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"Brain Computer Interfaces in Post Stroke Rehabilitation: A Machine Learning-based Meta-analysis"

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Abstract

Background: Motor impairments after stroke have debilitating consequences on the quality of life of patients. Brain computer interfaces (BCIs) have been proposed as a novel approach to neurorehabilitation, providing tools for a therapy in which activity-dependent brain plasticity can be induced.

Objective: This paper evaluates the efficacy of BCIs in motor recovery after stroke and examines the conditions under which BCI-based rehabilitation is successful.

Methods: The systematic review compiles the available studies in which BCI systems have been used for upper and lower limb post-stroke rehabilitation. Through a literature search, we identified 532 papers which had the keywords “brain computer interface”, “stroke” and “stroke rehabilitation”, out of which 59 were included in our analysis. The selected studies met all the following criteria: studies including stroke patients with hemiplegia or hemiparesis who undergo upper or lower limb rehabilitation; studies using electroencephalography (EEG) or magnetoencephalography (MEG)-based BCI interventions, regardless of the employed cognitive strategies or the associated feedback modalities; studies in which clinical assessment scores for motor function are reported for group baseline and outcome, regardless of which standardized evaluative measure has been used. Data from these studies was extracted, operationalized and further analysed in a meta-analysis.

Results: The analysis was conducted on group data from a total of 763 patients divided into 65 experimental conditions and 18 control conditions. Although numerous studies reported a moderate to significant improvement of patients’ motor function, we did not find strong evidence that BCI rehabilitation has an additional positive impact on motor rehabilitation compared to other rehabilitation methods.

Conclusion: More studies are needed in order to further assess the efficacy of a BCI-based post-stroke rehabilitation and the benefits of adding this form of therapy to other standardized methods. BCI rehabilitation might be particularly appropriate for patients with no residual movement who would not be eligible for other intervention methods.

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1. Introduction

1.1 Stroke and post-stroke motor rehabilitation

Stroke is a debilitating medical condition that affects approximately 15 million people worldwide on a yearly basis, causing severe motor impairments or paralyses. It occurs as a repercussion of a blockage in the blood supply to the brain or due to a leakage of blood from a brain artery. According to the World Health Organization (WHO) reports, 5 million stroke survivors are permanently disabled. As a consequence, medical treatments and rehabilitative interventions are required in order to maximize the patients' chances of recovery and to minimize the associated risks of the disease.

Rehabilitation is a lengthy and complex process that requires the involvement of medical practitioners, physical therapists and the active participation of patients and their families or caregivers. Due to the fact that numerous variables influence the rehabilitative process, it is considered improper to resume its evaluation to a specific method, and it is generally recommended to provide a description that encapsulates the full characterization of the disability and its particularities, the entire rehabilitative process and its specific goals and the behavioural changes that arise after the rehabilitation (Wade, 2005). The addition of BCI systems to post-stroke rehabilitation is a novel approach and specialists aim to explore the rehabilitative effects of BCI-based methods. However, no standard rehabilitation protocol has been developed. The effectiveness of such treatment methods is still under discussion and it is yet needed to determine what tools and strategies are needed, as well as what patient and illness characteristics are more likely to lead to the implementation of a maximally effective rehabilitation treatment.

Determining the effectiveness of any rehabilitative treatment poses challenges to researchers because of the complexity of factors that need to be taken into consideration. Firstly, the degree of disability, as well as the post-treatment improvement, are difficult to measure because they go beyond the objective data obtained from various assessment measures and involve the patients' subjective evaluation. According to Andrews (1991), a specific score may be experienced differently by different patients or even by the same patient at different points in time. Secondly, the environmental circumstances create variables that affect the rehabilitation outcome and cannot be properly separated from the effects of the treatment. More specifically, the medical personnel and physical therapists don't have access to an accurate representation of the patients' activities outside the rehabilitation centre. Attempting to repeat the movement exercises at home or to incorporate the affected limb in certain daily-life activities (e.g., attempts to pick an object) influence the rehabilitation outcome and these variables cannot be properly accounted for.

Lastly, designing randomized controlled trials to assess the efficacy of a method in motor rehabilitation raises certain specific problems. Establishing an adequate control condition raises ethical concerns due to risk of providing less effective treatment for one group. Additionally, because of the nature of intervention, which requires the patients' active participation, blinding the patients is not only unfeasible most of the time, but also not desirable, allowing pre-existing beliefs to influence the outcome of the treatment (Wade et al., 2010).

The purpose of this paper is to explore the research challenges imposed by the particularities of the disease and to evaluate the efficacy of BCIs in motor recovery after stroke. The literature review provides a comprehensive overview of the available research studies in which BCIs have been used in post stroke rehabilitation by taking into consideration the both patient- and treatment-related details, as well as the outcome of each method. Furthermore, we extracted all relevant patient and treatment data and, after operationalizing it, we conducted a meta-analysis in which we used both linear and multilinear models with the aim to determine which patient and treatment characteristics are good predictors of a significant increase in motor function. The outcomes of BCI-based intervention methods were also evaluated in comparison with the outcomes of the control groups in which other traditional rehabilitative methods have been used.

1.2. BCI-based post-stroke rehabilitation

The field of BCIs has a relatively recent history, as the first experiments involving human participants date from the early seventies. The primary focus in BCI research was the development of a communication system for locked-in patients - e.g., patients suffering from Amyotrophic Lateral Sclerosis - (Vidal, 1973). Concomitant with the advancement of technological devices and with the deepening of knowledge in neuroscience, a new domain of application has gained researchers' interest: the implementation of systems that could restore motor and sensory functions lost as a consequence of a brain trauma. In the context of post-stroke motor recovery, non-invasive BCI systems are used for neurorehabilitation, having the goal to restore motor functions which have been lost after the stroke event. This approach has been proposed as a rehabilitative method due to its potential to induce neural plasticity and to promote recovery through neurofeedback (Grosse-Wentrup et al., 2011).

Motor imagery (MI) serves as a method of volitionally modulating the sensorimotor rhythms (SMR), allowing the operation of a BCI system. The MI paradigm is used with predominance in motor rehabilitation because the intention of carrying out a movement activates the same brain regions as real motion. As a result, both lead to the desynchronization of sensorimotor rhythms (SMR) when motor information is processed and to the SMR synchronization during rest or idle periods (Van Dokkum et al., 2015). By pairing the detection of motor imagery with a response from the BCI system, the patient receives reinforcing feedback that facilitates motor re-education (Remsik et al., 2016). The most commonly met restorative approaches use BCI in conjunction with a robotic device attached to the impaired limb (e.g., exoskeletons, orthoses), with electrical stimulation applied to the impaired limb, with visual and with auditory feedback.

For research in the field of BCI-based post-stroke rehabilitation, the challenges are not only the ones related to the study of rehabilitation, but also the ones specific to the use of a technologically supported form of therapy and the ones related to the target demographic. Patients' psycho-emotional status, as well as their beliefs and expectations related to such systems, should be taken into consideration when evaluating the usability and efficacy of a BCI-based rehabilitation. The novelty of the method can greatly influence the way in which it is perceived by the patients, who might expect it to be more efficient than other rehabilitative methods they are accustomed to (e.g., physical therapy) or might experience anxiety and fear of incompetence. While the former expectation could increase patients' active participation, the latter negatively impacts the performance. The patients' understanding of technology also plays a relevant role in terms of a technologically-based form of rehabilitation. Fear of the BCI system and a low feeling of control over the technological components are shown to negatively impact the performance, ultimately affecting the outcome of the therapy (Jeunet et al., 2016). In their study, Bragoni et al. (2013) show that the motor outcomes of patients who undergo rehabilitation with robotic devices are more affected by anxiety and locus of control than the ones of patients who receive conventional therapy methods. Other factors that influence BCI performance are related to users' cognitive and emotional states (such as mood, motivation, attention), personality, cognitive profile and experience (Jeunet et al., 2016). It should also be taken into consideration that stroke patients are generally form the elderly age category, only 34% of patients being younger than 65 years old (CDC). Studies show that older adults are more likely to refuse the use of assistive technology, manifest more distrust towards it, believe that it is too complex and generally experience anxiety related to the use of such devices and it is recommended to take older adults' perspective and specific needs or belief into consideration when designing a technologically-based rehabilitative treatment (Yusif et al., 2016; Goher et al., 2017).

1.3. Controlled trials

Designing controlled trials with the purpose to evaluate the effects of a BCI-based post stroke rehabilitation in comparison with another rehabilitative method is a challenging, complex process. Researchers are confronted with difficulties in creating true blind patient groups, with implementing a control condition that raises similar expectations as the experimental condition and with comparing the outcomes of the two rehabilitative methods in a satisfactory manner. Additionally, target group characteristics and history biases should be taken into consideration. Through our literature research, we identified 20 controlled trials. From these, 5 use sham-conditions for control groups, 4 use two BCI-based experimental settings and the other 11 evaluate the outcome of a BCI-based intervention in comparison with the outcome of another therapy method (e.g., functional electrical stimulation, passive mechanotherapy). A series of design-related issues should be taken into consideration. Out of all controlled trials, 14 used more than one rehabilitative method, adding physical therapy for either one or for both experimental and control groups. This affects the interpretation of results because the outcome of the rehabilitation cannot be properly attributed to one specific form of therapy, creating difficulties in the examination of the effects of a BCI therapy alone. Double-blind designs were used only in the studies in which sham-interventions were administered to the control group. Only Ramos-Murguialday et al. (2013) investigated whether patients recognized the group allocation. All other studies either used single-blind designs in which either the patients or the motor recovery assessor were blinded in regard to the allocation or did not provide information regarding participant blinding. No mention regarding patients' expectations has been made. Another occurring issue is related to inequalities in the intensity of the treatment received by the patients, one study offering 136 trials per session for the BCI-Manus experimental group and 1040 trials per session for the Manus control group (Ang et al., 2015a). Additionally, less than half of the studies offered follow-up information. The time point for follow-up evaluations ranged between 2 weeks and 6 months, while the recommended time period of evaluating the intervention outcome is between 6 and 24 months after the intervention has finished (Wade et al., 2010).

