

SYSTEMATIC REVIEW OF THE STATE-OF-THE-ART IN BRAIN-COMPUTER INTERFACE ROBOTIC WALKING IN STROKE

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ABSTRACT: In stroke rehabilitation intelligent robots are required that can interpret walking intention accurately. This systematic review, guided by PRISMA and registered with PROSPERO (CRD42018112252), identifies current state-of-the-art in brain-computer interface (BCI) robotic walking in stroke using electroencephalogram (EEG). A detailed search strategy was applied across the following databases: PubMed (1949-2018), EMBASE (1947-2018), Web of Science (1945-2018), COMPENDEX (1967-2018), CINAHL (1982-2018), SPORTDiscus (1985-2018), ScienceDirect (1997-2018), Cochrane Library (1974-2018). Eligibility for inclusion was considered independently by two reviewers. From a total of 38895 publications, 2 studies comprising N=48 chronic stroke patients met inclusion criteria and rated moderate to strong in quality. Different exoskeleton devices were employed in studies (Ekso™; H2 exoskeleton). No study closed the BCI loop. Longitudinal training was noted to increase classification accuracy. Improved frontoparietal connectivity in the affected side was observed during robotic gait training. BCI robotic gait training after stroke is not reported in the literature to date but shows promise with adequate training for classification.

INTRODUCTION

Many patients with stroke experience a restriction in their mobility. Impairment of gait affects the functional ambulation capacity, balance, walking velocity, cadence, stride length and muscle activation pattern[1].

With conventional rehabilitation and gait training, 22% of all stroke patients do not regain the ability to walk[2]. Intensive gait training with or without body weight support (BWS), while associated with short term gains in walking speed and endurance does not increase the likelihood of walking independently [3]–[6]. Moreover, only patients with stroke who are able to walk benefit from such an intervention [3]–[6]. There is growing effort to increase the efficacy of gait rehabilitation for stroke patients using advanced technical devices. In the last decade, advances in robotic technologies, actuators & sensors, new materials, control algorithms and miniaturization of computers have led to the development of wearable lower-body exoskeleton robotic orthoses. There is also evidence that robotic-

assisted gait training has an additional beneficial effect on functional ambulation outcomes[7], [8] and increases the likelihood of walking independently[9].

Brain-Computer Interface (BCI) technology is also a growing field in stroke rehabilitation with promising results as a therapeutic intervention in upper limb training. [10], [11]. Gains in BCI based gait training in stroke lag behind and there is a critical need for reliable BCIs that interpret user intent directly from brain signals for making context-based decisions with respect to stepping.

EEG recording in stroke, where the pathology is at brain level has been problematic when compared to other neurological pathologies such as spinal cord injury. Uncertainty exists in the literature on the best choice of EEG metric [12]–[14] and in inherent difficulties in identifying the precise role of the motor cortex during phases of the gait cycle due to difficulty capturing low artefact EEG in an ambulatory context and the proximity of both motor cortices to each other [15].

Our overarching goal in this review is to summarize existing studies employing BCI robotic walking in stroke using EEG. Thereby providing a current state-of-the art summary of this research field. Current BCI robotic walking devices, algorithms, signal processing methods and classification methods described in the literature are presented.

MATERIALS AND METHODS

Study identification and selection

A systematic literature search was conducted. As this review is related to engineering and physiotherapy / rehabilitation, an automated search in the following main databases available were undertaken to identify relevant publications: PubMed (1949-2018), EMBASE (1947-2018), Web of Science (1945-2018), COMPENDEX (1967-2018), CINAHL (1982-2018), SPORTDiscus (1985-2018), ScienceDirect (1997-2018), Cochrane Library (1974-2018). The search terms and Boolean

ID	Stroke patients	RGD	EMP	BLC
1	40	Ekso™	FPEC CSE SMI	N
2	8	H2	Neural Decoding	N

Table 1 | Table of studies. In the first row the three selected studies are shown. (1) Calabrò et al., (2) Contreras Vidal et al. 2018. RGD: Robotic gait device; EMP: EEG Measurement Protocol; BLC: BCI loop closure achieved; FPEC: Frontoparietal effective connectivity; CSE: Cortico-spinal excitability; SMI: Sensory-motor integration

operators employed are summarised in figure 1. Only publications in English were considered. The following types of study were included: Randomized control trials, cross-over or quasi randomized control studies, case-control studies, cohort studies, cross-sectional studies, case series and case reports. Reviews, opinion pieces, editorials and conference abstracts were excluded.

Data extraction

Two independent researchers reviewed the literature at title, abstract and paper stages and performed the data extraction and the results were compared afterwards. Disagreements were resolved by broad discussion and observance of the set criteria. Data extraction fields focused on the following topics: Fields relating to achievement of BCI, description of bio-signal capture, description of hardware/software devices employed, description of bio-signal recording, description of processing methodologies employed and description of bio-feedback mechanisms.

Quality assessment

Risk of bias was assessed using the effective public health practice project tool (EPHPP). Two reviewers independently rated the studies under headings of selection bias, study design, con-founders, blinding, data collection methods and withdrawal and drop-outs, a final rating of strong, moderate or weak quality.

