorded bipolarly from above and below the right eye

Note. NI is information not included in the article.

activity. There are some advantages for carrying out this type of study.

- The stimulus to be applied can be controlled by the researcher. Therefore, a correlation can be established between the intensity of the stimulus and the intensity of perceived pain.
- The study can be carried out on a group of healthy subjects.

Given the needs of this type of study, it is imperative to carry out a careful selection of the type of stimulus, the application medium, and the area of the body in which the stimulus is going to be applied.

Another important variable that is considered in this type of study is the use of a pain perception test, intending to establish a correlation between the stimulus intensity applied, the pain perception of the subject, and the brain activity generated. The most common tools are the NRS and VAS. In addition, these tools sometimes are used individually or combined with other types of pain perception tests.

Tables 4a to 4e present a summary of studies of pain monitored by brain activity when a stimulus is applied. Although studies from the last ten years are considered for the development of this research, the tables only present studies from the last six years. Fifteen reported studies were selected according to the criterion defined in Table 1. In general, subjects of both sexes were studied, with an age range between 18 and 59 years.

IV. COMMON ELEMENTS AND METHODS IN THE STUDY OF PAIN THROUGH BRAIN ACTIVITY

From the selected studies, it was possible to identify the device to acquire EEG signals, stimulus application technology and technique, pain perception tool, additional questionnaires to assess the perception of physical and mental health, and the software to acquire and analyze brain activity. These elements are presented below, describing their main features.

A. DEVICE TO ACQUIRE EEG SIGNALS

One of the main elements to start with a study of pain through brain activity is the selection of a device to record EEG signals. It is worth mentioning that the selection of this device will depend on the need for the study. However, a hint that can facilitate this selection is considering the number of electrodes to be mounted. Commercial devices commonly handle the 10-20 mounting standard. Table 5 lists the devices used in the selected studies, as well as the brand and the number of electrodes used.

The way of acquiring the brain electrical activity in these studies is generally by the gold standard non-invasive EEG. Then two studies that were analyzed for the survey were excluded from Table 5, considering that the analysis of brain activity was performed through MRI for which an 8-channel BOLD-based fMRI [50] and 3 Teslas MRI scanner with 35 axial slices covering the entire brain was used [33]. Likewise, another two studies [27], [46] were carried out with rats, even though they used EEG recording. An invasive technique was used because screws were the active electrode, considering 12 channels in one of the cases and 3 in the other.

B. STIMULUS APPLICATION, TECHNOLOGY, AND TECHNIQUE

As previously mentioned, another type of pain study is considered. The acute pain studies are the application of a harmful stimulus in people with no disease. For these cases, it is crucial to consider properly what type of stimulus will be applied and the medium or device that will be used for the application because it is not intended to generate any

TABLE 4. Summary of methodologies for the study of acute pain.

