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TOPICAL REVIEW

Intracortical Hindlimb Brain–Computer Interface Systems: A Systematic Review

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ABSTRACT Brain-computer interfaces (BCI) can help people with motor disorders to regain their ability to communicate and interact with the surrounding environment. The majority of studies in this field pursue the development of BCI systems to enhance or restore the movement functionality of people with disability. Although the studies on the development of BCIs to restore hindlimb movements have shorter backgrounds compared to forelimb, several studies have investigated hindlimb BCIs and their results were promising. In the present study, we systematically reviewed the studies investigating the decoding of hindlimb movement parameters using intracortical signals. Three scientific databases (PubMed, Scopus, and Embase) were used to extract the articles and the experiment, recording, processing methods, and results of the included studies were discussed. Although several studies on upper-limb intracortical BCIs have been conducted on human subjects, almost all studies in hindlimb intracortical BCI field were performed on animal subjects. The most investigated task was walking on a treadmill, and the position of hindlimb joints and gait phase were the most studied continuous and discrete parameters, respectively. The included studies have mainly used spikes and linear decoders, which leaves the question of the effectiveness of using local field potentials and nonlinear decoders in this field unanswered. Although the results imply that hindlimb movement decoding using brain signals is feasible in laboratory conditions, further investigations are required to examine the hindlimb BCIs in real-life conditions.

INDEX TERMS Brain–computer interface, motor cortex, hindlimb, neural decoding, intracortical.

I. INTRODUCTION

Neural circuits continuously process various sensory signals and generate motor commands and cognitive functions, e.g., thoughts and decision-making, producing a mental feeling of consciousness and free will. Unfortunately, neurological disease or trauma might create significant disorders in such neural mechanisms whereby an individual cannot feel, move or communicate. However, most neurological diseases like Amyotrophic Lateral Sclerosis (ALS), Stroke, and Spinal Cord Injury (SCI), cannot be cured completely. In most neuro-motor disorders, spinal neural circuits generating

locomotor patterns for standing and walking remain intact. Even after an abrupt disconnection between spinal and supraspinal circuits by SCI, cortical and spinal circuits significantly maintain the capability of controlling prostheses [1]. Accordingly, embedded neural networks in the lumbosacral segments maintain the ability to create complex locomotor behaviors [2], [3], [4], [5], [6]. Thereby, one of the developing solutions for such patients rehabilitation is Brain-Computer Interface (BCI) based neural prostheses, which can lead to restoring the partial or complete movement of the body [7], [8], [9], [10].

BCI connects neural circuits to external devices like artificial limbs, communication devices, computers, functional electrical stimulation systems, and even other central nervous

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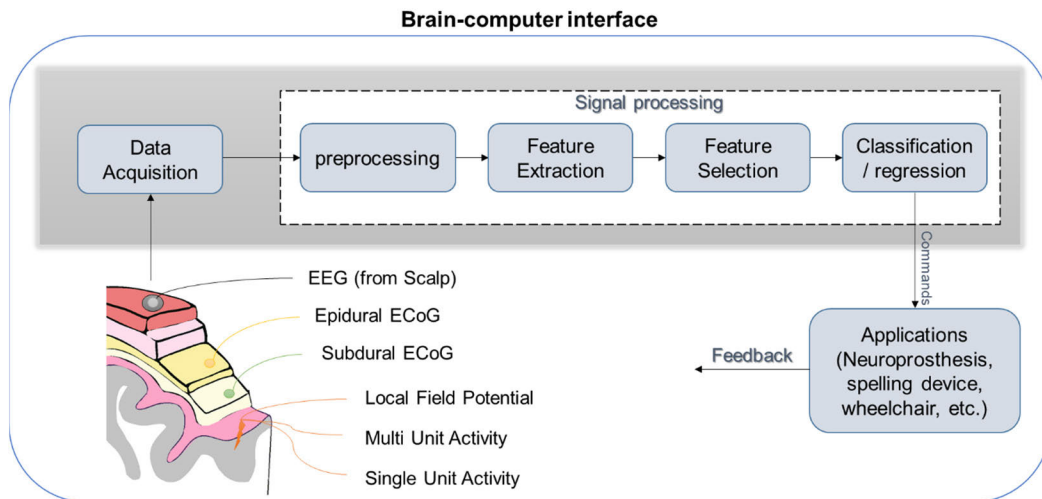


FIGURE 1. Schematic of principal BCI components: (1) data acquisition, (2) preprocessing, (3) feature extraction, (4) feature selection, (5) feature translation to classification/regression and device.

system parts [11]. As an illustration, the BCI approach to SCI includes a direct connection of effective regions of the brain, e.g., the sensory-motor cortex, to limb prosthesis [12], [13]. Fig 1 presents a schematic of the principal BCI components. The components involve data acquisition, preprocessing, feature extraction, feature selection, classification/regression, and an application interface. BCIs can connect the brain to a cursor, a robotic prosthesis, such as a robotic arm [14], [15], [16], exoskeletons for walking [17], [18], Wheelchairs [19], [20], drones [21], and automobiles [22]. In this regard, due to their importance in life quality improvement for individuals with movement disability, the development of BCIs focusing on the movement of arms and legs have special importance and has made significant progress [14], [23], [24].

Developing these systems requires a deep understanding of the way movement parameters are encoded in different regions of the brain and also the development of neural decoding algorithms. Improvement of our understanding in these areas can lead to BCI systems with higher degrees of freedom.

Among various brain signals, intracortical signals have been the main base of BCI systems development [25], [26], [27]. Also, invasive recording techniques, e.g., recording by microelectrode arrays inside the cortex, have a greater signal-to-noise ratio (SNR), providing the possibility of accurately identifying patterns or the continuous decoding of locomotor variables. Nevertheless, the pertinent risks to experimenting with these systems for human applications prevent invasive BCIs development for lower limb applications. Thereby, the development of BCI systems in lower limbs is being done on animals so that by developing algorithms and examining their feasibility, it is used for human applications in the future. According to evidence, intracortical recording during normal walking indicates distinct characteristics compared to when walking

on stairs or on a treadmill [28]. More importantly, the walking cycle and related parameters to locomotion like the Electromyography (EMG) of leg muscles and gait phase can be decoded via the processing of recorded signals from the brain cortex [29], [30], [31], [32], [33], [34]. For this purpose, only intracortical studies have been examined in this review.

Although most of the studies in BCI have focused on upper-limb movement and manipulation tasks so far, some studies investigated the decoding of hindlimb movement parameters with promising results for the rehabilitation of people with movement disabilities. These studies revealed that the neural circuits controlling forelimb movements are different from hindlimb controlling circuits [35], [36]. Thus, the current review focuses on studies investigating the role of brain cortical signals in decoding hindlimb movement information which was conducted to develop movement BCI systems.

Several reviews exploring the decoding of movement parameters from brain signals have been conducted. For example, Fatima et al. [37] systematically reviewed the studies which used intracortical brain-machine interface (BMI) to control upper limb robotic systems or functional electrical stimulation of muscles. They assessed 15 studies with human subjects which used brain-controlled robotic or functional electrical stimulation (FES) devices, which make body movements by electrically stimulating the muscles that are involved in producing the intended movement, to perform upper limb tasks and reported information about their subjects, robotic/FES device, BMI, and performances. Khaliq Fard et al. [38] performed a meta-analysis on 11 electroencephalogram (EEG)-based studies continuously decoding upper limb kinematic parameters. He et al. [39] compiled studies on BMI to control lower limb robotic systems. Their systematic review, which included 11 studies on robotic systems for lower limb movement controlled by BMI, reported the subjects, robotic devices and their performance,

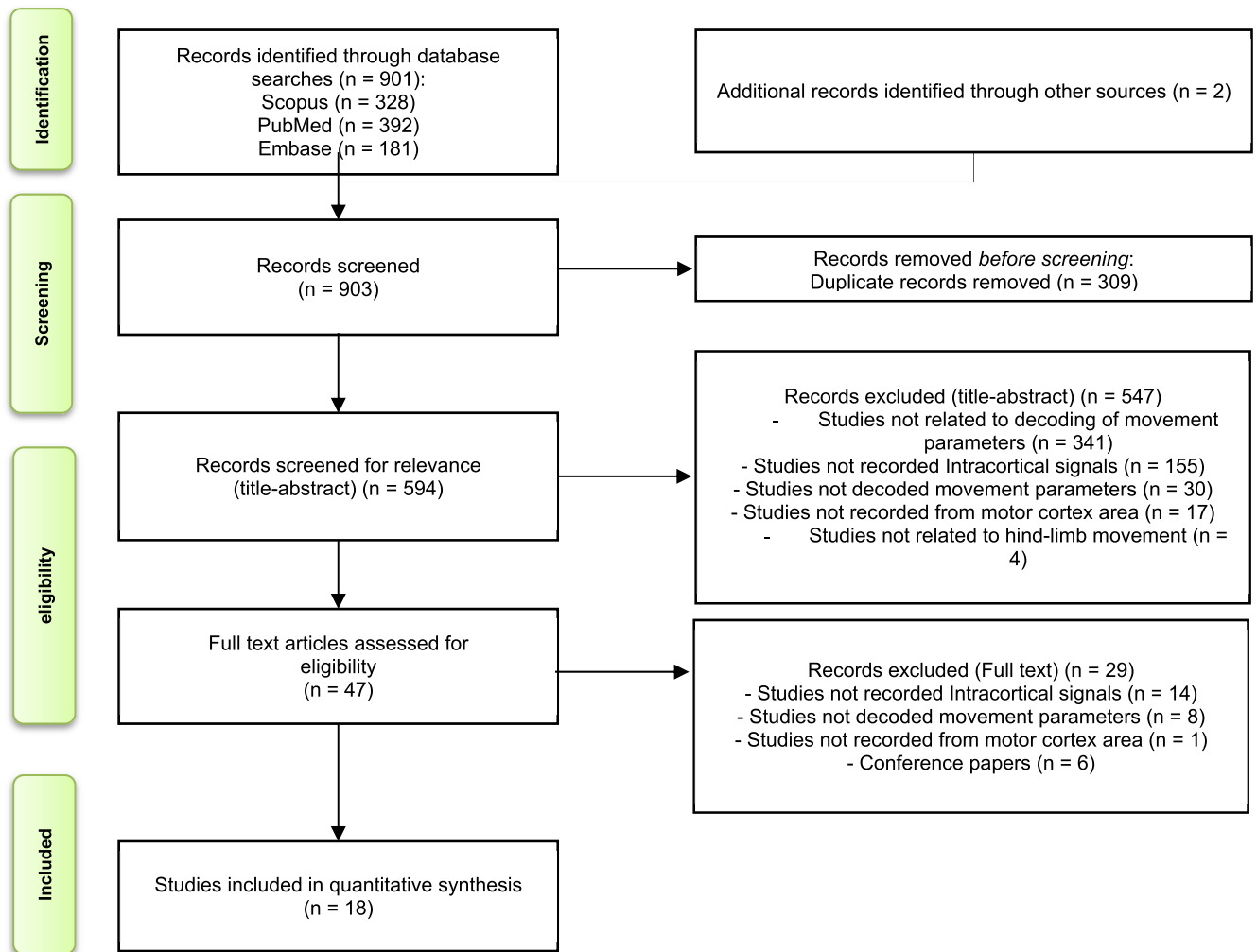


FIGURE 2. PRISMA flow chart of literature search procedures.