Selection biases also became apparent. Six studies had a 5 to 10 years difference in the mean age of the participants allocated to the experimental group and the ones allocated to the control group. When designing controlled trials, it is important to create groups of equally aged individuals because older adults have a more limited functional rehabilitation outcome compared to younger individuals (Bindawas et al., 2017). Similarly, there were intergroup differences in the amount of time that has passed since the stroke event. Ono et al. (2014) had a 38.9-month difference between two groups of chronic stroke patients in one study and a 31.5-month difference between one subacute and one chronic group (Ono et al., 2018). In the remaining studies included in our analysis, the differences ranged between 0.1 and 13.9 months. These differences should be taken into consideration particularly when the comparison is between subacute and chronic patients, given the fact that the first months after the stroke are most promising in terms of recovery and also allow the possibility for a natural recovery in motor function (Maulden et al., 2005). Lastly, none of the studies mentioned conducting any qualitative interviews with the patients, the caregivers or the patients' family. Not receiving information about the patients' activities outside the rehabilitation center and not investigating whether the patients attempt to repeat the motor exercises in a home setting can lead to unexplored history biases. Through their control group, Pichiorri et al. (2015) showed that motor imagery alone can lead to improvements in motor function. It would be perhaps relevant to note whether participants explore the therapeutic methods beyond the research setting.

Despite the challenges of designing and conducting these trials, the existing studies provide useful insight into the application of BCI-based rehabilitation. Our approach addresses both the advantages and the limitations of implementing a BCI-based post-stroke rehabilitative treatment and analyses the efficacy of the method using patient- and treatment-data extracted from the available studies. Through the literature review and the implemented linear and multilinear models, we provide a complex analysis of the state of the research and a comprehensive evaluation of the effectiveness of post-stroke rehabilitation using BCI systems in comparison with other traditional methods. The implemented strategies, the characteristics of the experimental groups and the rehabilitation outcomes are detailed and discussed in the results section of our paper.

2. Contribution of cognitive science principles to rehabilitation research

2.1. Need for an interdisciplinary approach

Research in the field of BCI-based post-stroke rehabilitation is intrinsically interdisciplinary, requiring a complex collaboration between professionals from various disciplines. With the purpose of understanding the pathology of stroke, the neurological and physical deficits it accompanies, neurology and neuroscience are two of the necessary fields of study. Additionally, in regard to the operation of BCI systems and the means of signal acquisition, data processing and feedback delivery, extensive knowledge and skills in the fields of computer science and engineering are needed.

Given this thesis, we make the argument that research in this field could greatly benefit from drawing inputs from psychology, recommendation motivated by a series of factors that are related to the psychological effects of stroke on the patients' emotional well-being, to the challenges of implementing a technologically based rehabilitation method and to the aim of elaborating engaging and motivating training environments.

Post-stroke depression. It should be taken into consideration that post-stroke patients oftentimes suffer from great psychological distress due to the newly acquired disability. Numerous studies indicate that almost a third of the stroke survivors experience depression, apathy and insomnia. Hackett et al. (2005) conducted a systematic review on 51 studies, analysing the data of 2865 stroke patients. The authors found that approximately 33% of patients experienced depression, the results being replicated in a more recent cross-sectional analysis conducted by Khedr et al. (2020). Additionally, in the longitudinal analysis conducted by Hackett et al. (2005), it became apparent that the symptoms, although potentially reoccurring in later stages of the rehabilitation, were commonly diminished within the first months after the event. However, as our analysis shows, the timing of the rehabilitation treatment correlates with its outcome, earlier interventions leading to a higher increase in motor function. The post-stroke depression might thus hinder the rehabilitative process, its symptoms (among which, according to the American Psychiatric Association (2013), are: apathy, feelings of hopelessness, diminished interest in various activities and lowered ability to concentrate on certain tasks) preventing the patient from actively engaging in the rehabilitative process. The addition of psychological support to post-stroke rehabilitation might contribute to increasing the efficacy of the rehabilitative treatment by accelerating the alleviation of depressive symptoms that commonly occur in the propitious recovery period.

Receptiveness towards the BCI therapy. As previously mentioned, BCI-based rehabilitation is a novel method that is based on an almost entirely technological process. The small amount of direct interaction with the therapist, as well as the general usage of such systems can give rise to feelings of distrust, fear of incompetence or to computer anxiety, especially in the case of older adults (Jeunet et al., 2016; Bragoni et al., 2013). Operating a motor imagery-based BCI system also requires certain skills that are gained through training and the learning process might prove to be difficult and demotivating for some of the patients (Karácsony et al., 2019). We thus suggest that patients would more easily adapt to the requirements of the system if they are provided with both cognitive and emotional support during the training period.

Contributions to research. As one of the main contributors to the efficacy of the rehabilitative treatment is the patients’ active engagement in the process, it is needed to develop stimulating and motivating BCI training environments. Qualitatively analysing the patients’ experience of undergoing a BCI-based rehabilitation would help researchers better understand the users’ needs and ultimately use the information to design more engaging tasks.

2.2. Paradigms

The motivation behind placing this research within the field of cognitive science is not only due to its highly interdisciplinary character, but also because the principles behind the BCI-based rehabilitation rely on concepts elaborated in various cognitive science paradigms.

Firstly, the BCI-based rehabilitation has its roots in approaches specific for conventional learning therapies, for which the behaviourist paradigm serves as a basis. The principle of operant conditioning, expounded by American psychologist B. F. Skinner (1953), is relevant when designing a rehabilitation treatment using BCI systems. The reinforcement feedback which is consistently offered during the therapy when motor imagery is detected not only positively impacts users’ motivation, but also facilitates motor re-education, as patients learn to associate the motor imagery to the actual movement (Remsik et al., 2016).

Secondly, body agency and embodied interaction are two relevant concepts in the context of the application of a BCI treatment. In this type of intervention, the sense of embodiment is construed from the relation between motor imagery (as internal, conscious cognitive phenomenon) and the associated movement produced by an external device (Alimardani et al., 2016b). An enhanced sense of embodiment is hypothesized to increase users' performance, experience of body control and motivation, reason why immersive VR environments using embodied avatar representations have been proposed as more efficient feedback modalities (Vourvopoulos et al. 2019c). However, more research is needed in order to determine the degree to which the sense of embodiment influences the BCI performance and what systems could better lead to an increased sense of embodiment. Additionally, most studies researching embodiment in BCIs target healthy participants or amputee patients, little studies targeting stroke patients.

3. Methods

3.1. Literature retrieval and selection criteria.

All articles which included the keywords: “brain computer interface” (BCI), “stroke” and “stroke rehabilitation” have been downloaded from the Web of Science database and from the PubMed database. As our selection method flowchart shows (Fig. 1.), from an initial compilation of 532 research papers, all duplicates and studies written in languages other than English were discarded, resulting in a set of 307 studies which have been further screened based on the information provided in the abstract.

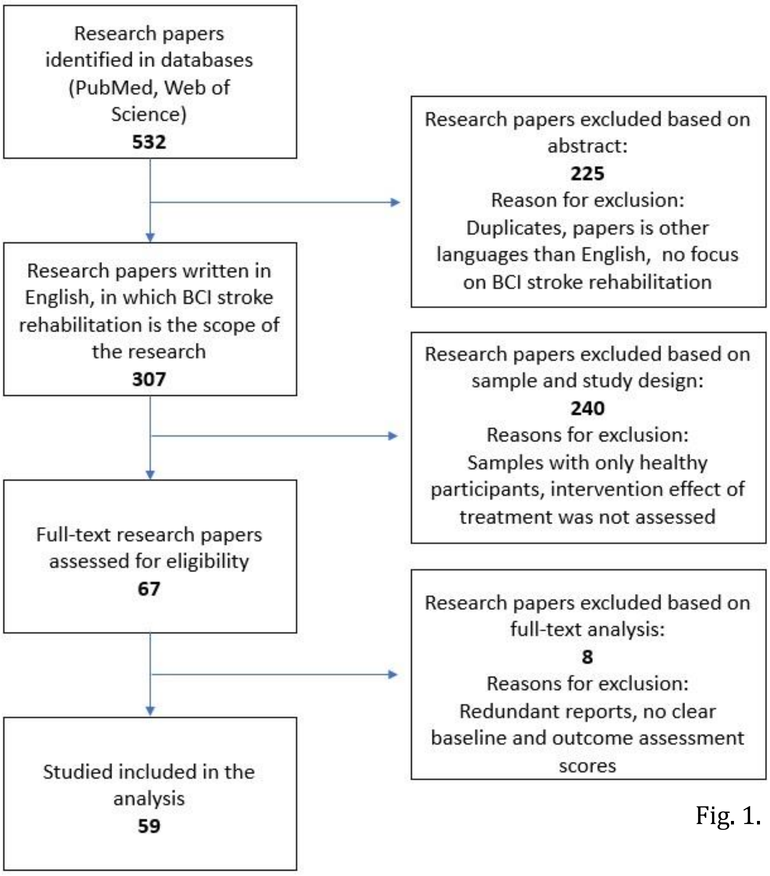

Fig. 1.