RESULTS

The search was completed across the databases in November 2018. Figure 1 summarizes the studies identified from the search and those included at each stage of the review process. A total of 2 studies were identified following full manuscript review that met the inclusion criteria. These were rated by the *EPHPP quality assessment* as moderate to strong in quality. Table 1 provides a summary of the key characteristics of these studies. Results are then synthesized narratively under headings of interest.

Feasibility of decoding walking from brain activity in stroke survivors

Contreras-Vidal et al. (2018)[16] investigated the feasibility of decoding walking from brain activity in stroke survivors during therapy by using a powered exoskeleton integrated with an EEG-based BCI in five chronic stroke patients. Classification accuracies of predicting joint angles improved with multiple training sessions and gait speed, suggesting improved neural representation for gait and the feasibility of designing an EEG-based BCI to monitor brain activity or control a rehabilitative robotic exoskeleton. EEG was recorded using a high-input impedance amplifier (referential input noise < 0.5µVrms @ 1÷20,000 Hz, referential input signal range 150-1000mVPP, input impedance >1GΩ, CMRR > 100 dB, 22bit ADC) of Brain Quick System PLUS (Micromed; Mogliano Veneto, Italy), wired to an EEG cap equipped with 21 Ag tin disk electrodes, positioned according to the international 10-20 system. The cortical activations induced by gait training were identified from EEG recordings by using Low-Resolution Brain Electromagnetic Tomography (LORETA). The brain compartment of the three-shell spherical head model used in LORETA was thereby restricted to the cortical gray matter using a resolution of 7 mm, thus obtaining 2394 voxels. The voxels were collapsed into 7 regions of interest (prefrontal, PF, supplementary motor, SMA, centroparietal, CP, and occipital, O, areas of both hemispheres) determined according to the brain model coded into Talairach space, by using MATLAB. Then, structural equation modeling technique (or path analysis) was employed to measure the effective connectivity (that assesses the causal influence that one brain area, i.e., electrode-group, exerts over another, under the assumption of a given mechanistic model) among the cortical activations induced by gait trainings.

This work builds from a previous publication (not included in this review) outlining a possible roadmap for EEG-based BCIs in lower body robotic exoskeletons using the NeuroRex System [Contreras-Vidal et al. (2013).

The second study identified for inclusion was an RCT by Calabrò et al.[17]. This study with 40 sub-acute and chronic stroke patients employed EEG to evaluate frontoparietal effective connectivity (FPEC) as a metric of neuroplasticity to identify if additional gains were made from Robotic gait training in addition to conventional rehabilitation and overground walking when compared with same duration therapy and overground training alone. The strengthening effect of robotic gait training on FPEC when compared with the control group ($r = 0.601$, $p < 0.001$) was observed. and were the most important factors that correlated with the clinical improvement following robotic gait training.

EEG was recorded in this study using a high-input impedance amplifier (referential input noise $< 0.5 \mu\text{Vrms}$ @ $1\text{--}20,000 \text{ Hz}$) of Brain Quick SystemPLUS (Micromed; Mogliano Veneto, Italy), wired to an EEG cap equipped with 21 Ag tin disk electrodes, positioned according to the international 10-20 system. An electrooculogram (EOG) was also recorded for blinking artefact detection. The recording occurred in the morning (about 11^{am}) and lasted at least 10 min, with the eyes open (fixing a point in front of the patient). The EEG and EOG were sampled at 512 Hz, filtered at 0.3-70 Hz, and referenced to linked earlobes. The cortical activations induced by gait training from the EEG recordings were identified by using Low-Resolution Brain Electromagnetic Tomography (LORETA; LORETA-KEY alpha-software)

DISCUSSION

This systematic review describes the current state of the art in robotic gait training with BCI integration in stroke. Following a scientifically rigorous systematic review identifying over 38,000 potentially relevant publications, only two studies met the criteria for inclusion by describing a clinical population of stroke, having a robotic gait training intervention and having registered EEG signals during gait training in the device. No study was identified that closed the BCI loop in robotic walking after stroke.

Many papers reviewed presented data from healthy norms during robotic gait and identified utility for populations such as stroke. However, these foundational works have not yet translated into the next phase of testing in the clinical population of interest, suggesting barriers to implementation. Inclusion of study participants with physical disability requires interdisciplinary expertise beyond engineering and barriers to EEG in clinical practice have been identified including the length of time needed to mount traditional AgCl EEG electrodes [12] and uncertainty regarding choice of EEG metric [12]–[14]. Advances in EEG hardware, recording electrodes, and software analysis methods may now overcome many of these barriers with dense-array systems with up to 256 electrodes showing improved spatial resolution [18] and newer computational methods for example, using partial least squares (PLS) regression has outperformed traditional EEG methods in capturing behavioral variation in stroke populations [19]. Renewed, interdisciplinary focus is now required in this field.

Of the two studies identified addressing robotic walking and EEG biosignals; data collection and processing were dealt with differently, limiting synthesis and future projections. Agreed standards in EEG capture and processing are required in this field to allow future meta-synthesis.