BMI structure (tasks, decoder, output commands, etc.), and the performance of the system in reviewed studies. Most of the included studies in the aforementioned review (10 out of 11) used EEG signals as the input to the BMI system.

In this review, we systematically explored the studies which used intracortical signals for decoding hindlimb movement-related parameters and no restrictions on subjects, movement parameters, or the presence/absence of a robotic systems were considered and task, recorded signals, subjects, decoders, features, and decoded parameters were summarized. This study aims to briefly investigate the currently available BCI systems for decoding hindlimb movement parameters and controlling robotic limbs and identification of the challenges and opportunities of this emerging field.

In section II, the methods for setting up this systematic review are presented. In section III, the results of the following items are presented: general results of the search in section III-A; subjects used in studies (III-B); signal type (III-C); recording area (III-D); tasks and experiments in section (III-E); kinetic and kinematic parameters (III-F); decoding

methods in section (III-G). Finally, in sections IV and V the discussion about the results and conclusion is presented.

II. METHOD

A. DATA SOURCE AND SEARCH STRATEGY

The articles in this review were searched and screened based on Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) [40] as depicted in Fig 2. Scientific literature databases are generally classified into two major groups; Academic Citation Databases (ACDB) including traditional Boolean string-based search engines such as Scopus and PubMed, and Academic Citation Search Engines (ACSE) such as google scholar and search engines operating based on semantic/natural language such as Microsoft Academic Search and semantic scholar [41]. In this review, three items of the first class of databases (ACDB) (PubMed, Scopus, and Embase) were considered. Two authors (AM and MG) searched the three mentioned databases (without using MeSH terms) through advanced search considering a vast set of keywords (Table 1). The last search took place on September 1st, 2021. The papers containing the selected

TABLE 1. Keywords used to search in the Scopus database and the results were 328 articles (see Fig. 2). Similar keywords are used for other databases.

	Keywords
Lower Limb	hind-limb* OR leg* OR lower limb* OR lower body* OR "lower extremity"
	AND
Decoding	Code** OR encode** OR decode** OR predict** OR regression OR classify OR discriminate OR discrimination OR BCI* OR BMI* OR "brain-computer interface"* OR "brain-machine interface"*
	AND
Area (Motor Cortex)	M1 OR "motor cortex" OR cortical OR sensorimotor OR cortex OR "primary motor cortex"
	AND
Invasive Recording	Intracortical OR microelectrode OR array OR spike OR LFP OR "local field potential" OR "single-unit activity"* OR "multi-unit activity"* OR neuron OR "neural ensemble" OR tetrodes OR array OR neural OR electrode OR signal OR "Spiking activity" OR "firing rate"
	AND
Movement	gait OR stepping OR movement OR treadmill OR motor OR "freely-moving" OR "freely moving" walking OR walk OR locomotion OR locomotor

*Phrases written in different forms including hyphen separated, space separated, and plural have been added to the search. **, Verbs in simple form, third person, with “ing” and past tense are added to the search.

keywords in title, abstract, or keywords were extracted. Only the papers of journals published in English were included. Science Direct database was excluded as the recent update of this framework limited us in entering all the keywords in the search keyword input section. However, since Science Direct and Scopus use the same database [42], this did not affect the comprehensiveness of our literature review. IEEE Xplore was not used as its search keywords were limited to 15 terms which were far lower than the number of keywords considered in this study (see Table 1). This also does not influence the comprehensiveness of our study as the papers in IEEE are also indexed in Scopus. ACSE was not taken into account due to the deficient repeatability and reproducibility of the search results [43], [44].

To set up an appropriate search phrase and make the decision-making less subjective and biased, a pre-search step was carried out by collecting a keyword list used by the lower limb BCI researchers, and to find optimum keywords we analyzed keyword combinations by taking the conducted search results (recorded from Scopus) to a metadata analysis software to have a greater picture from the nature of search engine results. To this aim, we used VOS-viewer [45] which performs clustering of search results based on title, keywords, and abstract and illustrates the results graphically (see Fig 3). The node size indicates the relative relevance based on the occurrence frequency of keywords and colors indicate

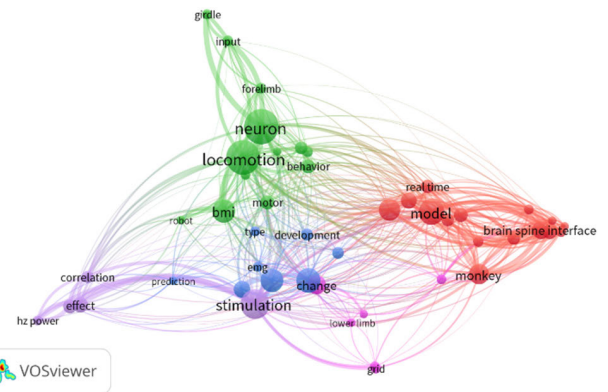


FIGURE 3. Word cloud showing the most frequent keywords in results (recorded from Scopus), visualized by the software VOS-Viewer.

the cluster to which a node belongs. This procedure was iterated and refined several times before arriving at the final search phrase listed in Table 1. Overall 903 papers were investigated in this review and 901 articles of which were retrieved from the three mentioned databases. Two articles were manually added. Fig 2 presents the PRISMA flow diagram which demonstrates the followed screening procedure. Any disagreement on the exclusion of studies between the authors (i.e. those placed on the borderline of the exclusion criteria) was resolved by mutual discussion and decision.

B. ELIGIBILITY CRITERIA

This review only addressed the studies which used intracortical signal recording using microelectrodes to decode the motor parameters or the BCI-controlled prosthesis. The following eligibility criteria were considered:

- 1) This study is specifically focused on the research works directly related to the decoding of hindlimb kinetic/kinematic parameters using cortical signals. The studies not focusing on decoding as an outcome, as well as those concentrating on cortex stimulation, were excluded.
- 2) The intracortical brain signals must be recorded from the sensorimotor cortex area.
- 3) The subject species was not specified (Table 1), however, as only intracortical signals were investigated, the included studies (except one) are all on animal subjects.
- 4) This review article did not exclude any studies based on the type of the recorded intracortical neural signal (spike/ field potentials).
- 5) No specific task was determined for hindlimb movements and all the studies decoding the kinetic/kinematic parameters of hindlimb motor tasks (walking, pedal pressing, squat, foot movements) were included.

The main exclusion criteria are mentioned in PRISMA flow diagram (Fig 2). Studies that did not address the decoding of the hindlimb parameters, those not including decoding by

TABLE 2. Information of subjects and type of signal recorded in each study.

Authors	Subjects (involved in decoding)				Recording		Recording Area	
	Subject	number	Gender	strain	Signal	Channel #	Area	Laterality
Fitzsimmons et al (2009) [33]	Monkey	2	F	Rhesus macaques	Spike	128 / 160	M1 and S1	CL/BL ^a
Song et al (2009) [29]	Rat	4	-	Sprague–Dawley	Spike	24	HL / trunk area of M1	CL
Song et al (2011) [30]	Rat	11	F	Sprague Dawley	Spike	24	HL / trunk area of M1 and S1	-
Manohar et al (2012) [46]	Rat	6	M	Long Evans	Spike	16	HL sensorimotor cortex	BL
Knudsen et al (2012) [47]	Rat	11	M	Long Evans	Spike	16	HL sensorimotor cortex	BL
Li et al (2014) [48]	Guinea Pig	3	-	Hartley Albino	Spike	9	M1	CL
Alam et al (2014) [31]	Rat	6	F	Sprague Dawley	Spike	7	FL and HL area of M1	CL
Schwarz et al (2014) [49]	Monkey	3 ^b	F, M	Rhesus macaques	Spike	384 / 576	M1 and S1 ^c	BL
Rigosa et al (2015) [28]	Rat	6	F	Lewis	Spike	32	sensorimotor cortex	CL / IL
Ma et al (2015) [50]	Monkey	2	M	Rhesus macaques	Spike	Acute	M1	CL / IL
Capogrosso et al (2016) [51]	Monkey	9	M	Rhesus macaques	Spike	96	HL area of M1	CL ^d
DiGiovanna et al (2016) [32]	Rat	16	F	Lewis	Spike	32	HL area of M1	CL
Knudsen and Moxon (2017) [52]	Rat	9	M	Long Evans	Spike	16	HL sensorimotor cortex	BL
Ma et al (2017) [53]	Monkey	2	M	Rhesus macaques	Spike	64	M1	CL
Vouga et al (2017) [54]	Monkey	1	F	Rhesus macaque	Spike	576	FL and HL area of M1	BL
Xing et al (2019) [55]	Monkey	5	M	Rhesus macaques	Spike	96	HL area of M1	CL ^d
Barroso et al (2019) [34]	Rat	7	F	Sprague Dawley	Spike, LFP, EFP	32 ^e	HL sensorimotor cortex	CL
Willett et al (2020) [56]	Human	2	M	-	Spike	192	the hand knob area	CL / IL

^a arrays were implanted bilaterally in one subject and contralaterally in the other subject; ^b one of the monkeys has done two tasks; ^c arrays were implanted only in the Hindlimb area of M1 and S1 in one monkey; ^d these items were inferred by the authors; ^e 16-electrode arrays were used for EFP recording. **Abbreviations:** F, female; M, male; HL, hind-limb; M1, Primary motor cortex; S1, primary somatosensory cortex; FL, Forelimb; BL, bilateral; CL, contralateral; IL, Ipsilateral.

intracortical data, and those that did not record the cortical signals were directly eliminated.