With the purpose of conducting the review and meta-analysis, we only kept the studies in which EEG or MEG-bases BCI systems were used for post-stroke upper or lower limb rehabilitation, excluding the studies in which BCI systems were used for rehabilitation after other forms of injury, the ones in which signal acquisition devices other than EEG or MEG were used, the ones in which the systems were only tested on healthy participants and the ones in which the pre- and post-intervention motor scores were not specified. The type of scale used to assess the sensorimotor impairment was not a selection criterion, however we included only the studies in which a standardized evaluative measure was used. For post stroke assessment of motor function, the most commonly used methods are the Fugl-Meyer Assessment (FMA) scale for upper and lower limbs, the Stroke Impairment Assessment Set

(SIAS) and the The Action Research Arm Test (ARAT) for testing the upper limb function. Based on these criteria, we identified 59 research papers that met the requirements given the scope of our analysis. Among these, 14 are case reports, 20 are randomized controlled trials and 25 are single group designs.

3.2. Data processing

Data extraction. For each experimental or control group, we extracted the following information: (1) sample size; (2) patient characteristics (gender, age); (3) stroke details (type: ischemic/haemorrhagic, location: cortical/subcortical/cortico-subcortical, side of impairment: left/right, amount of time that has passed since the stroke); (4) number of drop-outs and reason for drop-out; (5) method of signal acquisition (EEG/MEG); (6) task and feedback method used in the BCI conditions; (7) rehabilitation methods used for control conditions; (8) rehabilitation period and number of sessions; (9) physical therapy details (no/yes + type: conventional therapy, occupational therapy, action-observational therapy); (10) baseline measures; (11) outcome measures. Additional relevant information has been noted (i.e., mentions of fatigue, pain, participants’ motivation and engagement).

Data operationalization. The data was further prepared in order to consistently represent the features as categorical or numerical variables in the same unit of measure. All group-related numerical variables (for the "age" and "time since stroke" categories) are given as group mean.

For the conditions in which BCIs were used for rehabilitation, we identified a number of overlapping categories based on the type of feedback provided by the system: (1) BCI combined with actuated movements (BCI systems used to control a robotic device such as a robotic exoskeleton or a mechanic orthosis); (2) BCI combined with electrical stimulation (BCI systems used to trigger functional electrical stimulation (FES) or neuromuscular electrical stimulation (NMES)); (3) BCI with visual feedback (successful detection of motor imagery is represented on a screen or as a projection); (4) BCI combined with a virtual reality system (the BCI system incorporates an immersive virtual reality environment); (5) BCI with auditory feedback (successful detection of motor imagery is represented through a sound system); (6) BCI combined with a vibrotactile device (BCI system used to control a vibrotactile device such as touch controllers).

Similarly, for the control conditions, we identified the following categories: (1) passive mechanotherapy (physical practice with the help of an exoskeleton or an orthosis); (2) electrical stimulation (FES, NMES); (3) visual representation of the motion or the following sham-conditions: (1) BCI in conjunction with a sham-actuated movement; (2) BCI in conjunction with sham-electrical stimulation; (3) BCI in conjunction with sham-visual feedback. An experimental or control condition can be placed in one or more categories, based on the particularities of the intervention.

Meta-analysis. For the statistical analysis we evaluated the intervention effect at group level. Based on author reports, the rehabilitation outcome for each group was labeled either as “significant improvement” or as “no significant improvement”. For the Fugl-Meyer Assessment (FMA), the most widely used measure to assess the level of impairment after a stroke, the minimal clinically important difference (MCID) is set for an improvement in scores between 4.25 and 7.25 points, with the general consensus that a score of 5.6 is a MCID for upper arm, 4.9 for wrist and hand and 6 for the lower extremity (Page et al., 2012; Hiragami et al., 2019; Pandian et al., 2016). For the Action Research Arm Test (ARAT), which is used to assess the limitations of upper limb movement, the MCID is a 6 point increase in score (Lang et al., 2008). It should be noted, however, that MCID values depend on context, initial deficits and stroke and patient-related variables (Lang et al., 2008). It is also recommended to set different MCID targets for subacute and for chronic stroke patients (Frolov et al., 2017).

Given the above-mentioned aspects and the fact that different assessment methods as well as various modified scales or subscales of these evaluative measures have been used across studies, we chose to categorize the outcome of the studies included in our analysis as it was reported by the authors. Using this categorization, we analyzed the characteristics of different rehabilitative strategies and their relation with the rehabilitation outcome.

Lastly, because the data was given per experimental and control group, individual motor improvement could not be included in the statistical analysis. For this reason, there are cases in which some participants in a sample had a significant improvement in motor function, but the group improvement did not significantly differ post-treatment compared to baseline and the group was therefore classified as having no significant improvement. However, detailed rehabilitation outcomes are discussed in the review section of this paper.

4. Results

The results section is divided into two parts, the first representing the literature review findings and the second consistig of our meta-analysis results. In our literature review, we investigated the implemented BCI-based rehabilitation methods and the respective reported outcomes, as well as the outcomes of the control groups in which other rehabilitative strategies have been used. Our meta-analysis investigates the correlations between patient demographic data (age, gender), stroke details (type of stroke, the amount of time that has passed since the stroke occurred, location of stroke), rehabilitation details (type of feedback offered through the BCI system, number of sessions, physical therapy details) and rehabilitation outcome, as reported by the authors. We further examined whether these factors can predict the rehabilitation outcome by implementing a logistic regression model.

4.1. Literature review

A total of 59 research studies have been included in our analysis. After screening an initial number of 532 paper, we identified 14 case reports, 19 randomized controlled trials and 24 single group designs that met our selection criteria. For a more detailed evaluation of the intervention effect of each rehabilitative method and BCI system, we further grouped them into studies in which only one intervention method is used (i.e., single design studies and case reports) and studies in which multiple BCI-based and traditional methods are implemented and compared (randomized trials).

4.1.1. Single design studies and case reports

For the literature review, we considered 24 single design studies (E) and 14 case reports (CS) in which BCI-based systems were paired with different feedback modalities and used for post-stroke rehabilitation. Electrical stimulation was used in 4 studies, visual feedback in 6 and a virtual reality (VR) system in 2. The majority of studies used more than one feedback modality, automated movement paired with visual feedback being identified in 15 studies, electrical stimulation with visual feedback in 10 and multi-modal systems with automated movement, electrical stimulation and visual feedback were used in 2 studies.

Electrical stimulation. Functional electrical stimulation (FES) is a rehabilitative method that aims to improve motor function by using the application of electrical currents to stimulate the nerves of paretic or plegic muscles in order to facilitate or generate movement (Vafadar et al., 2015). Its efficacy in post stroke rehabilitation has been evaluated in a series of systematic reviews and meta-analyses and researchers reported that early interventions can reduce shoulder subluxation and that, in addition to physical practice, it yields better results than conventional therapy (Ada and Foongchomcheay, 2002). The passive application of electrical stimulation can help modulate the patients' neural activity and promote motor relearning (IJzerman et al., 2009). It is thus hypothesized that rehabilitation with a BCI system that offers electrical stimulation as real-time feedback has the potential to enhance post-stroke motor recovery by combining a neuroplastic with a neuromodulatory approach (Young et al., 2014b).

From the 24 single group design studies identified, three used electrical stimulation as a sole feedback modality (Table 1). McCrimmon et al. (2014) targeted lower limb rehabilitation and reported that all three participants had possible improvements in dorsiflexion. Song et al. (2015), who had 15 participants, reported no improvement in group performance, however, 7 participants had some improvement in motor function, 3 achieving MCID. Ib´an˜ez et al. (2017) found a significant improvement in motor function of the 4 participants included in the study. This therapy method has also been presented in one case study, Mukaino et al. (2014) reporting a significant improvement in the patient's motor function.

BCI + electrical stimulation								
Author	Study design	N	Gender	Mean age	Mean time since stroke	Number of sessions	Physical therapy	Outcome
McCrimmon et al. (2014)	E	3	N/A	67.3	21	3	No	No significant improvement
Song et al. (2014)	E	13	8M/5F	61.9	23.4	15	No	No significant improvement
Ibanez et al. (2015)	E	4	4M	54	48	8	No	Significant improvement
Mukaino et al. (2014)	CS	1	1 M	38	14	10	Yes	Significant improvement

Table 1: Single group design studies and case reports using BCI + electrical stimulation

BCI paired with visual feedback. With the scope of post stroke rehabilitation, there are different methods of pairing a BCI system with visual feedback. The visual feedback can be presented on a screen as a game (e.g., 8-point face game or "hitting the target"-task) when it is offered in conjunction with other feedback modalities such as actuated movements. However, it is also used as a single feedback modality (e.g., a projection of a virtual limb or visually engaging games), having the ability to enhance the users' sense of embodiment (Alimardani et al., 2016a).