Reference	Subjects				EEG Montage			Stimuli			Pain Perception Tool Used	Acquisition and Analysis	
	Quantity	Sex M/F	Age Range M, Sd	Health Conditions	Device	# of Electrodes	Electrodes Position	Type	Device to Apply It	Part of the Body for Application	Scale	Software	Models
(Furman et al., 2018) [44]	44	22/22	Mean age = 28.4, age-range = 19–42	Chronic Pain-free	Vision actiCAP system (Brain Products GmbH	64	International 10–20 system	Chemical and thermal heat	Topical capsaicin, 30 x 30 mm Medoc Pathway ATS Peltier device	Volar surface of participant's left forearm	0–100 point scale	Brain Vision Recorder software (version 2.1), EEGLAB 13.6.5b	Infomax (extended) independent component analysis (ICA), Fourier transform, Hanning taper, center of gravity (COG) method, independent samples t-test, Pearson's correlation coefficient, Spearman's rank-order correlations
(Bright & Nottage, 2018) [24]	34	12/22	18 - 59 years	Healthy	MyndPlay version 2013	3	Ear lobe and two placed onto the forehead	Pressure	Wagner Force Dial™ FDK 40 with a 1cm rubber-tipped probe	Right thenar eminence, common extensor tendon of the forearm and the levator scapula muscle	NRS	MyndPlay version 2013 2.3.0 pro, Excel version 14 (Microsoft), Analyse-it version 3.76	Spearman's Correlation, Multiple regression approach, Shapiro-Wilks' test and Q-Q, Mann/Witney-U test
(Almarzouki, Brown, Brown, Leung, & Jones, 2017) [45]	44	25/19	19–41 mean age = 25.6 years, SD = 6.7	Pain-free	Brain Vision actiCAP and Neuroscan headbox and amplifier system	59	Extended 10–20 system	Heat by laser	Thulium laser	Right forearm	NRS, Fear of Pain Questionnaire-III (FPQ-III), a Manipulation check	Brain Vision Analyzer 2.0, LORETA Key, SPSS version 20	ANOVA
(Blanco-Mora & Díaz-Méndez, 2017) [46]	20	NI	NI	Healthy	EEG system (g.HIamp of g.tec company)	128	Intra-hemispheric short: Intra-hemispheric long: Inter-hemispheric short: Inter-hemispheric long	Cold pressor test	Cold water 4±1 °C	Right hand	NI	EEGLAB MATLAB toolbox	ICA, Phase Lag Index (PLI), Weighted Phase Lag Index (WPLI), Hilbert transform, Bonferroni correction
(Lancaster, Mano, Callan, Kawato, & Seymour, 2017) [25]	14	10/4	21-35 years	Healthy	ActiCAP Xpress Brain Products	16	FP1, FP2, FC6, FC2, FC1, FC5, Fz, C4, Cz, C3, P4, Pz, P3, O2, Oz, O1	Noxious Cold Pain	Thermode PATHWAY ATS 30x30 mm, Medoc	Left volar forearm	NI	Brain Vision Recorder software	ICA, Hamming-window short-time Fourier transform, Sparse Logistic Regression (SLR)
(Nickel et al., 2017) [26]	39	21/18	Age 24.3 ± 5.6 years	Healthy	Easycap, Brain Products	64	Fpz, CPz, POz, Oz, Iz, AF3/4, F5/6, FC1/2/3/4/5/6, FT7/8/9/10, C1/2/5/6, CP1/2/3/4/5/6, TP7/8/9/10, P5/6 and PO1/2/9/10	Thermal Heat	Thermode (TSA-II, Medoc)	Dorsum of the left or the right hand	VAS	Software environment R, lme4 package, MATLAB and the Psychophysics Toolbox, BrainVision Analyzer software Brain Products, FieldTrip toolbox	ANOVA, Hilbert transform, linearly constrained minimum variance (LCMV), realistically shaped three-shell boundary-element volume conduction model, linear mixed models (LMM), false discovery rate (FDR), the region of interest (ROI)
(WW Peng et al., 2017) [27]	12 rats	12/0	Adult	Sprague Dawley rats weighing between 300 and 400 gr of weight	Screws were used as electrodes	12	Positions are set according to Bregma coordinates in mm; positive X and Y axis values indicate right and anterior locations, respectively	Radiant nociceptive stimuli	Infrared neodymium: yttrium–aluminium–perovskite (Nd: YAP) laser with a wavelength of 1.34 mm	Animal paws through the holes (5-mm diameter) on the floor of the chamber	0 to 4 numerical rating scale (NRS)	Brain Products and EEGLAB	ANOVA, FT Hanning window, PCA, decomposition with Varimax rotation, bootstrapping test, pseudo-t statistic, P values, multiple linear regression with dispersion term, Pearson R
(Alshelh et al., 2016) [34]	61	14/47	50.6±2.8 (with pain) 45.9±2.0 (no pain)	17 with chronic orofacial NP, 44 pain-free	3 tesla MRI scanner	35 axial slices covering the entire brain	180 gradient echo-planar	Hypertonic saline (5%) injection	Catheter connected to a syringe filled. Infusion pump with a 10 ml syringe placed	Right masseter muscle midway between its upper and lower borders	VAS, Pain Catastrophizing Scale, McGill Pain Questionnaire	MATLAB, SPM toolbox REST, DPARSF toolbox, SPM12	Gaussian filter, Fast Fourier transforms, local homogeneity analysis, Kendall's coefficient of concordance (KCC)
(LeBlan, Bowary, Chao, Lii, & Saab, 2016) [47]	44	44/0	NI	Male Sprague-Dawley rats, weight 200-300 g	Stereotaxic apparatus and Stainless steel "screw" electrodes	3	S1 hindlimb area bilaterally and prefrontal cortex (PFC)	Chemical Capsaicin (0.1%, 20 mL) intradermal.	Injection	Left hind paw	Rats show evidence of neuropathic pain such as guarding the affected hind paw	Spike 2 (COHER script), MATLAB R2012b	Fast Fourier transform, magnitude squared coherence function, Hamming window, Bonferroni correction, Bartlett test, P-value
(Li et al., 2016) [28]	43	43/0	22±3 years	Healthy	Neuroscan system	64	Extended international 10–20 system	Innocuous and Noxious	Two automated syringe infusion pumps	Left masseter muscle to a depth of 1 cm	NRS	EEGLAB	Paired-sample t-test, RM-ANOVA, independent component analysis (ICA), linear mixed model (LMM)

long-term harm to the participant. Table 6 presents stimulus applied in the revised studies and the way the stimulus was applied.

From this survey, it was possible to identify that at least 60% of the cases use commercial equipment to apply a controlled stimulus. It stands out that 28% of the equipment used belongs to the Medoc brand, which provides specialized commercial equipment to evaluate pain from different perspectives, such as research, clinical use, and clinical trials. Another 28% of the cases used some type of laser to apply

TABLE 4. ***(Continued.)*** **Summary of methodologies for the study of acute pain.**

(Dario, Eleonora, Chiara, & Laura, 2015) [48]	75	75/0	Mean± SD: 22± 1.8 years	Healthy	Quick-Caps from Compumedics/Neuroscan	32	International 10–20 System	Mechanical pressure applied	Deep pressure algometer (Wagner Instruments, Green- wich CT)	Second costochondral junction (the joint between the second ribs and costal cartilage in the front of the rib cage	NRS	SPSS.15 package	Recurrence Quantification Analysis (RQA), Determinism (DET) and Entropy (ENT), BIS and total BAS scores, ANOVA, Greenhouse Geisser ε correction
(Blöchl, Franz, Miltner, & Weiss, 2015) [14]	12	4/8	Mean 21.75 SD ±1.96 years	Healthy	ActiCAP, Brain Products	64	Frontal (F3, Fz, F4) and central (C3, Cz, C4) - scalp channels. 10/10 system	Steady-state, transcutaneous electrical stimulation	Transcutaneous concentric stimulation electrodes	Dorsum of both hands	Modified NRS	BrainVision Analyzer 2.0, Brain Products, SPSS 21	ANOVA, FastICA, FFT; Hamming window
(Hadjileontiadis, 2015) [49]	17	9/8	23.22 ± 1.72 years	Healthy	Emotiv EPOC headset, Emotiv Systems Inc	14	AF3, F7, F3, FC5, T7, P7, O1, O2, P8, T8, FC6, F4, F8, and AF4	Tonic cold	Iced water on 0.51 plastic bottle (−1 ◦C± 0.5 ◦C)	Dominant hand	NRS	Microsoft Visual Studio 2010, MATLAB R2014	Wavelet higher-order spectral (WHOS), complex Morlet wavelet, Gaussian-windowed complex sinusoid

Note. NI is information not included in the article.