C. DATA EXTRACTION AND PRESENTATION

Data were extracted based on a structured template form; the following information was extracted:

- 1) Subject (species, strain, gender, and number of subjects)
- 2) Recorded signal (type of signal, number of the recorded channels, recording area, and laterality)
- 3) Experiment design (including task type and experiment conditions)
- 4) Data analysis (decoded parameters, neural features, and decoder)
- 5) Major findings.

All the identified studies and some of the main properties related to the type of recording and subjects are summarized in Table 2. Table 3 also lists the information regarding the tasks and their corresponding decoder. Decoded parameters are also presented in Table 4. In this review, “identified studies” and “included studies” refer to the selected studies.

III. RESULTS

A. LITERATURE SEARCH

The flow diagram is plotted in Fig 2 based on PRISMA [57]. 901 papers were retrieved from PubMed, EMBASE, and Scopus. Two other articles, which were related but did

not appear in search results, were also added manually. From the 903 papers, 309 items were omitted due to duplication; 341 papers were excluded due to their irrelevance to the decoding of motor parameters. Moreover, by investigating the abstract and full text of the papers, 169 cases were excluded due to signal type and recording. 18 papers were excluded as they recorded data from other brain regions. 4 articles were excluded due to their irrelevance with the hindlimb movement and 38 were omitted as they did not address decoding. Fig 2 illustrates the details of the papers. Finally, 18 papers [28], [29], [30], [31], [32], [33], [34], [46], [47], [48], [49], [50], [51], [52], [53], [55], [56], [58], [54] were included in this systematic review.

B. SUBJECTS

Except for one study which decoded human movement parameters [56], all other papers addressed various species and strains of animals. In total, 76 rats (50% of the papers, $n = 9$), 24 monkeys (38.88% of the papers, $n = 7$), 2 humans (5.56% of the papers, $n = 1$), and 3 guinea pigs (5.56% of the papers, $n = 1$) were used as subject. Fig 4A shows the percentage of each species (by considering the number of subjects in each study) in included studies. The studied rats belonged to Long Evans (34.21% $n = 26$), Sprague Dawley (36.84%, $n = 28$), and Lewis (28.95% $n = 22$) strains. Considering the studies using rat subjects, except for [29] in which the gender of subjects was not mentioned,

TABLE 3. Task and neural decoding methods were used in each study.

Authors	Task			Decoder		
	Task	Intervention	Quadrupedal or Bipedal	Neural feature	Classifier	Regression
Fitzsimmons et al (2009) [33]	Treadmill Walking	-	B	FR	-	Wiener Filter
Song et al (2009) [29]	Treadmill Walking	AW	Q	FR	-	Multiple Linear Regression
Song et al (2011) [30]	Treadmill Walking	AW	Q	FR	-	Linear model
Manohar et al (2012) [46]	Pedal Press	SCI	-	FR	PETH-based classifier	Wiener Filter
Knudsen et al (2012) [47]	Pedal Press	-	-	FR ISI	ISI-based classifier	Wiener Filter
Li et al (2014) [48]	Treadmill Walking	SCI, AW	Q	FR	Thresholding	-
Alam et al (2014) [31]	Treadmill Walking	SCI, AW	Q	FR	Thresholding	-
Schwarz et al (2014) [49]	Treadmill Walking	-	B & Q	FR	EM, SVM and k-means.	Unscented Kalman Filter
Rigosa et al (2015) [28]	Treadmill Walking Runway Walking Staircase Walking	AW	B	FR SMFR	SVM	SVR
Ma et al (2015) [50]	Squat	-	-	FR	-	MISO
Capogrosso et al (2016) [51]	Treadmill Walking Runway Walking	SCI	Q	FR	rLDA	-
DiGiovanna et al (2016) [32] ^a	Treadmill Walking Runway Walking Ladder Walking Staircase	-	Q	FR	-	LS
Knudsen and Moxon (2017) [52]	Pedal Press	SCI	-	PSTH	PSTH-based classifier	-
Ma et al (2017) [53]	Squat	-	-	FR	-	Standard Kalman Filter Unscented Kalman Filter
Vouga et al (2017) [54]	Tracking a cursor in 2D plane on screen	EX	B	FR	-	Linear regression
Xing et al (2019) [55]	Treadmill Walking Runway Walking Ladder Walking	-	B & Q	FR	-	Wiener Filter
Barroso et al (2019) [34]	Treadmill Walking	-	Q	FR/BP	-	Wiener Filter & RNN
Willett et al (2020) [56]	Movements of body parts (head, face, arm, leg, etc)	TP	-	FR	Gaussian Naïve Bayes	-

^a decoding was only done on treadmill and runway walking tasks. **Abbreviations:** Q, quadrupedal; B, bipedal; FR, firing rate; BP, band power; ISI, Inter-Spike Interval; PSTH, Peri-stimulus time histogram; EM, expectation–maximization; SVM, Support vector machine; RNN, Recurrent neural networks; SMFR, Statistical moments of firing rate; SCI, spinal cord injury; TP, tetraplegia; AW, Assisted Walking; EX, Exoskeleton.

other studies on rats investigated 63.89% female ($n = 46$) and 36.11% ($n = 26$) male rats. Male rats were only used in studies with Long Evans strain, while studies that used other two strains, merely worked with female rats. All studies addressing monkey subjects, used rhesus macaque species ($n = 24$); 20.83% female ($n = 5$) and 79.17% male ($n = 19$). Fig 4B illustrates the number and subject type of each study. The precise information on the animal type, species, gender, and number can be found in Table 2.

C. INPUT TO THE BRAIN-COMPUTER INTERFACE

Following an extensive search for post-SCI neuro-regenerative strategies, three decades of progression in neural engineering have led to alternatives to replace the lost sensory-motor functions. The development of high-density neuronal recording devices [59], [60], along with high-performance computation capacity, has resulted

in the identification of the principles through which the brain cortex can contribute to movement coordination [61]. Various neural recording methods are developed to be used in the fabrication of BCI systems, each of which can deliver different temporal and spatial resolutions depending on their biological and physical principles. Invasive brain signal recording methods deliver higher SNR as microelectrodes directly record neural signals from a small area in the vicinity of neurons. Depending on the task type and the aim of study, microelectrode arrays can be implanted in various regions of the brain cortex. In this study, only intracortical recording methods were assessed which can be divided into three major classes: a) single-unit activity (SUA), b) multi-unit activity (MUA), and c) local field potentials (LFP). Table 2 lists the type of neural data in the studied articles. As can be observed, except for one case [34], other studies recorded and used spike signals (single-unit or multi-unit activity). In [34],

TABLE 4. Decoded parameters in each study.

Authors	Low-level parameters					High-level parameters				
	Position	Angles	Velocity	EMG	Acceleration	Press Parameters (Continuous)	Gait phase	Intention	Task	Press Parameters (Discrete)
Fitzsimmons et al (2009) [33]*	✓	✓	✓	✓			✓		✓	
Song et al (2009) [29]	✓	✓	✓							
Song et al (2011) [30]	✓									
Manohar et al (2012) [46]	✓					✓				✓
Knudsen et al (2012) [47]						✓				✓
Li et al (2014) [48]							✓	✓		
Alam et al (2014) [31]							✓	✓		
Schwarz et al (2014) [49]	✓								✓	
Rigosa et al (2015) [28]	✓	✓		✓			✓	✓	✓	
Ma et al (2015) [50]				✓						
Capogrosso et al (2016) [51]							✓	✓		
DiGiovanna et al (2016) [32]		✓						✓		
Knudsen and Moxon (2017) [52]										✓
Ma et al (2017) [53]	✓		✓	✓	✓					
Vouga et al (2017) [54]	✓									
Xing et al (2019) [55]	✓	✓					✓			
Barroso et al (2019) [34]	✓	✓		✓						
Willett et al (2020) [56]									✓	

* for this study velocity indicates the instant speed of walking, not joint velocity