Four single group design studies have been administered a BCI treatment with visual feedback (Table 2). Prasad et al. (2010) used a BCI system with an on-screen basketball game and reported that 2 out of 5 participants had a MCID improvement. The participants in the researches of Morone et al. (2015), in which a virtual limb system has been implemented, and of Foong et al. (2019), who used an engaging game provided by the nBETTER system, had significant group improvements. Lioi et al. (2020) conducted a pilot study on 4 stroke patients and used both unimodal EEG-based neurofeedback and bimodal EEG-fMRI neurofeedback to apply the treatment. The researchers offered visual feedback as a puzzle game and reported that 2 participants had an increase in motor function, one reaching the MCID on the FMA scale, 1 had no change and one patient had a decrease in motor function. Among the case reports, Mottaz et al. (2015) and Pichiorri et al. (2017) used a visual feedback system. The former presented the case of one patient who had a significant improvement after receiving visual feedback as an on-screen task, while the latter discussed the cases of two participants who used a virtual limb system, from which one had no change in motor function while the other had a significant improvement.

Lastly, virtual reality was used as an immersive feedback modality in Vourvopoulos et al. (2019a), who reported no significant improvement. The effects of the system were further investigated, and the results presented in a case study by Vourvopoulos et al. (2019b), who used the VR system in conjunction with vibrotactile and auditory feedback and reported a significant increase in the patients' motor function.

BCI + Visual feedback								
Author	Study design	N	Gender	Mean age	Mean Time since stroke	Number of sessions	Physical therapy	Outcome
Prasad et al. (2014)	E	5	4M/1F	52	28	12	No	No significant improvement
Morone et al. (2015)	E	8	6M/2F	60	6	12	No	Significant improvement
Foong et al. (2018)	E	11	6M/5F	55.2	11.1	18	Yes	Significant improvement
Lioi et al. (2020)	E	4	2M/2F	64.25	30	5	No	No significant improvement
Mottaz et al. (2014)	CS	1	1 M	57	40	7	No	Significant improvement
Pichiorri et al. (2017)	CS	1	1 F	77	1	11	Yes	Significant improvement
Pichiorri et al. (2017)	CS	1	1 M	20	12	22	Yes	No significant improvement
BCI + VR								
Vourvopoulos et al. (2019)	E	4	3M/1F	60	105.8	8	No	No significant improvement
Vourvopoulos et al. (2019)	CS	1	1 M	60	10	10	Yes	Significant improvement

Table 2: Single group design studies and case reports using BCI + visual feedback

Exoskeletons and orthoses. The addition of exoskeletons and orthoses to a BCI-based therapy can enhance the neuroplastic rehabilitative effect by providing proprioceptive feedback to the modulations of the sensorimotor rhythms, reinforcing the connection between movement-related brain activity and actual movement (Lopez-Larraz et al., 2018). In our findings, the reported efficacy of such systems varies across studies, no significant improvement being reported in seven case reports and single group design studies, while significant improvement is reported in eight research papers (Table 3).

No significant improvement. In one of the earliest research studies in BCI post-stroke rehabilitation, Buch et al. (2008) had 8 participants with no residual hand movement and reported no improvement for any of the patients. Shindo et al. (2011) had a sample of 8 participants with moderate to severe paresis and reported an improvement of finger function in five and an improvement in arm paresis and a decrease in finger spasticity in two participants. Tung et al. (2015) reported an improvement in seven out of nine participants and a deterioration in one, however the group improvement did not significantly increase. Similarly, Kotov et al. (2017) reported an increase in motor function in some of the participants, although the FMA scores at the end of the rehabilitation treatment did not significantly differ from the baseline scores. The authors also reported that participants with improvements in cognitive parameters also had a higher recovery. Lastly, Norman et al. (2018) had a three phase-design, the BCI rehabilitation beginning with proprioceptive feedback offered by an exoskeleton, continuing with a visual feedback and ultimately consisting of simultaneous visual and proprioceptive feedback. For the Box and Block

Test (BBT), they reported a modest group improvement. However, they noted that patients who achieved BCI control could resume some daily life activities after the treatment.

A BCI system which incorporated actuated movements and visual feedback was used in 5 case studies, out of which Silvoni et al. (2013) and Dzhalagoniya et al. (2018) reported no significant improvement.

Significant improvement. Bundy et al. (2017) reported a 6.2 mean increase on the FMA scale for the 10 participants included in the sample. Kotov et al. (2018) had 7 participants who received multiple courses of treatment over the first year after stroke. The patients have been hospitalized three times and had a significant improvement after each hospitalization.

However, the motor function deteriorated during each break between treatment sessions. The authors also monitored patients' motivation levels and suggested that poor motivation affects the results of the procedure, while the desire to return to pre-stroke levels of functioning was associated with increased rehabilitation effects. The studies of Chowdhury et al. (2018) and Rathee et al. (2019) had similar designs, both providing physical practice with a hand exoskeleton prior to the BCI treatment and both reported a significant difference in the ARAT scores pre-and post-treatment. Sullivan et al. (2017) used only actuated movement as BCI feedback and reported a statistically significant increase in motor function.

From the case reports, Broetz et al. (2010) and Darvishi et al. (2017) reported a significant increase in motor function. The same rehabilitation design was used by

Frolov et al. (2018b), who presented the case study of a patient who had been hospitalized three times and had a significant increase after each hospitalization.

BCI + Actuated Movement + Visual Feedback								
Author	Study design	N	Gender	Mean age	Mean time since stroke	Number of Session	Physical therapy	Outcome
Buch et al. (2008)	E	8	6M/2F	52	23	17.6	No	No significant improvement
Shindo et al. (2011)	E	8	8 M	59	28	14.8	No	No significant improvement
Tung et al. (2015)	E	9	N/A	N/A	N/A	10	No	No significant improvement
Kotov et al. (2017)	E	21	13M/8F	59.1	11	10	No	No significant improvement
Norman et al. (2018)	E	8	8 M	59.5	N/A	12	No	No significant improvement
Bundy et al. (2016)	E	10	N/A	58.6	73.6	N/A	No	Significant improvement
Sullivan et al. (2017)	E	6	3M/3F	57.6	51.5	12	No	Significant improvement
Kotov et al. (2018)	E	7	6M/1F	N/A	N/A	N/A	No	Significant improvement
Chowdhury et al. (2018)	E	4	2M/2F	44.7	7	14	Yes	Significant improvement
Rathee et al. (2018)	E	5	2M/3F	61.6	28.3	5	Yes	Significant improvement
Broetz et al. (2010)	CS	1	1 M	67	14	3	Yes	Significant improvement
Silvoni et al. (2013)	CS	1	1 F	25	84	6	No	No significant improvement

Darvishi et al. (2017)	CS	1	1 M	65	45	10	No	Significant improvement
Dzhalagoniya et al. (2018)	CS	1	1 M	62	10	10	No	No significant improvement
Frolov et al. (2018)	CS	1	1 F	42	16	30	Yes	Significant improvement

Table 3: Single group design studies and case reports using BCI + actuated movement + visual feedback

BCI with electrical stimulation and visual feedback. Another commonly met feedback pairing is between electrical stimulation and visual feedback. According to the reports, the intervention led to a significant improvement in motor function in 6 out of 10 single group design studies and case reports (Table 4). No significant improvement was reported in 2 single group design studies. Two case reports, each including two participants, reported a significant improvement for one out of two patients.

No significant improvement. Qiu et al. (2018) incorporated a virtual limb system as visual feedback and showed on a screen the motion that served as a basis for motor imagery. In this study, 5 out of 10 had an increase on the FMA scale, with only three participants achieving a MCID. Kakui et al. (2018) added physical therapy to the rehabilitative program, however reported similar results, all patients having moderate improvement. Because the intervention was conducted in the early stages of recovery after the stroke event, the authors note that it is unclear whether the improvement is a result of the treatment or a normal part of the natural recovery process.

Significant improvement. Tabernig et al. (2018) and Remsik et al. (2018) reported a significant difference between the mean outcome and baseline scores of their samples. Similarly, Cho et al. (2018), who used a first-person avatar mirroring system to deliver the visual feedback, reported a significant group increase in motor function. From the case studies, Daly et al. (2009), Young et al. (2014a) and Marquez-Chin et al. (2016) used a BCI-based rehabilitation with electrical stimulation and visual feedback and reported that patients had a significant improvement. Cho et al. (2017) and Ortner et al. (2015) used a similar design and presented clinical reports of two participants each, in both cases one participant having an increase in motor function and the other no significant change.

Lastly, Nishimoto et al. (2018) and Takasaki et al. (2019) used BCI systems that incorporate visual feedback, electrical stimulation and a robotic device and both reported significant increases in motor function at group level.