TABLE 5. **EEG signals recording systems used in the selected studies of pain. The devices range from largest to smallest number of electrodes.**

Reference	Device to Acquire EEG Signals	Brand	Number of Electrodes used for the Study
[46]	g.HIamp	g.tec company	128
[36] [44][14]	ActiCAP System	Brain Products	72/64
[50][26][29]	Easycap	Brain Products	64
[28][45]	NeuroScan System	Compumedics Neuroscan	64
[42][20]	Ag-ACl active-two electrode system	Biosemi	64/34
[45]	Brain Vision ActiCAP and Neuroscan head box and amplifier system	Brain Products	59
[48][39]	Quick-Caps	Compumedics Neuroscan	32/26
[43]	Mitsar-201 amplifier	Nova- Tech	19
[25]	ActiCAP Xpress	Brain Products	16
[49][37]	Emotiv EPOC	Emotiv Systems Inc	14
[31]	AgCl electrodes placed on the scalp	Developed by researcher	7
[22]	Standard EEG recorder	Recorders & Medicare Systems	7
[24]	MyndPlay	MyndPlay	3
[12]	HXD-I EEG Monitor	Heilongjiang Huaxiang Technology Co., Ltd.	2

heat stimuli. With a lower percentage, 14% used chemical stimuli, such as injection of solutions or application of topical capsaicin, another 14% used the application of electrical stimuli, 9% applied pressure, and 9% used cold water controlling the temperature.

Once the equipment to apply the stimulus is selected, it is important to determine the part of the body where it will be applied. From this survey, it was found that 38% of the studies applied the stimulus to the hands (commonly on the dorsum), 33% on the forearm (commonly on the volar surface), 9% on the masseter muscle, 4% on the second costochondral junction, 4% on the index finger, and considering that two studies in rats were included, they were applied to the paws. It is important to highlight that 42% of the stimuli were applied in the left parts of the body, 28% in the right parts, 19% in both parts of the body, and only 4% considered the application in the dominant hand.

C. PAIN PERCEPTION TEST

As a common technique for the study of pain, several researchers considered parameters extracted from the EEG signal to establish a correlation with the perception of the pain of participants. One-dimensional scales are used to give a qualitative pain value experimented by the subject. The reviewed studies use the scales either individually or in combination.

- Numerical Rating Scale (NRS) [12], [24], [51], [28], [30], [31], [38], [45], [48]–[50]
- NRS variations [14], [22], [27],
- Visual Analogue Scale (VAS) [12], [22], [26], [29], [32], [34], [36], [52],
- Pain intensity (PI) [12],
- Psych ache Scale (PS) [20],
- Likert scale [33],
- 0–100 Point scale [44].

D. ADDITIONAL QUESTIONNAIRES TO ASSESS THE PERCEPTION OF PHYSICAL AND MENTAL HEALTH

Some researchers incorporated multidimensional questionnaires that identified information on the physical and mental health of the subjects, in order to correlate these variables with the perception of pain obtained and the result of the brain activity generated as an additional source of information. Table 7 presents a classification of the tools used by the selected studies.

E. SOFTWARE TO ACQUIRE AND ANALYZE THE SIGNALS

An essential tool for studies of pain through brain activity is the software through which the signals will be recorded and analyzed, as well as the visualization and study tools. Table 8 includes a list of software and tools used for the acquisition and analysis of brain activity.

TABLE 6. Harmful stimulation techniques applied to study pain through brain activity.

Type of Stimulus	Device to Apply It	Part of the Body to Apply It	Reference
Thermal heat and Chemical	30 x 30 mm Medoc Pathway ATS Peltier device Topical capsaicin	Volar surface of participant's left forearm	[44]
Thermal heat	Thermode (TSA-II, Medoc)	Dorsum of the left or the right hand	[26]
Thermal Heat	Medoc Thermode, peltier type 3x3 cm	Left volar forearm	[51]
Tonic heat	PATHWAY sensory evaluation system, Medoc Ltd.	Non-dominant (left) volar forearm	[30]
Heat by thermode and laser	Thermode (TSA-II, Medoc) and Tm:YAG Laser (Starmedtec GmbH)	Dorsum of the left hand	[29]
Heat by laser	Thulium laser	Right forearm	[45]
Heat by laser	Infrared neodymiumyttrium aluminum perovskite laser with a wavelength of 1.34 μm	Dorsum of the right and left hands	[31]
Heat by laser	Starmedtec Tm:YAG laser	Dorsum of the left hand	[50]
Laser stimuli	ND YAP Laser DEKA system	Dorsum of the left hand	[32]
Radiant nociceptive stimuli	Infrared neodymium: yttrium–aluminum–perovskite (Nd: YAP) laser with a wavelength of 1.34 mm	Animal paws through the holes (5-mm diameter) on the floor of the chamber	[27]
Cold pressor	Recipient with cold water at controlled temperature of 4±1 °C	Right hand	[46]
Noxious Cold Pain	Thermode PATHWAY ATS 30x30 mm, Medoc	Left volar forearm	[25]
Tonic cold	Iced water on 0.51 plastic bottle (−1 ◦C± 0.5 ◦C)	Dominant hand	[49]
Hypertonic saline (5%) injection	Catheter connected to a syringe filled. Infusion pump with a 10 ml syringe placed	Right masseter muscle midway between its upper and lower borders	[34]
Chemical	Injection	Left hind paw of the rats	[47]
Innocuous and Noxious	Two automated syringe infusion pumps	Left masseter muscle to a depth of 1 cm approximately	[28]
Pressure	Wagner Force Dial™ FDK 40 with a 1cm rubber-tipped probe	Right thenar eminence, common extensor tendon of the forearm and the elevator scapula muscle.	[24]
Mechanical, pressure applied	Deep pressure algometer (Wagner Instruments, Green- wich CT)	Second costochondral junction (the joint between the second ribs and costal cartilage in the front of the rib cage	[48]
Steady-state, transcutaneous electrical stimulation	Transcutaneous concentric stimulation electrodes	Dorsum of both hands	[14]
Electrical pulses	Digitimer Constant Current Stimulator, model DS7A	Right index finger, following light abrasion of the finger (cathode—distal phalanx; anode—middle phalanx)	[33]
Noxious electrical	Pain Vision system PS-2100, Nipro Co	Right forearm	[52]