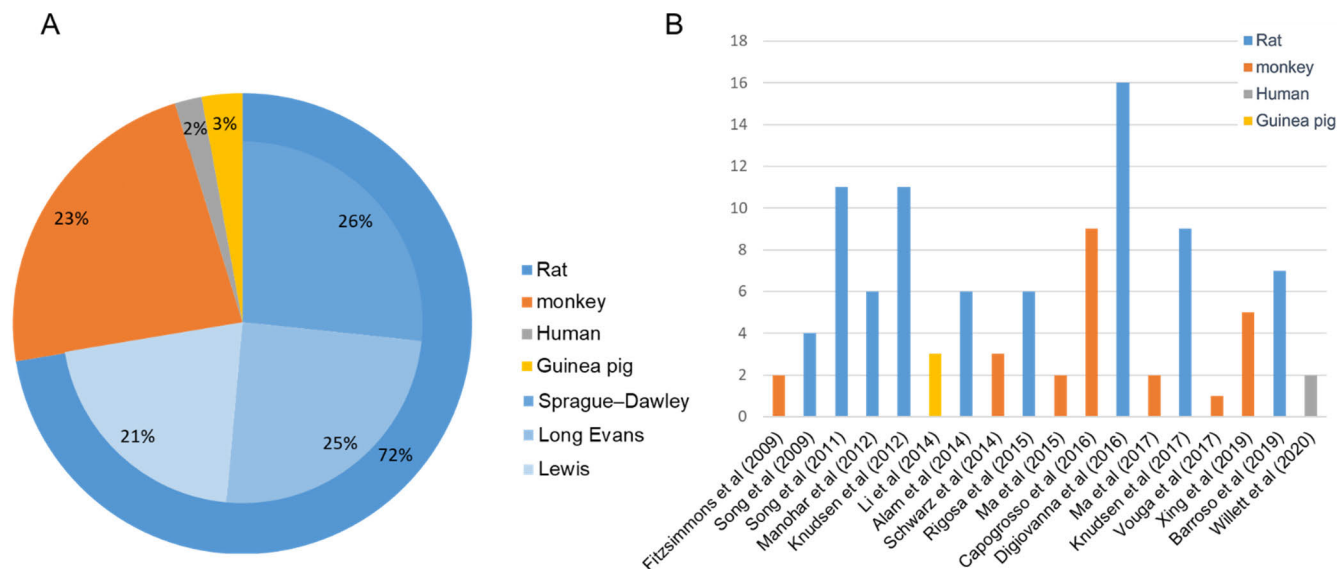


FIGURE 4. Visualization of Subjects information among the identified studies. (A) The Percentages of type and strain of subjects. (B) The number and type of subjects.

however, LFP and epidural field potential (EFP) data were used in addition to MUA to decode kinematic and kinetic parameters related to walking. Over time, SUA and MUA data vanishes gradually which is one of the main challenges in the application of long-term BCIs based on spike activities.

On the other hand, the stability of LFP signals over time, has attracted attentions in recent years and many studies have examined the feasibility of using these signals

in BCIs. In particular, LFP has gained attentions and has been used in studies on forelimb BCI in animals, in which the informativeness of these signals and their stability over time were investigated [24], [62]. In hindlimb BCI, however, LFP signals have been less noticed. The limited number of studies in this area indicated that useful information can be extracted from LFP signals of the primary motor cortex (M1) regarding various walking parameters

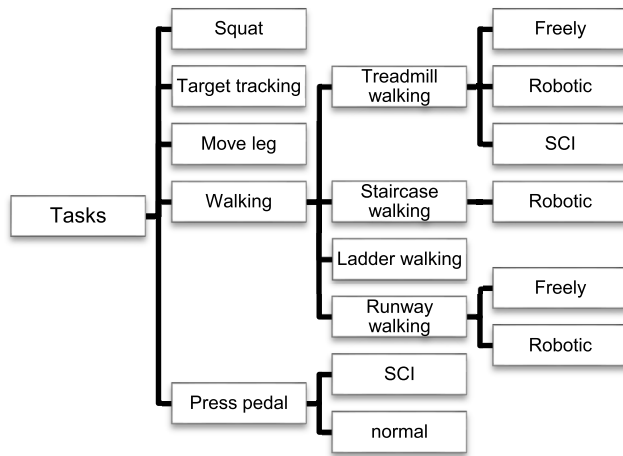


FIGURE 5. Tasks used to decode Hindlimb movement parameters.

[34], [63], [64], [65]. Comparison of the walking parameter information contained in various brain signals of rats walking on a treadmill showed that MUA signals encompassed more information than LFP signals [34]. The results of this study show that EFP does not provide any information about the kinetic and kinematic parameters of hindlimb, whereas LFPs deliver comparable results for decoding these parameters to MUA [34]. A comparison of the previous works using EFP data for decoding movement parameters with the aforementioned study showed that the decoding accuracy was far lower which the authors claimed that it can be assigned to the smaller size of the epidural electrodes. Overall, the type of brain signal plays an important role in the feasibility, accuracy, and lifetime of a BCI system.

D. RECORDED CORTICAL AREA

In this review, the studies which decoded hindlimb motor parameters using intracortical neural signals are investigated. In all the addressed studies, recording electrodes were invasively implanted in the cortex and the brain signals of subjects were recorded simultaneously with the hindlimb movement task. The motor cortex consists of several regions, each of which is related to the movement of a specific part of the body. Thus, electrodes were implanted in different areas of the motor cortex based on the body part being investigated. Table 2 presents the investigated region in each study. The recorded areas included the hindlimb/trunk area of M1, premotor cortex, and hand knob area of the premotor cortex. Moreover, some papers mentioned the sensorimotor cortex as the recorded region and some of the assessed studies recorded the signals of S1 in addition to the motor cortex but only used motor cortex signals in decoding.

As reported in Table 2, all studies had the signal recording from the contralateral hemisphere to the investigated limb in their recording areas. In addition, in several studies [33], [46], [47], [49], [52], [54], the electrode arrays were bilaterally implanted. Also in two studies [28], [56] the electrode arrays were implanted only on one hemisphere, and the decoding of movement parameters was investigated

for both ipsi- and contralateral limbs. Rigosa et al. [28] recorded brain signals only from one hemisphere and tried to use the recorded cortical signals to decode movement parameters of both hindlimbs. Willett et al. [56] also recorded one hemisphere and decoded the motions of both sides of the body.

The number of recorded channels and the type of recorded signal were also investigated in this review. Only one of the included studies [50] used acute recording to decode the motor parameters. In the rest of the included articles, the lowest and highest channels were 7 [31] and 576 [49], [54], respectively. Table 2 lists the number of recording channels in the included studies as well as the information related to their subjects and recording area. 88.89% of the studies considered more than (or equal to) 16 channels, and 50% and 33.33% of the studies used more than 32 and 96 channels for neural signal recording, respectively. As mentioned before, all the studies, except for one [34], recorded and analyzed spike data.

E. EXPERIMENT DESIGN AND TASKS

Movement parameters can be decoded by analyzing brain activities. The decoding ability is basically due to a correlation between the brain activities, firing rate of neurons, and motor parameters [66]. Studies in this field have shown that intracortical signals recorded from the cortex are related to movements of the fore and hindlimbs. Decoding algorithms of BCI systems convert these neuromodulations into desired output signals (cursor motion or determining the spatial position of a prosthetic limb). Decoding algorithms are often developed and validated offline using previously recorded neural data and the final experiment can be conducted in real-time in such a way that the subject can directly control the actions of the external device by their brain activities. The type of the decoded parameter and the degree of freedom of the developed system have a direct relationship with the designed task and its implementation. Therefore, this systematic review investigated and compared the type of the implemented tasks to finally evaluate the parameters investigated by these tasks. Table 3 demonstrates the type of task in the reviewed papers for decoding the hindlimb movement parameters. The studies in which the condition of performing tasks were not as similar as normal were indicated under “intervention” column in Table 3. Four types of intervention are specified: (a) spinal cord injury (SCI) indicates studies in which the subject has performed the task after SCI, (b) assisted walking (AW) indicates studies in which the subject performed walking task using a robotic device, (c) tetraplegia (TG), and (d) exoskeleton (EX) indicates performing the task using exoskeleton. The type of tasks in the included studies is also depicted in Fig 5.

Based on Table 3, 61% of the included papers used locomotion-related tasks to decode hindlimb movement parameters. Using treadmill to force the subjects to walk, is one of the highly used tasks for decoding hindlimb movement parameters (used in 58% of the studies addressing

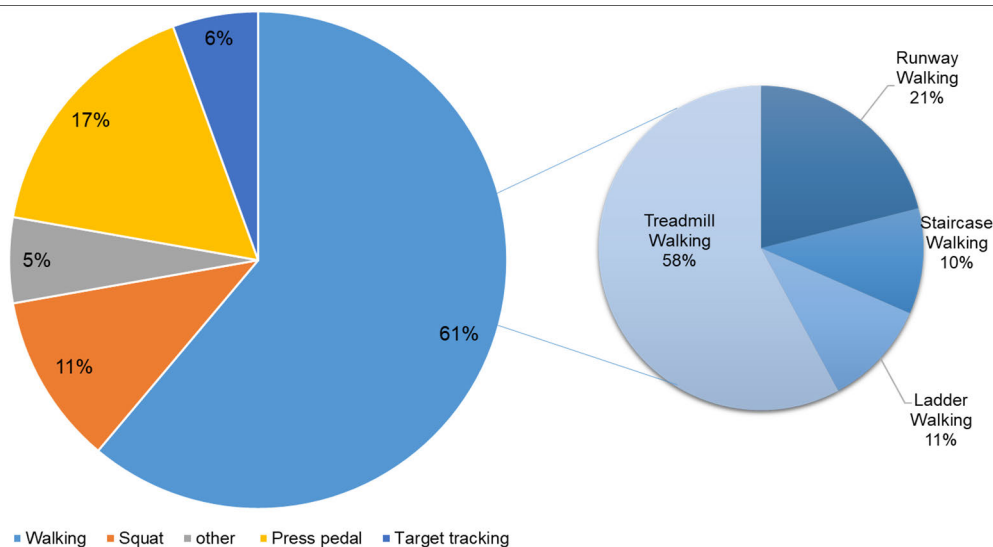


FIGURE 6. The contribution of different tasks in decoding the movement parameters, left shows the different types of tasks. The right side shows the different walking tasks.

the movement parameters during walking tasks). Studies on decoding the hindlimb movement parameters during walking on a treadmill addressed this task in two ways: a) walking on a treadmill with some sort of intervention in the normal walking of the subjects (for instance, by attaching a robotic arm to the animal), in which the bipedal or quadrupedal walking of the subjects was investigated [28], [29], [30], [48] and b) freely walking on a treadmill [31], [32], [33], [34], [49], [51], [55] in which subjects stepped normally on the treadmill. The latter task provides data under conditions closer to natural circumstances for walking which may result in better generalization. Bipedal locomotion, however, has some advantages (compared with quadrupedal walking) in investigating the decoding of hindlimb movements using cortical activities. This posture allows for separating the contributions of the brain activities related to forelimb and hindlimb and by eliminating the movements of forelimb resolves one of the major uncertainties in decoding the hindlimb movements. This is important as there is a correlation (with a relatively constant time lag) between the movements of forelimb and hindlimb during quadrupedal walking, which may raise the question of whether the BCI decodes the movements of hindlimb or forelimb with a specific time lag. Moreover, the robotic interface helps the subject in maintaining its balance, making it possible to record under various conditions and tasks [28]. However, robot-assisted walking or bipedal locomotion walking is different from the natural walking of the animal and possibly alters the contribution of various central nervous system regions in coordinating the movements. Therefore, brain activities during freely walking on a treadmill may be more similar to the ones during natural walking.