BCI + Electrical Stimulation + Visual Feedback								
Author	Study design	N	Gender	Mean age	Mean time since stroke	Number of sessions	Physical therapy	Outcome
Qiu et al. (2018)	E	10	7M/3F	49.5	37.4	12	No	No significant improvement
Kakui et al. (2018)	E	4	3M/1F	67.4	0.3	3.3	Yes	No significant improvement
Tabernig et al. (2018)	E	8	6M/2F	61.2	38.6	30	No	Significant improvement

Cho et al. (2018)	E	7	5M/2F	58.6	110.4	25	Yes	Significant improvement
Remsik et al. (2018)	E	21	11M/10F	61.6	37.5	15	No	Significant improvement
Daly et al. (2009)	CS	1	1 F	43	10	9	No	Significant improvement
Young et al. (2014)	CS	1	1 M	48	4	12	Yes	Significant improvement
Ortner et al. (2015)	CS	1	1 F	61	2.5	21	No	Significant improvement
Ortner et al. (2015)	CS	1	1 F	40	48	10	No	No significant improvement
Chin et al. (2016)	CS	1	1 M	64	72	40	No	Significant improvement
Cho et al. (2017)	CS	1	1 M	53	11	25	No	Significant improvement
Cho et al. (2017)	CS	1	1 F	54	350	25	No	No significant improvement
BCI + Visual Feedback + Electrical Stimulation + Robotic device								
Nishimoto et al. (2018)	E	26	N/A	50.3	47.3	10	Yes	Significant improvement
Takasaki et al. (2019)	E	8	4M/4F	58.4	29	7	No	Significant improvement

Table 4: Single group design studies and case reports using BCI + electrical stimulation + visual feedback and multi-modal feedback

Overall, out of 24 single group design studies, 13 reported a significant group improvement, while from 18 patients included in case studies, 12 had a significant improvement in motor function. Based on these findings, it can be inferred that BCI-based rehabilitation can yield positive results. However, the data does not provide insight into the rehabilitative efficacy over other traditional methods, therefore an evaluation of randomized controlled trial results is needed.

4. 1. 2. Randomized trials

In our analysis, we included 20 trial studies, out of which 4 had two experimental conditions (Table 5), 5 had a sham-condition for the control group (Table 6) and the remaining 11 administered other rehabilitation methods to patients allocated to control groups (Tables 7-9).

Studies with two experimental conditions. Ono et al. (2014) allocated 6 participants with severe limb paralysis to a BCI-group with somatosensory feedback group and 6 to the BCI with visual feedback group. Both groups received an equal amount of treatment, however participants in the first group underwent therapy once or twice a week for a time period of 4 to 7 months, while participants in the second group received therapy 5 days per week for a month. The authors reported that only 3 participants from the former group had an improvement in finger function, while no changes in the clinical scores of patients of the second group were identified. Ang et al. (2015b) also had two experimental groups receiving an equal amount of BCI treatment in conjunction with a robotic device and visual feedback, out of which one received an additional 20 minutes of transcranial direct current stimulation (tDCS) and the second received 20 minutes of sham-tDCS prior to each BCI intervention. The authors reported a significant improvement for both at the two-week follow-up but not upon completion of treatment, with no intergroup differences identified at any point in time. Kasashima-Shindo et al. (2015) had two experimental groups, out of which one received additional tDCS, and reported significant improvements for both conditions, with no intergroup difference upon completion of treatment. Lastly, Ono et al. (2018) applied an identical BCI treatment to participants in both experimental groups, the difference consisting in the fact that one group received one day of therapy, while participants in the second group alternated between control and experimental conditions for a treatment length of 14 days. In addition, the patients who underwent the two-week treatment also received physiotherapy and occupational therapy. One day of treatment, according to the authors, led to a significant alleviation in muscle spasticity. Moreover, patients in the experimental condition had significant increases in motor function compared to the control condition.

Two experimental groups							
Author	N	Gender	Mean age	Mean months since stroke	Number of sessions	Physical therapy	Outcome
Ang et al. (2015) EG1: BCI + Manus + Visual + tDCS EG2: BCI + Manus + Visual + sham-TDCS	10 9	6M/4F 8M/1F	52.1 56.3	35.3 32.6	10 10	No No	No significant improvement for either upon completion, significant for both at follow-up
Kasashima-Shindo et al. (2015) EG1: BCI + orthosis + visual + tDCS EG2: BCI + orthosis	11 7	6M/2F 4M/2F	53.5 48	46.2 56.4	10 10	Yes Yes	Significant increase in both groups upon completion, tDCS

+ visual							group higher at follow-up
Ono et al. (2014) EG1: BCI + orthosis EG2: BCI + visual feedback	 6 6	 N/A N/A	 56.1 59	 50.1 11.2	 16 16	 No No	 Improvement for the BCI+orthosis group only
Ono et al. (2018) EG1: BCI + exoskeleton (1 day) EG2: BCI + exoskeleton (14 days)	 27 9	 17M/10F 6M/3F	 63.9 64.3	 34.9 3.4	 1 14	 No No	 Significant improvement in both groups

Table 5: Randomized trial studies with two experimental conditions

Controlled studies with sham-conditions. Five studies had a sham-controlled group. Ramos-Murguialday et al. (2013) used a BCI system with a robotic orthosis for the experimental group and with sham-orthosis movements for the control group and reported a significant increase in motor function in patients of the experimental group only. Out of 14 participants in the control group, 8 had a decrease in the FMA scores and the authors reported a significant decrease in the group score for the motor activity log (MAL). Frolov et al. (2017) used a BCI-based rehabilitation in which visual feedback and automated movements were provided for the experimental group and sham-feedback was given to the control group. In addition, both groups underwent the same amount of conventional therapy, massage and neuromuscular electrical stimulation sessions. Participants in both groups had a significant motor improvement. However, the number of patients in the experimental group who achieved MCID was 4.3 on ARAT and 2.3 on FMA higher than in the control condition. Leeb et al. (2016) who used BCI systems with neuromuscular electrical stimulation (NMES) for the experimental group and sham-NMES for the control group reported an increase in motor function in both conditions, significant improvement being reported for the experimental group only. Biasiucci et al. (2018) offered a BCI triggered FES feedback to the experimental group and sham-FES to the control condition. Both groups received intervention and physical therapy in equal amounts. The authors reported a significant improvement in the motor function of patients in the experimental group only. For the control group, they reported a decrease in motor function in 2 patients, no change in 4 and moderate improvements in 7 patients. Lastly, Mrachacz-Kersting et al. (2016) had lower limb rehabilitation as focus of their research and used BCI with electrical stimulation for the experimental group, which had a moderate increase in motor function. For the control condition, they used sham-electrical stimulation and reported a group decrease in motor function, the mean of the FM scores being 26.44 before the intervention and 24.44 afterwards.

Experimental group and sham-condition for control group							
Author	N	Gender	Mean age	Mean months since stroke	Number of sessions	Physical therapy	Outcome
Ramos Murguialday et al. (2015) EG: BCI + orthosis CG: BCI + sham-orthosis	 16 14	 9M/7F 9M/5F	 46.5 49.8	 67.5 66	 17.8 17.8	 Yes Yes	Significant improvement for the experimental group only
Leeb et al. (2015) EG: BCI + electrical stimulation CG: BCI+sham electrical stimulation	 9 9	 N/A N/A	 N/A N/A	 N/A N/A	 10 10	 No No	Significant improvement for the experimental group only
Mrachacz-Kersting et al. (2016) EG: BCI + electrical stimulation CG: BCI + sham electrical stimulation	 13 9	 11M/2F 8M/1F	 46.3 55.2	 15.3 18	 3 3	 No No	Increase for the experimental group, decrease for the patients in the control condition
Frolov et al. (2017) EG: BCI + exoskeleton + visual feedback CG: BCI + sham-exoskeleton	55 19	34M/21F 14M/5F	58 58	8 8	10 10	Yes Yes	Significant improvement in both groups, higher for the experimental group
Biasiucci et al. (2018)							Significant improvement for

EG: BCI+electrical stimulation	14	6M/8F	56.3	39.7	10	No	the experimental group only
CG: BCI+sham electrical stimulation	13	10M/3F	59	33.4	10	No	

Table 6: Randomized controlled trial studies with sham-control condition

Controlled trials with BCI paired with actuated movement and visual feedback. Four studies have implemented a BCI system with automated movement and visual feedback for the experimental group and offered passive mechanotherapy for the control group (Table 7). Varkuti et al. (2013) reported a significant improvement of motor function in both groups, with an average FMA gain of 6.3 points for the control group and 5.6 for the experimental group, indicating that the control group had a slightly higher improvement. Similarly, Ang et al. (2015a) reported a significant increase in the motor function of both groups, participants in the experimental condition gaining 4.5 points on the FMA scale and the ones in the control gaining 6.3 points. It should be noted that participants in the control group had 1040 trials per session, while the ones in the experimental group only 136 trials. Lyukmanov et al. (2019) found that all patients, who underwent 40 minutes of robotic therapy to which physical therapy was added, had a significant improvement on the ARAT and FMA scales, but only the ones in the experimental group had an improvement on gross arm movement, ball grasp and finger pinch grip. Cheng et al. (2020) used a BCI-based soft robotic glove system (SRG) for the experimental group and only SRG for the control group and reported that only the control group had a significant increase in motor function upon the completion of the treatment, but not at follow-up, while the experimental group had a significant increase compared to baseline 6 weeks post-treatment.