It is essential to consider that the selection of the software depends on the application and the device used to monitor the EEG activity. Also, it is important to know that some of these toolboxes for MATLAB are available on their main webpage, for example: EEGLAB, Psychophysics, SPM, DPARSF, and Letswave. Another tool available online is the software LORETA-KEY as free academic software.

V. DISCUSSION

With this survey, it was identified that there are two main ways to study pain through brain activity: studies that consider subjects suffering from some type of chronic physical pain and studies that are based on the application of some type of painful stimulus to healthy subjects. It should be noted that similar elements are used in both studies despite the possible difference in the origin or mechanisms involved.

Regarding the number of participants, there is no constant to consider. Among the selected studies, it was identified that the study with the least number was seven subjects [31], and the one with the most subjects was 211 [12]. There is also no constant regarding sex consideration in test subjects who are part of the studies. Only one study was found where only female test subjects were considered. In that case, it was for the study of pain associated with fibromyalgia, and it is consistent with other reports about a higher incidence in females [42]. On the other hand, three cases were found in which only male subjects were considered. These studies were performed in healthy subjects to whom a painful stimulus was applied[28], [48], [52]. Two studies were also included in which the subjects were rats, and in that cases too, only male rats were considered [27], [47].

Concerning the equipment to record brain activity, it was found that 87% of the EEG signal acquisition equipment used in the revised studies was commercially available and there is no constant about the type of equipment used. As for the number of electrodes used to record EEG activity, there is significant variability. The study with the lowest number was two electrodes [12]. In comparison, studies with the largest number of electrodes use 128 [46]. Two studies considered for the survey present analysis of brain activity using an MRI for which an 8-channel BOLD-based fMRI [51] and 3 Teslas MRI scanner with 35 axial slices covering the entire brain [34]. Likewise, another two studies using rats [27], [47], in which an invasive technique was used because screws were the active electrode, considering 12 channels in one of the cases and 3 in the other. This last technique proved to be a valuable complement to understand the functioning of the brain.

For the cases that considered the study of pain caused by a stimulus, it was possible to identify that at least 60% of cases use commercial equipment to apply a controlled stimulus, but regardless of the equipment used or the type of stimulus

TABLE 7. Multidimensional questionnaires to complement the pain study by brain activity.

Parameter	Questionnaire
General	Activation-Deactivation Adjective Checklist (AD-ACL)
	Edinburgh Handedness Inventory
	Euro Qol Quality of Life Questionnaire EQ-5D
	Questions on Life Satisfaction QLS
	Stanford Hypnotic Susceptibility Scale (SHSS)
	BIS/BAS questionnaire
Pain	Fear of Pain Questionnaire-III (FPQ-III)
	Pain Catastrophizing Scale
	McGill Pain Questionnaire (SF-MPQ)
	Pain vigilance and awareness questionnaire (PVAQ)
	West Haven–Yale Multidimensional Pain Inventory
	Orbach & Mikulincer mental pain (OMMP)
	Pain Perception Scale PPS, Chronic Pain Grade CPG
	The general intake form of the Interdisciplinary Pain Unit and CONSORT checklist
Physical health	Clinical MTPS examination
	Fibromyalgia Impact Questionnaire (FIQ)
	Modified Fatigue Impact Scale (FIS)
	Neuropsychological/neurophysiological testing
Mental, emotional health	Beck Depression Inventory (BDI)
	Beck hopelessness scale (BHS)
	Beck scale for suicide ideation (BSS)
	Spielberger State Anxiety Inventory (STAI)
	Positive and Negative Affect Schedule (PANAS)
	Brief Symptom Inventory BSI
	Hospital Anxiety and Depression Scale HADS
	State-Trait-Anxiety Inventory

applied, similarities were found in the results regarding the type of wave generated from the application of the painful stimulus. Oscillations in alpha waves were reported as a result of heat stimulation [44]. In the case of beta waves, an increase was shown as a result of the application of cold as a stimulus [25], [46]. The brain wave that most commonly appeared independently of the stimulus was gamma because it was presented when heat [26], [29]–[32], cold [25], pressure [24], injection of solutions[28], and electrical stimuli [14], [33] were applied.