In addition to walking on a treadmill which could be free or robot-assisted in bipedal and quadrupedal form, walking on a ladder has been also regarded as one of the tasks

in this field [32], [55]. In comparison with previous tasks, this task requires more attention and care. As mentioned before, one of the hypotheses about the motor cortex expresses that the main role of this region is the production and coordination of precise and complex movements [67]. Previous studies have indicated that in locomotion, precise control of stepping requires specific functions of the motor cortex [68], [69]. This conclusion was based on the results of studies which used lesion and inactivation of cortical areas that revealed the essential role of the motor cortex for accurate stepping [70], [71]. Recording experiments also indicated a significant correlation between the motor cortex function and the required position of the feet on confined surfaces during passing a series of obstacles or walking on a horizontal ladder [69], [71]. Studies on rats and cats demonstrated the prominent role of the motor cortex in the voluntary adjustment of movements [32].

Walking on a flat surface is another task which has been used to investigate decoding locomotion-related information [28], [32], [55]. Compared to walking on a treadmill, this task is more similar to the natural walking condition as there is no force for walking, and walking is done volitionally, usually to receive a reward. Although the studies experimenting on the walking of rats on a flat surface were only conducted with robotic arm assistance [28], [32], this task was investigated on monkeys without a robotic arm and in a completely volitional mode [55]. Fig 6 shows the percentage of various tasks as well as the walking-related tasks in the included studies.

Walking under abnormal conditions (force application on body) is another task that confirms the role of the cortex in regulating motor parameters under abnormal conditions. Song et al. [29] compared walking in two different states (without and with force application by a robot) and revealed that the presence of load can slightly improve movement decoding. In their subsequent study [30] they investigated

the adaptation of the motor cortex to different locomotion conditions. They have examined the motor cortex neural activities in normal locomotion, under an elastic field applied to the pelvis and under an elastic field in which the force is determined by neural activities (BMI with elastic load) and observed that rats could manage to maintain their pelvic height in BMI control condition without significant difference with the natural condition. When subjects faced new conditions, the cortex becomes more activated, initially and after a period of time the cortical activity decreases. They concluded that the use of BMI in the period of confrontation with new conditions can change the adaptation of cortical activities [30].

For a better understanding of the role of M1 in various hindlimb movement tasks, Rigosa et al. [28] investigated the prediction of detail hindlimb movement parameters under various behavioral conditions and indicated that the prediction of hindlimb kinematics and EMG of hindlimb muscles during bipedal walking along a runway or staircase is significantly less accurate than walking on a treadmill. They concluded that the prediction of hindlimb movement parameters is not robust under various behavioral conditions; although it is not clear why these predictions are less precise during complex tasks which require voluntary adjustment of the walking patterns [28], which is believed to increase the contribution of cortex in coordinating movements.

In addition to the mentioned tasks which were focused on walking parameter decoding using intracortical recordings from the motor cortex, some studies have also decoded hindlimb parameters using movement tasks other than walking. Among these tasks, pedal pressing by hindlimb [46], [47], [52], and squat [50], [53] tasks can be mentioned. As listed in Table 3, three studies used pedal pressing to decode hindlimb movement parameters. All these studies considered rat subjects and this task was not investigated with monkey subjects. Knudsen and Moxon [47] investigated whether the duration of pedal pressing is encoded by the hindlimb area of sensory-motor cortex neurons and whether the brain activities of animals pressing a pedal for a specific duration to receive a reward are different from those pressing it with no duration condition. Manohar et al. [46] investigated the neural activities of rat sensorimotor cortex during behavioral and neural control of a pedal before spinal cord injury. After spinal cord injury, although the neural activity of the motor cortex was reduced, they still managed to control a BCI by neural activities of this area and their performance in doing the task increased gradually. This study also revealed that the activity of neurons in the hindlimb area of the sensorimotor cortex is related to more than one movement parameter, suggesting that the cortical cells of the hindlimb can simultaneously encode several kinematic parameters. These findings were in line with previous studies on encoding forelimb/arm and hindlimb movements. The limitation of this study was that the muscular activities were not recorded; therefore, after removing the pedal, the extent of the rats' muscles involvement in the movement is not

clear (i.e. neural activity was due to the movement or not). Knudsen et al. [52] resolved the mentioned limitation and repeated pedal pressing by rats (normal and SCI) with neural and EMG recording.

The squat is another task employed for decoding hindlimb movement parameters. Ma et al. [50] conducted visually guided stand and squat tasks and acutely recorded the spikes of hindlimb area in M1 to examine the neural modulation during various movement phases. They also tried to estimate the EMG of six muscles of monkeys' leg using neural data recorded from a limited number of neurons. The same group [53] also attempted to decode EMGs recorded from eight leg muscles of each monkey with the help of spike data recorded by 16-channel arrays. Vouga et al. [54] also designed the real-time control of a continuous virtual tracking task by which a trained monkey could control a cursor on a display to track a target.

In addition to the above-mentioned tasks on animals, Willet et al. [56] conducted a study to decode movement parameters using neural data of the hand knob area of two human subjects. They employed various tasks including different movements of face, hands, legs, and head versus doing nothing to classify these tasks. They finally showed that the hand knob area could be used for decoding the movement parameters on both sides of the body. As mentioned before, the task of a BCI system plays an important role in studies or in the practical applications of the system and can have a significant impact on decoding parameters, generalizability and even on the contribution of cortex in performing it. Table 3 lists the tasks of the included studies.

F. Hindlimb KINETIC AND KINEMATIC PARAMETERS

Hindlimb-related movement parameters can be divided into two major groups: low level parameters and high level ones, which different decoding techniques must be used for each group. High level parameters provide a general description of the movement and often decode the parameters using a classifier (or discrete decoder). The high level parameters that were investigated in the included studies are as follows: 1) gait phase or foot contact with the treadmill is one of the most basic and important high level parameters which indicates the stance/swing phase of one foot [28], [30], [31], [33], [55]. 2) The walking direction (discrimination between forward and backward walking) which was addressed in [14]. 3) The intention to move [28], [31], [48], [51], which is defined in this study as the onset of hindlimb movement. Studies decoding this parameter can be found in Table 4 in the "intention" section. Studies differentiating the instant stance/swing phase are also included in this group, as the onset of swing phase is equivalently the onset of target hindlimb movement. Note that in gait phase decoding, a gait phase (e.g. stance) is assigned to a period of time (e.g. 100 ms), whereas in decoding the intention to move, time is divided into small time bins (e.g. 20 ms bins) and each time bin is assigned to either onset of movement or otherwise. 4) The performed task also falls

into this category. For example, Rigosa et al. [28] decoded different tasks (walking tasks on a treadmill, on a flat surface, and climbing stairs) using intracortical signals recorded from the M1. Moreover, in [56] various tasks such as moving the hands, feet, and head were also decoded using intracortical signals.

Low level parameters such as position and speed of limb joints generally describe the details of movement and these parameters are continuous in nature. As mentioned before, many studies have used walking tasks to investigate decoding hindlimb movement parameters. The continuous parameters examined in hindlimb tasks will be introduced in the following. The position of the hindlimb parts such as toe, iliac crest, hip, ankle, knee, and metatarsal-phalangeal joints are the most important parameters that have been decoded in different studies using brain signals [28], [29], [30], [33], [34], [55]. Another evaluated parameter is the angle of the joints such as hip, ankle, knee, as well as some other angles defined by the authors [28], [29], [32], [33], [34], [55]. Velocity and acceleration of hindlimb joints [29], step length, step frequency, and instant speed of walking [33] were the other decoded parameters. EMG and muscle synergies are also decoded in some of the previous studies [28], [32], [33], [34]. Table 4 lists the decoded parameters in each article. In the velocity and acceleration column, studies which decoded the first (velocity) and second (acceleration) derivative of joints position are marked, respectively. In pedal pressing tasks the position of paw while pressing a pedal is investigated, which is also marked under the position column in Table 4.

G. DECODING ALGORITHMS

This section describes the decoding algorithms used in the reviewed studies in detail. These algorithms resemble EEG/ECOG-based decoders that have been evaluated in several review articles [72], [73]. Here only the literature on hindlimb movement decoding using intracortical signals will be reviewed. Decoding of movement parameters from intracortical signals is achievable as the modulation of neuronal activities is consistently related to tasks and changes in movement parameters [66].

Recording using multichannel arrays provides neural activities of several neurons or regions around each electrode (very small spheres around each electrode with a maximum radius of a few hundred micrometers), which in comparison with single electrode recording, can enhance the performance of decoders with richer inputs. A decoder takes the intracortical data as the input and estimates the desired parameters (including, but not limited to, presence/absence of movement, type of movement, position of a limb, joint angle) as the output. Thus, many machine learning methods can be used for this purpose. The signal processing for neural decoding consists of several steps, which are shown in Fig 1. After recording brain signals, the raw data is processed and several features are extracted from the processed signal, which may contain information about the BCI task or desired

parameters. The extracted features may be redundant or not related to the desired parameters which may be omitted from further processes in feature selection step. Next, a training algorithm fits a model to solve the problem of classification or regression. Classification algorithms solve the problem of matching the input with one of the predefined discrete classes, while the regression algorithms continuously match the input signals with the outputs. As an example, swing/stance identification is a classification problem, whereas knee joint trajectory decoding is a regression problem.