Lastly, Ang et al. (2014) had two control conditions. Participants in the BCI group received visual and movement feedback with the use of a haptic knob. Patients included in the first control group received passive mechanotherapy with the haptic knob and had the same number of trials per sessions as the patients in the experimental group, all participants from both groups undergoing 30 min movement therapy after each treatment session. The patients in the second control group received one hour of standard arm therapy and 30 minutes of movement therapy per session. The authors reported that all groups had a significant improvement with no intergroup difference upon the completion of the treatment. However, only the patients in the experimental group and the ones in the control group who received passive mechanotherapy maintained the improvement at follow-up. Wu et al. (2020) also reported a significant improvement for patients in both experimental and control groups, the former receiving a BCI-based therapy with actuated movement and the latter conventional and occupational therapy.

Experimental condition with BCI+actuated movement and visual feedback							
Author	N	Gender	Mean age	Mean months since stroke	Number of sessions	Physical therapy	Outcome
Varkuti et al. (2012) EG: BCI+MIT Manus + visual feedback CG: MIT Manus	6 3	5M/1F 2M/1F	40.9 50.6	11.6 6.8	12 12	No No	Significant improvement for both groups, higher for the experimental group
Ang et al. (2014) EG: BCI + visual feedback + haptic knob CG1: Haptic knob CG2: Standard arm therapy	6 8 7	4M/2F 6M/2F 4M/3F	54 51.1 58	9.5 13.2 15.18	18 18 18	Yes Yes Yes	Significant improvement for all groups, no intergroup difference upon completion
Ang et al. (2014) EG: BCI+MIT Manus + visual feedback CG: MIT Manus	11 15	9M/2F 7M/8F	48.5 53.6	12.7 7.8	12 12	No No	Significant improvement for all groups, no intergroup difference
Wu et al. (2020) EG: BCI + exoskeleton CG:Conventional, occupational therapy	14 11	9M/5F 9M/2F	62.9 64.8	2.1 2	20 20	Yes Yes	Significant improvement in both groups, higher for the experimental group

Cheng et al. (2020) EG: BCI + soft robotic glove + visual feedback	5	3M/2F	62.4	15.8	18	Yes	Significant improvement for the control group upon completion
CG: Soft robotic glove	5	2M/3F	61.4	29.7	18	Yes	

Table 7: Randomized controlled trial studies with BCI+actuated movement

Controlled trials with BCI paired with electrical stimulation. Three studies used a BCI condition in which patients received electrical stimulation as feedback (Table 8). Li et al. (2014) and Jang et al. (2016) explored the differences between BCI-based therapy with electrical stimulation as feedback modality and passive electrical stimulation, while providing conventional therapy to both groups. The former, who used additional visual feedback, reported a significant increase for both groups on FMA and ARAT scales with no intergroup difference upon completion of treatment, while the latter reported a significant motor improvement for participants from both groups, the experimental group having a significantly higher improvement compared to the control group. Kim et al. (2016) followed a similar design, offering BCI-based electrical stimulation, visual and auditory feedback on top of conventional therapy for the experimental group and only conventional therapy for the control group. They reported a significant improvement of motor function for both groups, with significantly higher scores for the experimental group in FMA total, shoulder, wrist scales.

Experimental condition with BCI + Electrical stimulation							
Author	N	Gender	Mean age	Mean months since stroke	Number of sessions	Physical therapy	Outcome
Li et al. (2013) EG: BCI + FES CG: FES	 8 7	 5M/3F 6M/1F	 67 67.1	 2.6 2.7	 8 8	 Yes Yes	Significant improvement for both groups, no intergroup difference upon completion
Kim et al. (2015) EG: BCI + FES + visual and auditory feedback CG: Conventional therapy	 15 15	 6M/9F 6M/9F	 50 59.9	 8.2 7.8	 20 20	 Yes Yes	Significant improvement for all groups, higher for experimental group
Jang et al. (2016) EG: BCI + FES CG: FES	 10 10	 6M/4F 4M/6F	 61.1 61.7	 4.4 4.1	 30 30	 Yes Yes	Significant improvement for all groups, higher for experimental group

Table 8: Randomized controlled trial studies with BCI + electrical stimulation

Controlled trials with BCI + Visual feedback. Lastly, visual feedback has been used as a sole feedback modality in two controlled trials (Table 9). Rayegani et al. (2014) had three intervention groups, all participants receiving occupational therapy: participants from one group (OTNF) received neurofeedback training with visual and auditory feedback presented as a boat race game, the ones in the second group

(OTBF) underwent biofeedback therapy with a puzzle game as visual feedback and participants in the last group received occupational therapy only (OT). Significant improvement in hand function according to JHFT scores was reported for all participants. Additionally, improvement in Brunnstrom stage was reported for 3 participants from OT, 2 from OTNF and one from the OTBF group. Pichiorri et al. (2015) used a BCI-based virtual limb system as well as verbal feedback from the therapist for the experimental group and only motor imagery training for the control group. Both groups received motor, occupational and cognitive therapy and the authors reported a significant increase in both, with a significantly higher improvement for the experimental group.

Experimental condition with BCI + visual feedback							
Author	N	Gender	Mean age	Mean months since stroke	Number of sessions	Physical therapy	Outcome
Rayegani et al. (2014)							
EG: BCI + visual and auditory feedback	10	6M/4F	51	8.5	10	Yes	Significant improvement in hand function for all patients
CG1: Biofeedback	10	5M/5F	53	8.7	10	Yes	
CG2: Occupational therapy	10	6M/4F	54	8	10	Yes	

Pichiorri et al. (2015) EG: BCI + visual feedback	14	N/A	64.1	2.7	12	Yes	Significant improvement for both groups, higher for the experimental group
CG: MI training	14	N/A	59.6	2.5	12	Yes	

Table 9: Randomized controlled trial studies with BCI + visual feedback

4.2. Meta-analysis

For the analysis, we used data from all 59 research papers, having a total number of 763 participants who either received a BCI-based intervention or were part of control groups. 564 patients were allocated to experimental conditions, with a mean age of 55.4 +/- 9.7 years old and a mean of 32.9 +/- 48.1 months since stroke. 199 patients were allocated to control conditions, the participants having a mean age of 57.3 +/- 4.9 years and a mean of 14.08 +/- 16.1 months since the stroke event. Detailed sample information is given in Table 10. Overall, there were 65 experimental conditions and 18 control conditions.

Participants overall N=763	Age (in years)	Gender (M/F)	Impairment side (L/R)	Stroke location (C/S/C-S)	Stroke type (I/H)	Months since stroke
Patients who underwent BCI treatment N=564	55.4 +/-9.7	314 M / 168 F	231 R / 254 L	25 C / 205 S / 68 C-S	187 I / 122 H	32.9 +/-48.1

Patients who were allocated to control groups N=199	57.3 +/- 4.9	113 M / 63 F	94 R / 60 L	25 C / 52 S / 42 C-S	74 I / 40 H	14.08 +/- 16.1

Table 10: Patient data. “Age” and “Time since stroke” are given as mean SD. “Gender” is given in number of male and female participants for each condition; “Impairment side” is given in number of patients with left or right impairment for each condition; “Stroke location” is given as number of patients with cortical, subcortical, cortico-subcortical for each condition; “ Stroke type” is given as number of patients with ischemic and haemorrhagic stroke for each condition. All values represent the data before the imputation procedure.

Representativity of the sample. The fact that the number of male participants (N=427) is almost double compared to that of female participants (N=231) indicates that the sample is not representative for the general population and it highlights a strong research bias. Specialized literature states that women generally experience more stroke events compared to men, finding explained by the fact that stroke has a higher incidence in advanced ages and women have a longer life expectancy (Reeves et al., 2008). This bias should be taken into consideration in the context of stroke rehabilitation due to the fact that findings indicate that men have statistically better chances of recovery compared to women (Niewada et al., 2005). However, before the age of 54, the prevalence is slightly higher for men than for women. The average age for all participants included in our sample is 55.8 years old, slightly smaller than the one of an average stroke patient. A large-scale study with 12.370 participants investigating the age trends of a first-time stroke reported a mean age of 63.9 years old (Oh et al., 2017). Lastly, the majority of patients included in the sample had a subcortical stroke (N=283), while fewer had a cortical stroke (N=59) or a cortico-subcortical stroke (N=130). However, we do not necessarily consider that this is an indicator of selection biases, given the fact that subcortical stroke leads most commonly to motor impairments, while cortical stroke is associated to higher cognitive disruptions such as aphasia, neglect.

4.2.1. Correlations

We conducted Pearson correlations to determine the linear relations between study outcome and patient-related and design-related variables. Permutation tests were conducted over 10.000 iterations to determine the p-value of each correlation.

Correlations between patient characteristics and rehabilitation outcome. Our analysis did not identify any significant correlation between gender or age and rehabilitation outcome. For the gender variable, the data included in our analysis represented the percentage of female or male participants from each study. The amount of time that has passed since the stroke had a significant negative correlation with improvement ($r=-0.27$, $p=0.0$), indicating that earlier interventions have higher chances to result in a positive outcome (Table 11). Research regarding the optimal time for rehabilitation after stroke is inconclusive. Clinical practice has generally recommended an early mobilisation, however, a large scale study has found that early interventions (within 24 hours after the event) can prevent motor recovery, while another randomized controlled trial conducted on a smaller sample correlated an early intervention to a significant improvement (Bernhardt et al., 2015; Chippala and Sharma, 2016). The most effective rehabilitation period is said to be within the first months after the event (Maulden et al., 2005).