Contreras-Vidal et al. showed in their publication/s a foundation step towards EEG-based BCI controlled lower-limb rehabilitation using the NeuroRex system after stroke. They identified the feasibility of accurately decoding lower limb movements during robotic gait training after stroke, an important first step and presented a clinical neural interface roadmap for EEG-based BCIs in lower body robotic exoskeletons, identifying requirements that include: a reliable BCI system with an option of shared control between the user and the robotic device; appropriate risk assessment and a better understanding of the neural representation for the action and perception of bipedal locomotion at cortical level. fMRI-EEG.

Calabrò et al. showed utility of EEG as an outcome measure for neuroplasticity, identifying a strengthening in the frontoparietal effective connectivity and demonstrating promise for robotic gait training as an intervention after stroke to driving positive brain plasticity over and above usual physiotherapy and overground gait training.

CONCLUSION

The small number of studies available in robotic gait in stroke and EEG limit conclusions that can be drawn about BCI integration in the future. A lack of standardization around EEG data capture and processing was evident that limited data synthesis. However, the current review revealed encouraging preliminary results in the road to BCI integration in robotic gait training after stroke.

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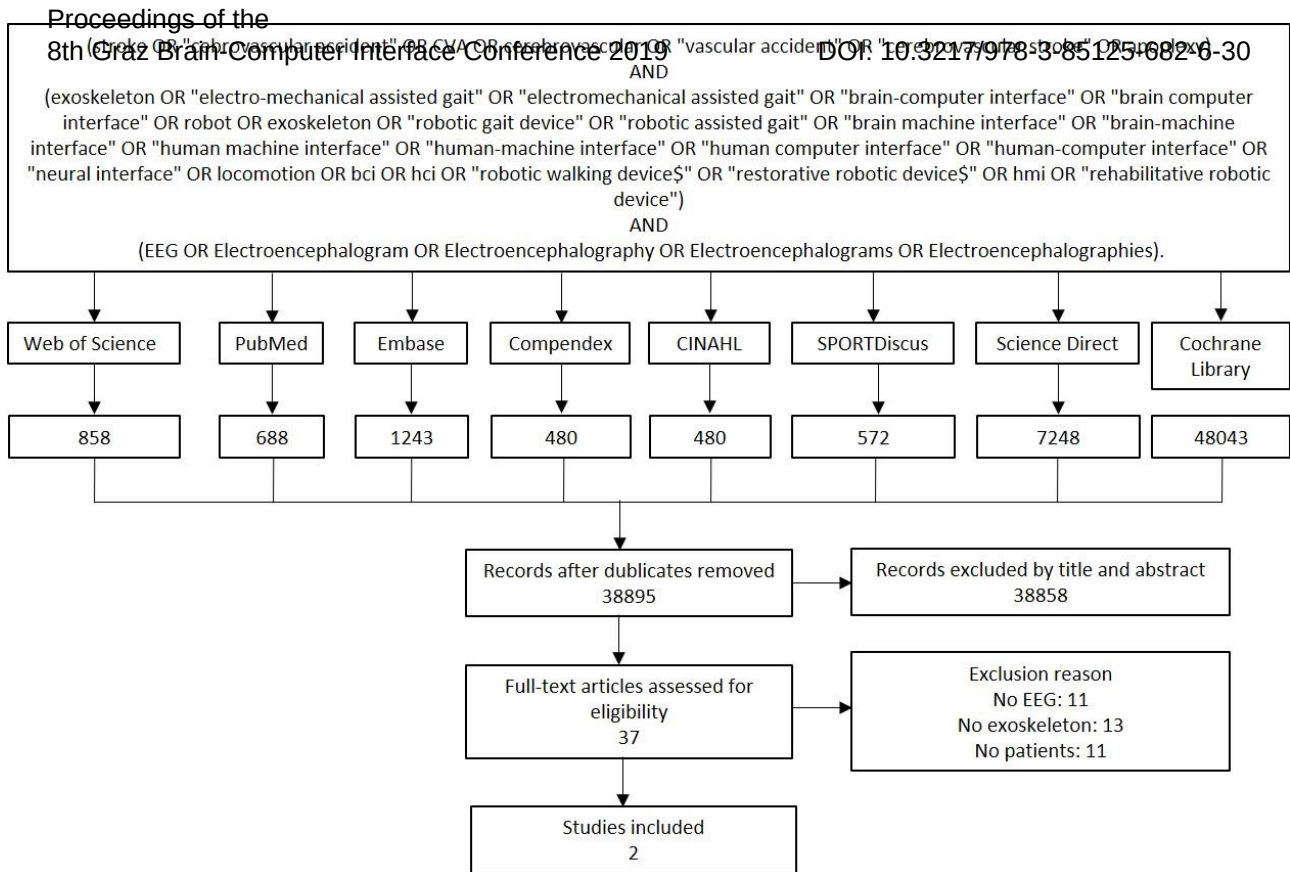


Figure 1 | Scheme of systematic review search process.