Preprocessing and denoising play a vital role in the development of intracortical BCIs. The preprocessing techniques (e.g. filtering, and artifact removal) used in BCIs can significantly affect the accuracy of BCI systems in decoding user's intent via intracortical neural signals. All of the included studies used frequency filtering to extract the spike/LFP signal from recorded neural activities. Spike detection was done using thresholding [29], [30], [31], [33], [34], [46], [47], [53], [55], [56], and a continuous wavelet-based method [28] presented in [74]. Several studies used Plexon online and offline spike sorting sorter softwares to obtain single-unit activities [29], [30], [46], [49], [52], [53], [56]. In addition, Barroso et al. [34] used a weighted common average reference method to denoise the LFP and EFP signals, and Rigosa et al [28] used wavelet filter bank to reduce the coupling between electrodes.

Depending on the type of the recorded signal (spikes or LFP), the considered features of the included studies are different. The features extracted from the recorded spikes include firing rate [28], [29], [30], [31], [32], [33], [34], [46], [47], [48], [49], [50], [51], [53], [55], [56], [54] (94.44% of included studies, $n = 17$), peri-stimulus time histogram (PSTH) [52] (5.56% of included studies, $n = 1$), and inter-spike interval (ISI) [47] (this study also used FR as feature, 5.56% of included studies, $n = 1$). Spike information was used in all of the included studies. However, Barroso et al. [34], in addition to spike data, analyzed LFP signals and used the power of LFP in several frequency bands (8-19, 20-69, 70-129, 130-199, 200-300 Hz) to decode the movement-related parameters. The features used in included studies are summarized in Table 3. Various decoding schemes were employed in the included studies which can be divided into two categories depending on the discrete/continuous nature of the decoded parameters: A) Discrete decoding, for discriminating several states. Methods such as Gaussian Naïve Bayes [56], PSTH-based classifier [52], rLDA [51], thresholding [48], [52], support vector machine (SVM) [28], [49], expectation maximization (EM) [49], and k-means [49] are examples of these decoders. B) Continuous decoding, for estimating a continuous parameter, such as studies that have continuously reconstructed the trajectory of a joint movement. In this section, different methods such as Wiener Filter [33], [34], [46], [55], Kalman Filter [53], Unscented Kalman Filter [49], [53], linear regression [54], multiple linear regression [29], [50], least-square [32], RNN [34], and support vector regression (SVR) [28] have been employed.

TABLE 5. Achievements of included studies.

Authors	Subject	Achievements
Fitzsimmons et al (2009) [33]	Monkey	The first BCI decoding hindlimb kinematics and EMG from monkey's intracortical neural signals during bipedal forward/backward walking, proposing a switching decoder to increase accuracy.
Song et al (2009) [29]	Rat	The first study to decode rat hindlimb kinematics during walking, demonstrating that rat hindlimb motor cortex is mostly involved in locomotion at high-level parameters, except when corrections are required.
Song et al (2011) [30]	Rat	Rat motor cortex adaptation can be used in BMIs for locomotion and engaging a BMI in the period of cortex adaptation in response to new conditions can alter and stabilize changes in neural activity, which can be used in BMIs.
Manohar et al (2012) [46]	Rat	The first neural control of hindlimb movements to press a pedal in the absence of visual feedback and after spinal cord transection in rats.
Knudsen et al (2012) [47]	Rat	Observed climbing activity of a portion of neurons during pedal pressing by hindlimb, and that temporal scaling of climbing activity only happen when the task requires an estimation of the elapsed time.
Li et al (2014) [48]	Guinea pig	"Motolink" system which directly links the cortex to the spinal cord to detect the neural "intent" of walking and stimulate the spinal cord accordingly.
Alam et al (2014) [31]	Rat	An interface between brain and muscle to decode locomotive state transition and gait cycle to trigger muscle stimulation system.
Schwarz et al (2014) [49]	Monkey	Chronic, wireless, and large-scale neural recording system for recording neural activities of primate cortex during freely performing different tasks and removing the constraining conditions of tethered neural recording during task execution.
Rigosa et al (2015) [28]	Rat	The first study on decoding hindlimb high and low-level kinematic parameters and EMG in the absence of forelimb movement in rats during bipedal walking. High-level movement parameters are well suited for BMI applications due to higher accuracy and robustness.
Ma et al (2015) [50]	Monkey	The first study on hindlimb movement-related neural activity during stand/squat task in primates, which obtained topographical information of motor cortex neurons tuned to different stand/squat phases.
Capogrosso et al (2016) [51]	Monkey	The first brain-spinal cord interface to restore weight-bearing locomotion in primates with spinal cord injury which links cortical dynamics with spatiotemporal neuromodulation therapies and could restore locomotion in unilaterally spinalized monkeys.
Digiovanna et al (2016) [32]	Rat	Motor cortex modulations are related to the volitional engagement and complexity of the task, neuronal responses of rat hindlimb motor cortex in different locomotion tasks are comparable to cats.
Knudsen and Moxon (2017) [52]	Rat	BMI training makes neurons more efficient at encoding information about the task and can reorganize neuronal populations to restore information to levels before spinal cord injury. Adapting the decoder to sensory feedback can better restore function than decoders which only consider information about the intention to move.
Ma et al (2017) [53]	Monkey	Decoding hindlimb EMG and kinematics during the execution of stand/squat task, a voluntary and non-cyclic task. Unscented Kalman filter outperforms standard Kalman filter in decoding kinematics and EMG.
Vouga et al (2017) [54]	Monkey	The first brain-controlled lower limb exoskeleton for rhesus macaques that the decoded positions/velocities are directly mapped onto the exoskeleton's motions, which in turn moves the monkey's legs.
Xing et al (2019) [55]	Monkey	Low-dimensional latent dynamics of motor cortex can well demonstrate kinematics and gait phase during directed locomotion (ladder walking) and autonomous locomotion (treadmill and corridor walking).
Barroso et al (2019) [34]	Rat	Multiunit activities and LFPs of motor cortex can be used to decode kinematics and EMG of hindlimb during locomotion, while EFPs are uninformative. Recurrent neural network can decode the parameters with higher accuracy than linear methods.
Willett et al (2020) [56]	Human	Hand knob area of premotor cortex in humans represents whole body (four limbs) movements by limb-coding and movement-coding. This area can be used for target decoding in intracortical BCIs.

The decoding methods of each study are tabulated in Table 3. Regarding the differences in species of subjects and the tasks in the assessed studies, it is not possible to directly compare the results and the decoding performances.

IV. DISCUSSION

This systematic review summarizes the studies on the use of intracortical signals in decoding the hindlimb movements for BCI systems. To the best of the authors' knowledge, this is the first systematic examination of intracortical BCIs focusing on lower limb movements. 18 studies were included in this study and the subjects, recorded signal, experiment design, decoding method, movement parameters, and major findings of these studies were summarized.

Table 5 summarizes some of the achievements of included studies that are mostly related to this review. These studies have investigated hindlimb neural decoding from different perspectives. However, there are several questions that need to be investigated more deeply. Decoding hindlimb

high-level and low-level movement parameters has been investigated in several studies and it is necessary to develop strategies for using important parameters, that can be accurately decoded, in online systems for patients. Although Barroso et al. [34] investigated the amount of information that can be extracted from MUA, LFP, and EFP of rat motor cortex about locomotion, more studies are needed to investigate this issue in monkeys and humans. The subject's balance while standing or walking, due to its importance for the subject's safety, is also one of the issues that needs to be further investigated in BCI studies. This issue may affect the generalizability of the results obtained by studies on animal models. In addition, during daily life walking, some actions such as obstacle avoidance or change in direction may be necessary which can be investigated more deeply in future studies. Examining the performance of different preprocessing, feature extraction, dimensionality reduction, and decoding methods - as examined in upper limb studies - as well as investigating the performance of deep neural

networks can provide a clearer picture of the amount of information that can be extracted from brain signals about hindlimb movements. Finally, more studies on online BMI systems with human subjects are needed to investigate the performance of these systems on their end-users or cases with similar conditions as them.

The results of this study indicated the appropriate possibility of decoding numerous kinematic and kinetic parameters of hindlimb movements using intracortical signals of the sensorimotor cortex. Some of these parameters were decoded online; by receiving feedback, the subjects managed to better control a BCI system consisting of an exoskeleton [54]. In another study, after spinal cord injury, the subjects could conduct pedal pressing tasks by brain control to receive the reward and control the BCI system [46]. Moreover, online brain control can result in functional plasticity in neuronal networks [14], [46], [75]. Additionally, the use of advanced BCI technology can offer a better understanding of the neural representation of various motor parameters which may improve the efficiency of these systems.

The type of signal used and the temporal stability of the BCI systems are among the significant parameters in the development of these systems. Although other issues such as computational costs and sampling rate, availability of the required technology, and costs are also among the determining features of the signal type, time stability of the signal has been one of the main challenges in the development of these systems. Today, various recording methods have been developed to record brain data and use them in the fabrication of BCI systems. Each of these methods can offer different spatial and temporal resolutions depending on their underlying biological and physical principles. The recording methods vary from single/multi-unit recording techniques, involving microelectrode insertion into the brain, to non-invasive approaches such as EEG, magnetoencephalography (MEG), functional near-infrared spectroscopy (fNIRS), and functional magnetic resonance imaging (fMRI). One of the clinically important factors in the development of neural prostheses is the durability of the recording method. Implanted multi-electrode arrays measure the brain activities at high spatial (single neuron level) and temporal (at spike level) resolutions. Multi-electrode array (MEA) based BCIs have been investigated on rats [29], [62], [76], non-human primates [75], [77], [78], and humans [13], [79], [80]. The degree of freedom presented by such BCIs is continuously growing [81], [82].