Patient characteristics	Percentage of female participants	Age	Time since stroke
Pearson Correlations (r)	0.03	0.08	-0.27
Permutations (p)	0.77	0.45	**0.0***

Table 11: Correlations between patient characteristics and rehabilitation outcome. *p<0.05 statistically significant

In regard to the stroke-related details, none of the stroke-related variables had a significant correlation with the rehabilitation outcome (Table 12.).

Stroke characteristics	Percentage of ischemic stroke patients	Percentage of haemorrhagic stroke patients	Percentage of cortical stroke patients	Percentage of subcortical stroke patients	Percentage of cortico-subcortical stroke patients
Pearson Correlations (r)	0.08	-0.08	0.17	0.22	-0.31
Permutations(p)	0.57	0.58	0.33	0.22	0.08

Table 12: Correlations between stroke characteristics and rehabilitation outcome. The data represents the percentage with which each variable is included in the study. *p<0.05 statistically significant

Correlations between rehabilitative therapies and rehabilitation outcome. Out of all rehabilitative strategies included in the analysis, none of the BCI interventions showed a significant correlation with the outcome (Table 13). The addition of physical therapy to the rehabilitative program, however, had a significant positive correlation with motor improvement (r=0.36 p=0.0), which is in line with clinical recommendations in which the importance of repetitive physical practice is underlined (NIN). Among different physical practice-based rehabilitative strategies, conventional therapy has been found to be of significance (r=0.25, p=0.03) (Table 15). In regard to the control conditions, we identified only one significant correlation with the outcome (Table 14). Sham-electrical stimulation negatively correlated with motor improvement (r = - 0.30, p=0.01), indicating that the sham condition might be potentially harmful for patients.

Rehabilitative strategies experimental groups	BCI + actuator	BCI+ electrical stimulation	BCI + visual feedback	BCI + VR
Pearson Correlations (r)	-0.02	0.06	0.02	-0.06
Permutations (p)	0.84	0.57	0.79	0.74

Table 13: Correlations between rehabilitative therapies and rehabilitation outcome for experimental groups. *p<0.05 statistically significant

Rehabilitative strategies control groups	BCI + sham-actuated movement	BCI + sham-electrical stimulation	Electrical stimulation	Passive Mechanotherapy
Pearson Correlations (r)	-0.01	-0.29	0.18	0.19
Permutations (p)	0.72	**0.01***	0.13	0.07

Table 14: Correlations between rehabilitative therapies and rehabilitation outcome for control groups. *p<0.05 statistically significant

Physical therapy	Addition of any form of physical practice	Occupational therapy	Conventional therapy	Action Observational training
Pearson Correlations (r)	0.38	0.21	0.23	0.12
Permutations (p)	**0.0007***	0.07	**0.02***	0.47

Table 15: Correlations between physical practice therapies and rehabilitation outcome. *p<0.05 statistically significant

The fact that our multiple comparison analysis did not find any significant correlation between any type of BCI-based intervention and an improvement in motor function is an indicator that, beyond the shortcomings of our category-based approach, there is no strong evidence that BCI rehabilitation has a significant positive impact on post-stroke motor recovery. Additionally, the significant correlations between presence of physical therapy, movement therapy as a rehabilitative intervention and improvement in motor function raises questions regarding the efficacy of BCI-based rehabilitation in comparison with other traditional methods.

4.2.2. Logistic regression

As the correlation analysis operates under the assumption that the effects of each variable are independent from one another, it may not provide an accurate representation of the complex interaction between variables. Given the multifaceted nature of the data, a multilinear model is better suited for the analysis.

For this reason, we built a logistic regression model that predicts study outcome from the data which includes demographic and intervention details. The statistical model uses the rehabilitation outcome as a categorical dependant variable (“significant improvement in motor function” and “no significant improvement in motor function”) and it models the probability with which a data instance representing patient-, stroke- or treatment-characteristics belongs to one of the two outcomes.

From the extracted data, all the missing entries have been imputed using the mean of available data for numerical variables and the most frequent category for the categorical variables. For the analysis, data was split into training (80%) and testing data (20%) using a stratified split which guarantees the same distribution of labels in training and test set. For training the logistic regression classifier, the scikit-learn library was used (Pedregosa et al., 2011). The average prediction accuracy over 10.000 train-test splits is 69% with a standard deviation of 16%. Based on the ”significant improvement” to ”no significant improvement” ratio, always predicting the former group would have a 70% accuracy, i.e. our model performs below baseline.

The confusion matrix (Fig.2) shows that the “no significant improvement” class is more often classified as “significant improvement” than as “no significant improvement”. Overall, the model has issues with accurately predicting the correct class. According to the trend of our model’s learning curves (Fig. 3), more data might improve its performance. However, based on the currently available data, the model cannot accurately predict the rehabilitation outcome.

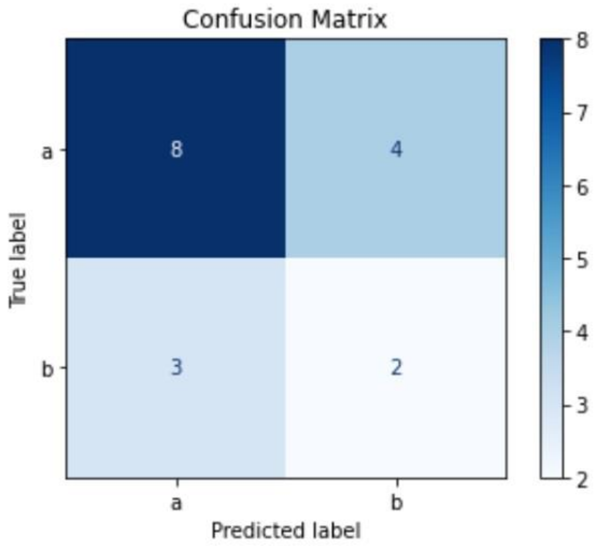

Fig. 2. Confusion matrix

a – “significant improvement of motor function”

b – “no significant improvement of motor function”

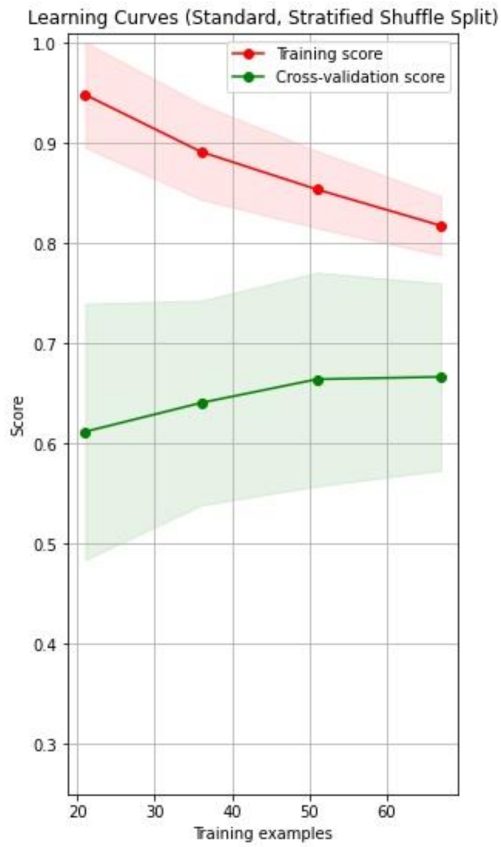

Fig. 3. Learning curve

We also employed the permutation feature importance technique which gives information about how important a specific feature is for the model’s overall accuracy, hence it can be used to evaluate what the predictive power of each data unit is. The values of each feature get permuted in order to break its relationship to the outcome variable and then the changes in the model’s accuracy are reported. In our case, this change in accuracy was averaged over 500 permutations as well as over 50 train-test splits. The computed values show that the features, ”MI training” ”Sham-TDCS”, “BCI + Sham-assisted movement”, “MI training”, “Action observational training”, “Visual feedback”, “BCI+VR”, “BCI + Vibrotactile device”, and “BCI + Audio feedback” related to the rehabilitation treatment, do not change the model’s performance at all (having an importance value of 0.000 or +/- 0.001). The remaining features had a varying importance, none of the ones related to the type of BCI feedback accounting for more than 1% difference in the prediction score. “BCI + FES” is the only BCI treatment-related feature that has a positive importance score of 0.009, while “BCI + actuated movement” has an importance score of -0.007.

Similarly, the features related to the addition of physiotherapy to the rehabilitative protocol and the different types of physiotherapy do not greatly influence the model’s predictive accuracy, also accounting for a maximum of 1% of the prediction score.

Lastly, among the patient and stroke characteristics, all features had an importance below 0.01, with the following exceptions: time since stroke accounts for 1.7%, cortico-subcortical stroke for 2.2% and subcortical stroke for 4.1% of the model’s variance.