Among the methods to analyze the signals, different tools were identified that provide accurate results in which brain activity can be used to monitor pain. However, there are other methods that allowed the generation of satisfactory results, like the methods presented in Tables 3a to 3e and in Tables 4a to 4d. Among these methods, the ICA and the FFT stood out. In terms of statistical analysis, ANOVA is a widely used tool [14], [26]–[28], [30], [39], [42], [45], [48]. Considering brain imaging, the study presented in [51] demonstrated that fMRI with SVM learning can assess pain without requiring any communication from the person being tested. On the other hand, the proposed approach by Hadjileontiadis [49] contributes with an alternative way to endeavor towards objective quantification of the subjective characterization of pain, considering the no stationarity and nonlinearity of the EEG-based brain responses to pain stimuli.

Considering the complementary methods, the additional technique of electrooculogram (EOG) was used to record the biopotentials generated by the movement of eyes to exclude trials contaminated with eye movements from further analysis [11], [36], [39]. Another additional tool was included in the SLBP patient testing protocol. A 25-minute massage was included and the results suggested that the complexity of EEG signals was reduced with the relief of pain after the massage therapy, and the change of pain of SLBP patients was closely related to the change of the rhythms of the brain in the massage therapy. Besides, the Approximate Entropy (ApEn) and the Hilbert-Huang Transform Marginal spectrum entropy (HHTMSEn) features could serve as a base for quantitative assessment of SLBP condition after the massage therapy [37]. An interesting challenge was presented by Kumar *et al.*, [22] working with patients in the Post Anaesthetic Care Unit (PACU). As a result, the developed pain scale by analyzing EEG signals of the patients in the post-operative period was correlated with Visual Analogue Scale (VAS) and was found to be accurate to estimate the level of pain when compared to the pain experienced by the patient.

TABLE 8. Common software and toolbox used in the pain study through brain activity.

Tool	Name
Software	• BrainVision • MATLAB • MyndPlay • LORETA-KEY • SPSS • R Studio • Excel • Spike 2 • Visual Studio • Delphi 5.0
Toolbox	• EEGLAB for MATLAB • Analyse-it for Excel • Ime 4 for R Studio • Psychophysics for MATLAB • Field trip for Brain Products • SPM for MATLAB • REST for MATLAB • DPARSF for MATLAB • Coher Script for Spike 2 • Letswave for MATLAB • SVM for MATLAB

In terms of the results obtained, it was also possible to identify some similarities and differences in the results of brain activity associated with pain. In a matter of results obtained through the selected articles, it was found that the activity associated with pain occurs mainly in the prefrontal, frontal, and central cortex [14], [20], [25], [26], [28], [29], [33], [38], [42], [47]. For the cases in which subjects with chronic physical pain are considered, brain activity associated with pain was found in the power bands: alpha [39], [43], beta [11], [37], [43], delta [11], [37] and theta [38], [42]. In studies where pain stimulus is applied, it was found that the brain activity changes commonly regarding the non-stimulus state in the gamma band [14], [24], [33], [50], [25]–[32]. However, some studies report an increase in alpha [44] and beta [25], [46].

VI. CONCLUSION

The objective of this article was to develop a survey considering studies of physical pain through brain activity to identify elements and the methodologies used in the last ten years. Initially, it was possible to identify that pain studies commonly address chronic pain caused by a physical condition and acute pain caused by some type of stimulus. For this survey, both types of studies were considered, and elements involved in the evaluation of these types of pain were identified, which are the number of subjects, the EEG setting, the stimulus applied, the pain perception test used, the tools for acquisition and analysis, and additional resources.

From the variables identified, it is concluded that in order to carry out a study of pain based on brain activity, it is necessary to identify the type of pain to be studied, since the requirements of the protocol to perform the tests will depend on this. For the studies of chronic pain, it is necessary to have access to a population sample with a chronic disease condition and to have a control group of healthy subjects with the same age range. In case of the acute pain study, it is crucial to identify the type of stimulus, the application conditions, and the part of the body where it will be applied. The stimulus that is commonly applied is heat or cold by thermode or laser; however, stimuli such as pressure and injection of solutions are also applied, commonly in the forearm or hand dorsum. Regarding the number of subjects, it is concluded that there is no evidence of a minimum number of subjects or sex to be able to develop a pain study. Commercial equipment is commonly used. In this case, there is no constant in the number of electrodes to consider but the 10-20 standard for electrode montage was used. For processing and extracting characteristics of the brain signals, Brain Vision and MATLAB are among the mostly used, but both are licensed software. As perception evaluation, it is concluded that the numerical scale of pain (NRS) is one of the most used. Likewise, the use of additional questionnaires for the perception of physical and mental health is recommended.

In general terms, this survey shows that the technology for the study of pain from brain activity is mature. There are commercial software and devices to facilitate the work of neurophysiologists. Likewise, there is congruence between MRI with those of EEG and the results are showing that pain is capable of generating certain patterns of behavior at brain level, which is why the EEG is expected to be a pain monitor (biomarker). Once the pain can be measured through a biological indicator, accurate diagnoses can be provided to patients, as well as effective physical therapy treatments can be prescribed, resulting in costs reduction in a personal and social way.