This review only addressed BCIs based on intracortical signals which can be categorized into three groups: A) single-unit recording which is the basis for the studies in the field of neuroscience and the majority of the developments in BCIs rely on these signals and the results and knowledge obtained by them. SUA is obtained from the axon output near the recording electrode [83]; except for some cases [84], such information may be degraded or disappeared only several months post electrode implantation

[85], [86]. B) multi-unit activities which originate from neural outputs of several neurons placed in the vicinity of the tip of the implanted electrode. It has been shown that multi-unit activities have higher resistance by passing of time as compared to SUA [85], [87], [88]. C) LFP which is indicative of the firing of several neural cells which are sustained as time passes [85], [89]. The amount of obtainable information about movement from LFPs, compared to spikes, is not well investigated. Some studies have reported lower decoding accuracy of LFPs [24], [87], [90]; while some others indicated higher or similar precision [91], [92]. Although several studies have used LFP signals for decoding various kinematic and kinetic parameters of the forelimb with very good outcomes [93], [94], [95], [96], only one paper [34] has addressed the movement of hindlimb considering the potential of this type of signal. Therefore, decoding of kinematic and kinetic parameters of the hindlimb using LFP signals is one of the topics requiring further investigation as there is no comprehensive answer concerning the applicability of these signals in BCIs. Some studies have revealed that LFP signals can manage to maintain their stability at longer periods as compared with SUA and MUA; thus they are more suitable for long-term applications [62], [95]. Moreover, regarding the smaller frequency range of LFP compared to spike, signal sampling and transfer from the implanted arrays to the BCI signal processing system will be more cost-effective in terms of energy consumption and bandwidth. The lower energy consumption can significantly contribute to the development of portable BCIs. Regarding the higher noise susceptibility of LFP signals compared to spikes, LFP-based BCI systems should employ artifacts and noise elimination techniques [97], [98].

Preprocessing is one of the most important steps in analyzing neural signals. As neural signals are affected by different noises and artifacts, it is very important to preprocess these data before any further analysis. Several preprocessing methods have been developed and are widely used in BCI systems. Signal filtering in the frequency domain is widely used to remove high and low-frequency noise, and powerline artifacts, and to obtain the signal in the desired frequency range (spike/LFP). Other preprocessing methods include re-referencing methods such as common average referencing (CAR) [62], weighted CAR [34], [98], and Laplacian filtering [99], [100] and spatial filtering methods such as common spatial patterns (CSP) [65], [101], and regularized CSP [102], [103]. As EEG, ECoG, and LFP signals are usually contaminated by noise, several denoising methods have been developed such as wavelet denoising [65], [97], and minimum noise estimation [97]. However, as spike signals are less susceptible to noise and artifacts, using denoising methods in BCIs which use MUA or SUA is not as critical as in EEG, ECoG, and LFP-based BCIs. Frequency filtering and thresholding is done to detect multi-unit activities and in order to obtain single-unit activity, spike sorting methods are used. Although studies

that use single or multi-unit activities do not usually use other preprocessing methods, denoising and/or re-referencing methods are needed if high-frequency noise and artifacts are present in the recorded signal. Frequency filtering [28], [29], [30], [31], [32], [33], [34], [46], [47], [48], [49], [50], [51], [52], [53], [55], [56], [58], [54], spike detection [29], [30], [31], [33], [34], [46], [47], [53], [55], [56], and [28], spike sorting [29], [30], [46], [49], [52], [53], [56], coupling reduction between electrodes [28], and weighted common average reference-based artifact rejection [34] were used in the preprocessing stage of the included studies. The impact of using other preprocessing methods in intracortical hindlimb studies can be investigated in future studies.

The goal of feature extraction is to find the informative and low dimensional patterns in the signal which are related to the investigated target variables. Feature extraction is one of the most important steps in BCI, as the informativeness and interpretability of features are very important in making accurate and reliable BCIs. Several groups of features are used in different BCI systems, depending on the signal being used (EEG, MEG, ECoG, LFP, MUA, or SUA), type of BCI (discrete/continuous), and task. Features such as band power [104], time domain features [105], canonical correlation [17], [106], connectivity indices [107], the envelope of signal [62], firing rate (SUA [28], and MUA [34]), peri-stimulus time histogram [52], and inter-spike interval [47] have been shown to be informative and result in accurate BCIs. However, in the included studies focusing on decoding hindlimb movements, firing rate [28], [29], [30], [31], [32], [33], [34], [46], [47], [48], [49], [50], [51], [53], [55], [56], [54], PSTH [52], ISI [47], and the statistical moments (mean, standard deviation, and skewness) of the distribution of the entire population firing rate [28] of the spike data and band power of LFP signals [65] have been used as feature (see Table 3). The previously mentioned feature groups can also be investigated in LFP-based intracortical hindlimb BCIs which can provide useful knowledge about the expected accuracy of BCIs with LFP signals.

The features extracted from neuronal signals are high dimensional, which may lower the accuracy of BCI systems and their interpretability. In addition, the number of data points needed for training the decoding algorithms without overfitting is directly related to the dimension of features. This issue is more critical if non-linear decoding algorithms are used. Thus, several methods were proposed to reduce the dimensionality of features before training the final decoding model. These methods, called dimensionality reduction methods, aim to obtain a set of features with lower dimension, either by transforming features into a different space or by selecting a subset of features, in order to prevent overfitting and lower the computational cost. Several dimensionality reduction methods such as principal component analysis (PCA) [46], [52], [108], mutual information [109], statistical dependency [65], and neighborhood component

analysis [110] have been used in BCI studies. In the included studies, Rigosa et al. [28] selected and analyzed the stable single units, determined by spike shape and ISI distribution, Willet et al. [56], excluded electrodes with less than 1 Hz firing rate from analysis, Knudsen and Moxon [52], used PCA/ICA to obtain a low dimensional representation of neural activities which are mostly related to the task, and Xing et al. [55] used Poisson linear dynamical system to reduce dimensionality and compared it with PCA and predictive subsampling (PSS) presented by [111]. It is worth noting that selecting the best time-window and an optimized combination of narrow and broad frequency bands in LFP, ECoG, and EEG-based BCIs can significantly affect the system performance [109], [112].

The development of BCI systems for hindlimb requires the decoding of parameters related to this limb under different conditions and movement types. Various tasks have been developed to assess decoding accuracy using diverse brain signals and algorithms. Among the hindlimb-related tasks, the treadmill walking task has been the most popular one, followed by walking on a flat surface. However, daily walking includes various movements such as crossing obstacles, walking on different slopes, changing direction to both sides, as well as walking at different paces. Tasks covering these items have been neglected in decoding studies. As an instance, several studies have examined the encoding of hindlimb movement while walking and obstacle avoiding, but the decoding of movements in these tasks has been neglected. Kinetic parameters such as joint torque and endpoint force have not been directly addressed in hindlimb-related studies and only the decoding of EMG of hindlimb muscles has been studied. Decoding parameters such as joint torque can be very useful in the development of hindlimb-related BCIs, leading to BCI systems that allow the user to control the machine/prosthesis better and with higher precision in different walking conditions. In forelimb studies, these parameters have been examined with acceptable decoding results [62], [113]. Concerning hand-related BCIs, some studies were focused on the torque decoding of the wrist joints [114], [115] but this group of kinetic parameters were not considered in hindlimb-related BCIs. Moreover, decoding kinetic and kinematic parameters in tasks requiring higher attention, such as walking on a horizontal ladder, has not been conducted.

There are two general approaches concerning BCIs. The first approach involves accurate decoding of low-level kinetic and kinematic parameters using brain signals and the precise control of machine/prosthesis by these decoded parameters. The aim of the second approach is, however, decoding the high-level movement describing parameters, such as the type of task and the intention to start motion. These high-level parameters are used to determine the details of task execution using already developed algorithms. To achieve BCIs with high accuracy and stability applicable to daily activities, the second approach can be used in the case of

low decoding accuracy of some low-level parameters (such as 3D joint position). Therefore, accurately decoding high-level parameters is important for designing high-performance BCIs.

Concerning hindlimb movement tasks, high-level parameters such as gait phase, intention to step, and type of task (walking under different conditions, moving the hindlimb in a certain direction) have been assessed in some studies [28], [30], [31], [32], [56]. Schwarz et al. [49] reported that all employed discrete decoding methods (EM, K-means, SVM with linear kernel, and SVM with RBF kernel) had good decoding performance classifying the movements performed by subjects. SVM and Gaussian naïve Bayes classifiers were also used to decode gait phase and task in [28] and the intended limb to move and the movement in [56], respectively with high accuracies. Capogrosso et al. [51] have used rLDA classifier to decode gait phase and the movement initiation of the limb affected by unilaterally spinalized monkeys during walking and could efficiently alleviate walking deficits in these subjects. Moreover, in [47] and [52], classifying pedal press duration was done using ISI-based and PSTH-based classifiers respectively and had high and relatively similar true positive rates. However, although promising results have been obtained using deep neural networks in discrete BCIs [116], [117], [118], none of the included studies used these methods for hindlimb high-level movement parameters.

Walking can be regarded as the most important use of the hindlimb, therefore attempts to apply BCI to restore the walking ability can be considered more important than other uses. To this end, the ability to predict the swing onset of one leg during the walking task can be of crucial importance. In a study [51], researchers succeeded in restoring the walking ability of monkeys by accurate estimation of the onset of the movement of one leg, paralyzed by unilateral spinal cord injury, and stimulating the spinal cord with an optimal pattern. However, this type of walking was restricted and differed from the normal gait of a healthy monkey which can be investigated further to develop brain-spinal cord interfaces with higher degrees of freedom.

Studies in this field often considered rat (50% of studies) and monkey (38.88% of studies) subjects. Many preliminary studies have been conducted on the walking of cats considering the coding of walking data in different tasks such as walking on a treadmill, in lateral slopes (to the left or right), and also walking on a treadmill with obstacle. However, no study was found concerning decoding this data of cats' movement. Concerning the frequency, Sprague Dawley, Long Evans, and Lewis breeds were more frequently used in studies on rat subjects, respectively while Wistar rats have not been considered in any of these studies. Rhesus macaque was the only studied monkey breed. Male monkeys (79.17%) and female rats (59.375%) were more considered.