ABBREVIATIONS AND ACRONYMS

AD-ACL Activation-Deactivation Adjective Checklist
ANCOVA Analysis of Covariance
ANOVA Analysis of variance
ApEn Approximate Entropy
BDI Beck Depression Inventory
BHS Beck Hopelessness Scale
BSI Brief Symptom Inventory
BSS Beck Scale for Suicide ideation
COG Center of Gravity Method
CPG Chronic Pain Grade
EEG Electroencephalography/ electroencephalogram
eLORETA Exact low-resolution brain electromagnetic tomography
EOG Electro Oculographic
EQ-5D Euro Qol Quality of Life Questionnaire
FDR False discovery rate
FFT Fast Fourier Transform

FIQ	Fibromyalgia Impact Questionnaire
FIS	Modified Fatigue Impact Scale
FM	Fibromyalgia
fMRI	Functional Magnetic Resonance Imaging
FPQ-III	Fear of Pain Questionnaire-III
FT	Fourier transform
HADS	Hospital Anxiety and Depression Scale
HHTMSEn	Hilbert-Huang Transform Marginal spectrum entropy
ICA	Independent Component Analysis
ICC	Intraclass correlation coefficient
LMM	Linear Mixed Model
LORETA	Low-Resolution Electromagnetic Tomography
MRI	Magnetic Resonance Imaging
NP	Neuropathic Pain
NRS	Numeric Rating Scale
OMMP	Orbach & Mikulincer mental pain
PANAS	Positive and Negative Affect Schedule
PI	Pain Intensity
PLI	Phase Lag Index
PPS	Pain Perception Scale
PSD	Power Spectral Density
PVAQ	Pain Vigilance and Awareness Questionnaire
QLS	Questions on Life Satisfaction
ROI	Region of interest
SF-MPQ	McGill Pain Questionnaire
SHSS	Stanford Hypnotic Susceptibility Scale
SLBP	Specific Low Back Pain
sLORETA	Standardized low resolution brain electromagnetic tomography
SLR	Sparse Logistic Regression
SMV	Support Machine Vector
STAI	Spielberger State Anxiety Inventory
VAS	Visual Analog Scale
WHOS	Wavelet Higher Order Spectral
WPLI	Weighted Phase Lag Index

REFERENCES

[1] K. D. Davis, H. Flor, H. T. Greely, G. D. Iannetti, S. Mackey, M. Ploner, A. Pustilnik, I. Tracey, R.-D. Treede, and T. D. Wager, "Brain imaging tests for chronic pain: Medical, legal and ethical issues and recommendations," *Nature Rev. Neurol.*, vol. 13, no. 10, pp. 624–638, 2017.

[2] M. B. Milton, B. Börsbo, G. Rovner, Å. Lundgren-Nilsson, K. Stibrant-Sunnerhagen, and B. Gerdle, "Is pain intensity really that important to assess in chronic pain patients? A study based on the Swedish quality registry for pain rehabilitation (SQRP)," *PLoS ONE*, vol. 8, no. 6, Jun. 2013, Art. no. e65483.

[3] A. Covarrubias-Gómez, U. Guevara-López, C. Gutiérrez-Salmerón, J. A. Betancourt-Sandoval, and J. A. Córdova-Domínguez, "Epidemiología del dolor crónico en México," *Rev. Mex. Anestesiol.*, vol. 33, no. 4, pp. 207–213, 2010.

[4] M. Lynch, "Pain as the fifth vital sign," *J. Intravenous Nursing Off. Publication Intravenous Nurses Soc.*, vol. 24, no. 2, pp. 85–94, 2001.

[5] M. J. Hjermstad, P. M. Fayers, D. F. Haugen, A. Caraceni, G. W. Hanks, J. H. Loge, R. Fainsinger, N. Aass, and S. Kaasa, "Studies comparing numerical rating scales, verbal rating scales, and visual analogue scales for assessment of pain intensity in adults: A systematic literature review," *J. Pain Symptom Manage.*, vol. 41, no. 6, pp. 1073–1093, Jun. 2011.

[6] M. Bahreini, M. Jalili, and M. Moradi-Lakeh, "A comparison of three self-report pain scales in adults with acute pain," *J. Emergency Med.*, vol. 48, no. 1, pp. 10–18, Jan. 2015.

[7] M. Ploner and E. S. May, "Electroencephalography and magnetoencephalography in pain research—Current state and future perspectives," *Pain*, vol. 159, no. 2, pp. 206–211, 2018.

[8] K. D. Davis and D. A. Seminowicz, "Insights for clinicians from brain imaging studies of pain," *Clin. J. Pain*, vol. 33, no. 4, pp. 291–294, Apr. 2017.

[9] K. Tatu, T. Costa, A. Nani, M. Diano, D. G. Quarta, S. Duca, A. V. Apkarian, P. T. Fox, and F. Cauda, "How do morphological alterations caused by chronic pain distribute across the brain? A meta-analytic co-alteration study," *NeuroImage, Clin.*, vol. 18, pp. 15–30, Dec. 2017.

[10] M. Ploner, C. Sorg, and J. Gross, "Brain rhythms of pain," *Trends Cognit. Sci.*, vol. 21, no. 2, pp. 100–110, Feb. 2017.

[11] A. M. González-Roldán, I. Cifre, C. Sitges, and P. Montoya, "Altered dynamic of EEG oscillations in fibromyalgia patients at rest," (United States), *Pain Med.*, vol. 17, no. 6, pp. 1058–1068, 2016.

[12] J.-X. An, Y. Wang, D. K. Cope, and J. P. Williams, "Quantitative evaluation of pain with pain index extracted from electroencephalogram," *Chin. Med. J.*, vol. 130, no. 16, pp. 1926–1931, Aug. 2017.

[13] D. Morton, A. Jones, and J. Sandhu, "Brain imaging of pain: State of the art," *J. Pain Res.*, vol. 9, pp. 613–624, Sep. 2016.

[14] M. Blöchl, M. Franz, W. H. R. Miltner, and T. Weiss, "Captured by the pain: Pain steady-state evoked potentials are not modulated by selective spatial attention," *Brain Res.*, vol. 1603, pp. 94–100, Apr. 2015.

[15] M. Teplan, "Fundamentals of EEG measurement," *Meas. Sci. Technol.*, vol. 2, no. 2, pp. 1–11, 2002.

[16] E. R. John, L. S. Prichep, and E. Hiesiger, "System and method for pain detection and computation of a pain quantification index," U.S. Patent 9 402 558 B2, Aug. 2, 2016.

[17] T. L. Rich, M. Lixandrão, and A. Hoefer, "Reliability of the location of primary motor cortex using the international 10/20 electroencephalogram system (10/20 EEG)," *Sci. Pages Pediatric Neurol.*, vol. 1, no. 1, pp. 6–7, 2017.

[18] M. X. Cohen, "Where does EEG come from and what does it mean?" *Trends Neurosci.*, vol. 40, no. 4, pp. 208–218, Apr. 2017.

[19] H. Marzbani, H. Marateb, and M. Mansourian, "Neurofeedback: A comprehensive review on system design, methodology and clinical applications," *Basic Clin. Neurosci. J.*, vol. 7, no. 2, pp. 58–143, 2016.

[20] E. L. Meerwijk, J. M. Ford, and S. J. Weiss, "Resting-state EEG delta power is associated with psychological pain in adults with a history of depression," *Biol. Psychol.*, vol. 105, pp. 106–114, Feb. 2015.

[21] S. Sanei, *Adaptive Processing of Brain Signals*. Hoboken, NJ, USA: Wiley, 2013.

[22] S. Kumar, A. Kumar, A. Trikha, and S. Anand, "Electroencephalogram based quantitative estimation of pain for balanced anaesthesia," *Meas. J. Int. Meas. Confed.*, vol. 59, pp. 296–301, Jan. 2015.

[23] E. Silva, F. C. D. Queirós, C. L. Santos, M. A. D. Nascimento, C. H. Ito, M. Silva, D. B. N. Santos, S. Benevides, J. G. V. Miranda, K. N. Sá, and P. Montoya, "Electroencephalographic patterns in chronic pain: A systematic review of the literature," *PloS ONE*, vol. 11, no. 2, 2016, Art. no. e0149085.

[24] P. Bright and S. Nottage, "Is there a correlation between objective and subjective pain measurements and gamma oscillation frequencies," *J. Pain Manag. Ther.*, vol. 2, no. 1, pp. 1–7, 2018.

[25] J. Lancaster, H. Mano, D. Callan, M. Kawato, and B. Seymour, "Decoding acute pain with combined EEG and physiological data," in *Proc. 8th Int. IEEE/EMBS Conf. Neural Eng. (NER)*, May 2017, pp. 521–524.

[26] M. M. Nickel, E. S. May, L. Tiemann, P. Schmidt, M. Postorino, S. T. Dinh, J. Gross, and M. Ploner, "Brain oscillations differentially encode noxious stimulus intensity and pain intensity," *NeuroImage*, vol. 148, pp. 141–147, Mar. 2017.

[27] W. Peng, X. Xia, M. Yi, G. Huang, Z. Zhang, G. Iannetti, and L. Hu, "Brain oscillations reflecting pain-related behavior in freely moving rats," *Pain*, vol. 159, no. 1, pp. 106–118, Jan. 2018.

[28] L. Li, X. Liu, C. Cai, Y. Yang, D. Li, L. Xiao, D. Xiong, L. Hu, and Y. Qiu, "Changes of gamma-band oscillatory activity to tonic muscle pain," *Neurosci. Lett.*, vol. 627, pp. 126–131, Aug. 2016.

[29] E. Schulz, E. S. May, M. Postorino, L. Tiemann, M. M. Nickel, V. Witkovsky, P. Schmidt, J. Gross, and M. Ploner, "Prefrontal gamma oscillations encode tonic pain in humans," *Cerebral Cortex*, vol. 25, no. 11, pp. 4407–4414, 2015.