This review is limited to invasive BCI systems which are generally conducted on animal subjects. Except for one article [56], all studies were performed on animal subjects.

Due to the invasive nature of intracortical recordings, the possibility of performing experiments on humans is very limited. The very limited human candidates often have disabilities failing in performing the movements completely and accurately. This is one of the challenges hindering the development of invasive human BCIs for hindlimb control. The BCI development studies are thus performed on animals until reaching the minimum desired accuracy. During the article search, studies related to motor, pre-motor, and sensory-motor cortex were included. However, no mapping was found in these studies concerning the data of different parts of the motor cortex to decode kinetic and kinematic parameters of the hindlimb to make it possible, in a comprehensive investigation, to investigate the possibility of decoding these parameters using signals of various cortical areas and determine the available data applicable to BCI systems in various brain parts such as M1 and pre-motor cortex. Most studies on decoding of hindlimb parameters are limited to M1, which may not be a correct approach. For example, Willet et al. [56] showed that high-level movement parameters can be decoded at high accuracy by recording from the hand knob area in the premotor cortex. These studies can provide a more comprehensive insight into the potentials for achieving accurate and functional BCIs.

As mentioned before, upper limb intracortical BCIs are well advanced and several studies have been conducted to assess the performance of these systems in human subjects with movement disabilities [24], [119]. In comparing the results of upper and lower limb BCIs, several factors can affect the results of comparison and it is important to consider them. Upper limb and hindlimb tasks are different as the main functions of upper limb are doing precise actions such as reaching, grasping, and holding which need accurate control strategies with several degrees of freedom; while the main function of hindlimb is locomotion, which, although complex in nature, is a stereotypic and repetitive movement. So the considerations in one BCI type may not be applicable to the other. Hindlimb BCIs are mainly for people who lost their ability to move and control their feet and need assistance in balance and locomotion. One of the challenges in hindlimb BCIs is that these systems must provide solutions for weight-bearing and balance as well as locomotion, which may make the development of these BCIs for human subjects more complex and limit these studies. Several standard tasks are being used for upper limb BCIs such as center-out and reaching tasks, which makes the results of different studies comparable. Also, in hindlimb BCIs the treadmill walking task is used in several studies, but the conditions of walking (bipedal/quadrupedal, freely walking/robot assisted walking) are different in these studies. Moreover, the assessed movement-related parameters are also different. Because of the aforementioned factors, a direct comparison between the performance of upper and hindlimb BCIs may not represent their progress. Although, in general, as a result of the promising results that upper limb BCIs have obtained in

human subjects, these BCI systems are in more advanced stages than hindlimb ones.

As the main goal of developing BCIs is increasing the quality of life of people with movement disabilities, it is very important to evaluate BCI systems on human subjects to obtain a clear understanding of the shortcomings and potential applications of these systems for patients. To address these issues, several studies have focused on using intracortical BCIs for human subjects with movement disabilities and their results were very promising. These studies focused on decoding the subjects' intention to move their upper limb. Studies have shown that people with tetraplegia can use an intracortical BCI to control computer cursor [84], [120], prosthetic limbs [13], robotic arm [1], FES-based wrist and finger control [12], and FES-based whole arm control [121] with high accuracy. The results of these studies show that the idea of using BCI systems for human subjects is feasible and can significantly increase the quality of life for people with movement disabilities. Some studies used EEG signals to decode gait speed change during treadmill walking [122], hindlimb kinematic parameters during robot-assisted walking [123], and freely walking on a treadmill [124] in human subjects. However, as a result of lower attention to hindlimb intracortical BCIs, to the best of our knowledge, only one study [56] investigated the human hindlimb movement decoding using intracortical signals.

Most studies have considered linear decoding methods. However, studies such as [34] and [53] compared the performance of linear and nonlinear decoding methods and showed that nonlinear models offered higher accuracy, highlighting the significance of nonlinear algorithms in BCI studies. Ma et al. [53] showed that unscented Kalman filter significantly outperformed standard Kalman filter in decoding hindlimb EMG and kinematics in terms of the correlation coefficient. Barrosso et al. [34] also showed that recurrent neural network can decode the hindlimb EMG and kinematics with significantly higher accuracy in terms of variance accounted for (VAF) by MUA, LFP, and EFP. Noteworthy, many reviewed articles did not explicitly report the decoding results, making it difficult to compare the results of different investigations. Furthermore, the wide variety of movement tasks, subjects, and decoded parameters made it practically impossible to compare the results in most cases.

Recently, researchers reported that using deep neural networks (DNN) for decoding can improve decoding accuracy. Studies have used Restricted Boltzmann machine [125], long short-term memory (LSTM) [126], [127], [128], convolutional neural network (CNN) [129], [130], temporal convolutional network (TCN) [131], recurrent neural network (RNN), QuasiRNN [132], multiplicative RNN (MRNN) [133], gated recurrent unit network (GRU) [134], and combination of CNN and LSTM [117], [135] for discrete and continuous movement-related parameters decoding. DNN models need to be trained by large-scale datasets in order to avoid overfitting and obtain high accuracies [136], [137]. In addition

to recording more data, which may not be possible or cost effective in some cases, data augmentation methods can also be employed to address this issue [137], [138], [139].

The emergence and development of wireless recording systems in intracortical signal-based BCI studies of the hindlimb which can offer a comprehensive understanding concerning the role of the brain cortex in various hindlimb tasks [49], [51], [55] is remarkable and noteworthy. It is important for both neuroprosthetic applications and research studies, as the mobility of subject can be considerably improved. Several groups have worked, and currently are working, on developing wireless recording wearable systems [140]. Experiments in conditions closer to daily life with higher complexity than laboratory tests can lead to the development of BCIs with higher generalizability. Thus, the data collected using this recording method can significantly broaden our knowledge and increase the development speed of BCIs for clinical and real-life use.

Previously, researchers have shown that it is possible to control FES system by analyzing the residual activity of muscles or residual limb movements and using the analyzed data to control a set of switches to animate the upper limb [141], [142]. Recently, several studies investigated the possibility of using brain signals to control the FES systems for upper limb movement in paralyzed people. Bouton et al. [12] demonstrated that using intracortical BCI to control FES device on hand, can enable people with tetraplegia to perform daily life upper limb tasks. Ajiboye et al. [121] showed that people with tetraplegia can move their whole arm to perform reach and grasp using FES controlled by intracortical BCI.

Animating hindlimb by BCI-controlled FES system to perform complex movements such as walking can be challenging as several muscles must be stimulated with an appropriate and complex protocol. In addition, the contribution of motor cortex in coordinating hindlimb movements is not well investigated and the rhythmic and stereotypic patterns of hindlimb movements during walking are believed to be produced by central pattern generator (CPG) circuits in spinal cord [143]. Garasimenko et al. [144] showed that cats can walk quadrupedally by epidural electrical stimulation (EES) of spinal cord after complete spinal cord transection. Noteworthy, the stimulation was not triggered by the cat's intention or brain signals in this work. Studies have also shown similar results in rats [6] and human [145] subjects. These studies used externally controlled EES to animate hindlimb. However, several studies used BCI-controlled EES system to reanimate hindlimb after spinal cord transection. Alam et al. [31] used intracortical signals to decode gait phase and stimulate hindlimb muscles of spinalized rats during treadmill forelimb walking. Li et al. [48] used motor cortex spikes to detect the hindlimb movement intention of guinea pigs in order to trigger the spinal cord stimulation system to produce movement. Knudsen and Moxon [52] used motor cortex signals to stimulate the spinal cord to produce

long/short pedal press by hindlimb of completely spinalized rats. Capogrosso et al. [51] developed a BMI-controlled EES system to stimulate the spinal cord of unilaterally spinalized monkeys with an optimized protocol to animate the paralyzed hindlimb during walking on a treadmill and over ground. The results of this study are promising, which suggest that the brain-spinal cord interfaces can be considered as a practical solution for alleviating gait deficits for people with hindlimb movement disabilities.

V. CONCLUSION

In the present work, we systematically reviewed the studies decoding hindlimb movement parameters using intracortical signals and summarized subjects, type and specifications of the recorded signal, task, decoding algorithms, movement parameters, and major findings of included studies. The results of reviewed studies show that it is possible to decode several movement parameters of hindlimb from intracortical signals which can be used in brain-machine interface systems to help people with hindlimb movement disabilities. However, further investigations are required to determine which types of movement parameters and to what extent can be reliably decoded from intracortical signals to be used as commands, because of the small sample pool, lack of clinical trials in real-world conditions as well as laboratory conditions for human subjects and safety challenges.

ABBREVIATIONS

ACDB; Academic Citation Databases; ACSE; Academic Citation Search Engines; ALS: Amyotrophic Lateral Sclerosis; AW: assisted walking; BCI: Brain-computer interface; BMI: brain-machine interface; CAR: common average referencing; SCI: Spinal Cord Injury; CSP: common spatial patterns; CNN: Convolutional Neural Network; CPG: central pattern generator; DNN: deep neural networks; ECoG: Electrocorticography; EEG: Electroencephalography; EES: epidural electrical stimulation; EFP: epidural field potential; EM: expectation maximization; EMG: Electromyography; EX: exoskeleton; fNIRS: functional near-infrared spectroscopy; fMRI: functional magnetic resonance imaging; FR: firing rate; GRU: gated recurrent unit network; ICA: Independent Component Analysis; ISI: inter-spike interval; LFP: local field potentials; LSTM: long short-term memory; M1: Primary motor cortex; MEA: Multi-electrode array; MEG: Magnetoencephalography; MRNN: multiplicative recurrent neural network; MUA: multi-unit activity; PCA: principal component analysis; PSS: Predictive Subsampling; PSTH: peri-stimulus time histogram; PRISMA: Preferred Reporting Items for Systematic Review and Meta-Analyses; RNN: Recurrent neural network; SUA: single-unit activity; SNR: signal-to-noise ratio; SVM: Support vector machine; SVR: support vector regression; TCN: temporal convolutional network; TG: tetraplegia; VAF: variance accounted for.

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