[30] W. Peng, L. Hu, Z. Zhang, and Y. Hu, "Changes of spontaneous oscillatory activity to tonic heat pain," *PLoS ONE*, vol. 9, no. 3, pp. 1–11, 2014.
[31] Z. G. Zhang, L. Hu, Y. S. Hung, A. Mouraux, and G. D. Iannetti, "Gamma-band oscillations in the primary somatosensory cortex—A direct and obligatory correlate of subjective pain intensity," *J. Neurosci.*, vol. 32, no. 22, pp. 7429–7438, May 2012.
[32] L. Tiemann, E. Schulz, J. Gross, and M. Ploner, "Gamma oscillations as a neuronal correlate of the attentional effects of pain," *Pain*, vol. 150, no. 2, pp. 302–308, Aug. 2010.
[33] R. J. Croft, J. D. Williams, C. Haenschel, and J. H. Gruzelier, "Pain perception, hypnosis and 40 Hz oscillations," *Int. J. Psychophysiol.*, vol. 46, no. 2, pp. 101–108, Nov. 2002.
[34] Z. Alshelh, F. D. Pietro, A. M. Youssef, J. M. Reeves, P. M. Macey, E. R. Vickers, C. C. Peck, G. M. Murray, and L. A. Henderson, "Chronic neuropathic pain: It's about the rhythm," *J. Neurosci.*, vol. 36, no. 3, pp. 1008–1018, 2016.
[35] M. Purcell, M. Fraser, and A. Vuckovic, "Home used, patient self-managed, Brain-Computer Interface for treatment of central neuropathic pain in spinal cord injury: Feasibility study," in *Proc. 7th Graz Brain-Comput. Interface Conf.*, 2017, pp. 1–6.
[36] S. Schmidt, J. R. Naranjo, C. Brenneisen, J. Gundlach, C. Schultz, H. Kaube, T. Hinterberger, and D. Jeanmonod, "Pain ratings, psychological functioning and quantitative EEG in a controlled study of chronic back pain patients," *PLoS ONE*, vol. 7, no. 3, 2012, Art. no. e31138.
[37] X. Sun, H. Li, W. Du, W. Chen, F. Zhou, and L. Wang, "Analysis of electroencephalogram of patients with specific low back pain with the massage treatment," in *Proc. 39th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc. (EMBC)*, Jul. 2017, pp. 479–483.
[38] M. Case, S. Shirinpour, H. Zhang, Y. H. Datta, S. C. Nelson, K. T. Sadak, K. Gupta, and B. He, "Increased theta band EEG power in sickle cell disease patients," *J. Pain Res.*, vol. 11, pp. 67–76, Dec. 2017.
[39] M. D. Vries, O. H. Wilder-Smith, M. L. Jongsma, E. N. van den Broeke, M. Arns, H. Van Goor, C. M. van Rijn, "Altered resting state EEG in chronic pancreatitis patients: Toward a marker for chronic pain," *J. Pain Res.*, vol. 6, pp. 815–824, Nov. 2013.
[40] D. M. Torta, V. Legrain, A. Mouraux, and E. Valentini, "Attention to pain! A neurocognitive perspective on attentional modulation of pain in neuroimaging studies," *Cortex*, vol. 89, pp. 120–134, Apr. 2017.
[41] A. E. Dubin and A. Patapoutian, "Nociceptors: The sensors of the pain pathway," *J. Clin. Invest.*, vol. 120, no. 11, pp. 3760–3772, Nov. 2010.
[42] N. Fallon, Y. Chiu, T. Nurmikko, and A. Stancak, "Altered theta oscillations in resting EEG of fibromyalgia syndrome patients," (United Kingdom), *Eur. J. Pain*, vol. 22, no. 1, pp. 49–57, Jan. 2018.
[43] S. Vanneste, J. Ost, T. Van Havenbergh, and D. D. Ridder, "Resting state electrical brain activity and connectivity in fibromyalgia," *PLoS ONE*, vol. 12, no. 6, pp. 1–20, 2017.
[44] A. J. Furman, T. J. Meeker, J. C. Rietschel, S. Yoo, J. Muthulingam, M. Prokhorenko, M. L. Keaser, R. N. Goodman, A. Mazaheri, and D. A. Seminowicz, "Cerebral peak alpha frequency predicts individual differences in pain sensitivity," *NeuroImage*, vol. 167, pp. 203–210, Feb. 2018.
[45] A. F. Almarzouki, C. A. Brown, R. J. Brown, M. H. K. Leung, and A. K. P. Jones, "Negative expectations interfere with the analgesic effect of safety cues on pain perception by priming the cortical representation of pain in the midcingulate cortex," *PLoS ONE*, vol. 12, no. 6, pp. 1–18, 2017.
[46] D. A. Blanco-Mora and J. A. Díaz-Méndez, "Pain detection with EEG using phase indexes," in *Proc. IEEE Healthcare Innov. Point Care Technol. (HI-POCT)*, Nov. 2017, pp. 48–51.
[47] B. W. LeBlanc, P. M. Bowary, Y.-C. Chao, T. R. Lii, and C. Y. Saab, "Electroencephalographic signatures of pain and analgesia in rats," *Pain*, vol. 157, no. 10, pp. 2330–2340, Oct. 2016.
[48] D. Madeo, E. Castellani, C. Mocenni, and E. L. Santarcangelo, "Pain perception and EEG dynamics: Does hypnotizability account for the efficacy of the suggestions of analgesia?" *Physiol. Behav.*, vol. 145, pp. 57–63, Jun. 2015.
[49] L. J. Hadjileontiadis, "EEG-based tonic cold pain characterization using wavelet higher order spectral features," *IEEE Trans. Biomed. Eng.*, vol. 62, no. 8, pp. 1981–1991, Aug. 2015.
[50] E. Schulz, L. Tiemann, V. Witkovsky, P. Schmidt, and M. Ploner, "Gamma oscillations are involved in the sensorimotor transformation of pain," *J. Neurophysiol.*, vol. 108, no. 4, pp. 1025–1031, Aug. 2012.
[51] J. E. Brown, N. Chatterjee, J. Younger, and S. Mackey, "Towards a physiology-based measure of pain: Patterns of human brain activity distinguish painful from non-painful thermal stimulation," *PLoS ONE*, vol. 6, no. 9, pp. 2–9, 2011.
[52] H. Kang, A. Nakae, H. Ito, T. Minamoto, T. Ikeda, M. Osaka, T. Mashimo, Y. Fujino, S. Hagihira, and P. Vitayaburananont, "Effects of sedation on subjective perception of pain intensity and autonomic nervous responses to pain: A preliminary study," *PLoS ONE*, vol. 12, no. 9, 2017, Art. no. e0183635.

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