Compared to the Pearson correlations, this analysis provides additional information regarding the relationship of each individual variable and the outcome. Since it analyses whether there is a degradation of the model’s performance when one feature is permuted, the fact that the differences in prediction scores generally account for 1%, with the exception of time since stroke, cortico-subcortical and subcortical stroke which account for 1.7%, 2% and 4%, respectively, indicates that the predictor variables are either not entirely independent, since significant correlations were identified, or are not relevant given the outcome. All the scores are represented in Fig.4. The results of the permutation feature importance are, however, limited by the fact that the logistic regression model currently underperforms due to insufficient data. Based on the feature importance scores obtained, we cannot accurately determine which of the features are most relevant when predicting the rehabilitation outcome.

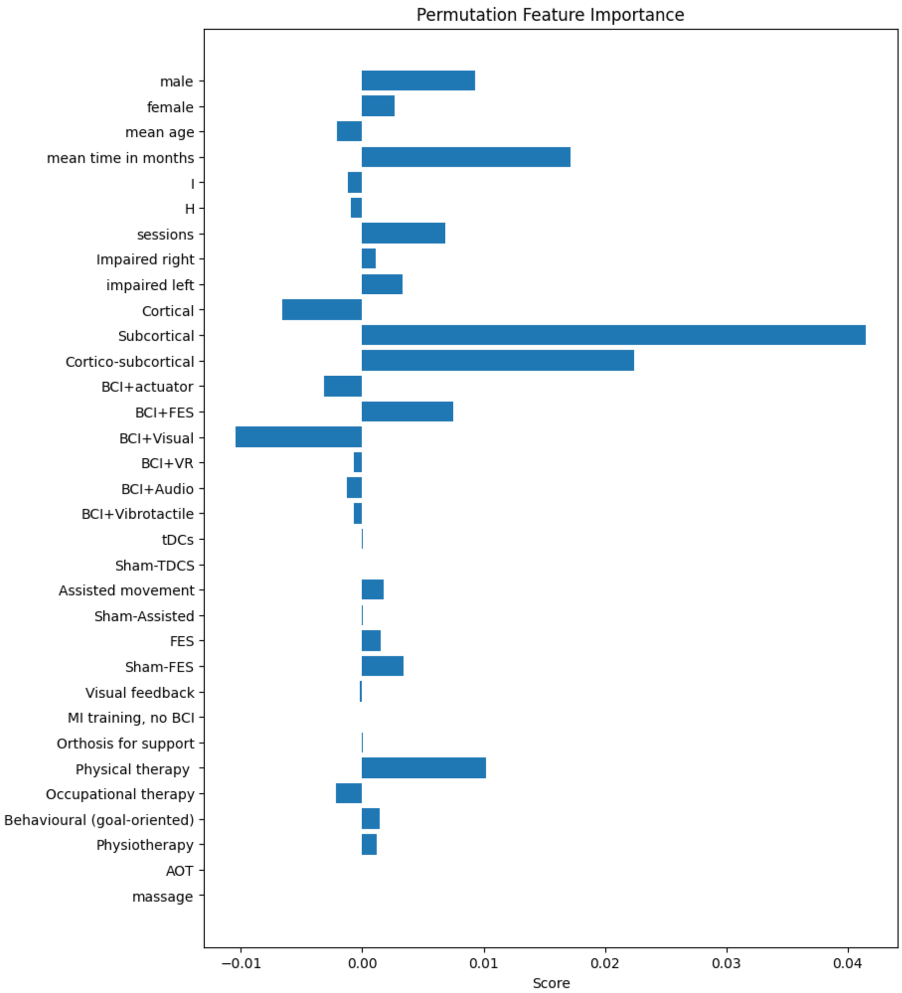

Fig.4. Permutation feature importance scores

In order to further examine how the model performs when only the features with a greater than zero importance are kept, we discarded the ones that had a negative or equal to zero score. In the new analysis, the model's average prediction accuracy over 10.000 train-test splits increased from 69% to 75%, performing over the 70% baseline. The permutation feature importance analysis conducted on the smaller dataset indicates that time since stroke accounts for 2.6% of the model's accuracy, subcortical and cortico-subcortical stroke account for 2.6% and 2%, respectively.

From the treatment-related features, addition of physical therapy to the rehabilitative treatment accounts for 1.9%, BCI+FES for 1.3%, the number of sessions for 0.7% and physiotherapy for 0.5%. From the features of the control conditions, sham-FES accounts for 0.5%, assisted movement for 0.4% and electrical stimulation for 0.1%.

However, as BCI+FES is the only BCI-related feature that has been kept, the model cannot predict the outcome of BCI-based therapies. Eliminating the features that have previously scored as having no difference on the model's predictive power greatly limits the scope of our analysis.

5. Psycho-emotional aspects in BCI-based rehabilitation

Rehabilitation has a subjective component that goes beyond the clinical setting and the objectively pre-defined clinically relevant differences in motor function that occur as the result of the treatment. The outcome is influenced both by the intervention and by the patients' active involvement in the rehabilitative process. BCI systems have the potential to facilitate patients' engagement by providing a motivating training environment (Graimann et al., 2007). Some of the studies we identified also investigate the patients' subjective experience while using the BCI system. From the 20 controlled trials included in our analysis, there were three qualitative reports. By means of questionnaires, Ramos-Murguialday et al. (2013) examined patients' expectations, reporting hopes for improvement and stable positive expectations for all participants. Pichiorri et al. (2015) reported an increased engagement from participants in the experimental BCI group compared to the control group due to the fact that motor imagery training was perceived as less demanding, while motor imagery-based BCI usage was considered more complex. Lastly, Cheng et al. (2020) administered a questionnaire to examine the rehabilitative method’s impact on daily living and the experience of imagined hand movement. They reported that all participants from the experimental group and none from the control group experienced vivid kinesthetic sensations in the paretic fingers. Additionally, three patients from the experimental group reported experiencing these sensations after the trial had ended and all considered that the BCI-rehabilitation had a positive impact on the daily living activities.

From the single group design studies, Prasad et al. (2010) administered the Visual Analog Scale for fatigue and mood (VAS) and reported that all participants had a clinically significant improvement in mood. The patients’ qualitative comments reflected that they were overall pleased with the rehabilitation method, most of them believing that it was beneficial, and one participant reported having the subjective perception of an improvement of motor function in the affected limb. However, most of them confirmed the need for more challenging and interesting game scenarios. Morone et al. (2015) administered the VAS for mood and motivation and the Questionnaire for Current Motivation and reported that the patient sample had a generally good mood and was highly motivated during the rehabilitation program. Along the sessions, there was an increasing trend in mastery confidence, while the fear of incompetence decreased towards the end of the training. They also evaluated the therapists’ experience of administering the rehabilitation and reported 3 commonly identified weaknesses of the procedure: the requirement of specialized skills to operate the system, the need to monitor a possible increase in spasticity and the lack of goal-oriented action feedback. Ibanez et al. (2017) reported that three out of four patients agreed with the intervention. One patient reported that the benefits of the intervention extended in the daily life activities, while two patients strongly disagreed that the rehabilitation was useful in carrying other activities out. Chowdhury et al. (2018) also used the VAS for fatigue, mood and motivation and their results showed no increase in fatigue and an increase in both mood and motivation levels. Vourvopoulos et al. (2019a), who used a VR environment, reported that participants were enthusiastic regarding the system and appreciated the new form of therapy. Lastly, Kotov et al. (2018) was the only research study in which patients' attitude to illness, as well as the patients' reintegration in daily life activities were examined. They reported that a positive attitude, motivation to recover and an appropriate interpretation of illness are the factors that lead to the best rehabilitation outcomes and that facilitate the adaptation to daily life.

6. Adverse effects of BCI-based rehabilitation

In general, studies reported no adverse effects of the rehabilitation methods. Chowdhury et al. (2018) measured participants' fatigue levels and reported no increase due to the intervention. Similarly, Vourvopoulos et al. (2019a), who used a virtual reality system, reported no simulation sickness, fatigue or pain. However, there is a limited number of studies in which adverse effects were reported. Prasad et al. (2010) reported a moderate increase in fatigue levels in 3 out of 5 participants and overall fluctuations of fatigue levels over the time of the intervention. Kotov et al. (2017) applied the Montreal Cognitive Assessment (MoCA) scale and reported that while 5 patients had an improvement in cognitive function, a worsening was observed in 6 patients. Ang et al. (2014) reported that one participant from the experimental condition, who was using a BCI-based intervention with a haptic knob and visual feedback, had to drop out of the treatment due to a mild seizure that occurred a couple of hours after the intervention. Ang et al. (2015a) reported that one participant from the control condition had to withdraw due to pain after using the MIT Manus robot. Bundy et al. (2017) had one participant drop out due to poor orthosis fit. Lastly, Frolov et al. (2017) reported multiple mentions of fatigue and headache. Results from participants in sham control conditions include cases in which participants had a decrease in motor function, indicating that sham conditions might affect patients' motor recovery.

7. Summary

Our review and meta-analysis included 59 research papers and a sample of 763 patients, out of which 564 received a BCI-based rehabilitation treatment, while 199 were allocated to control groups. In regard to single group design studies and case reports, BCI paired with electrical stimulation was reported to have a significant improvement on the group's motor function in 50% of the cases, BCI paired with electrical stimulation and visual feedback in 66% of the cases and BCI paired with electrical stimulation, visual feedback and actuated movement in 100% of the cases. A MCID was reported in 57% of the studies in which only visual feedback was used, while only 2 out of 5 patients who used a VR system had a significant difference in motor function. Lastly, 53% of the single group design studies and case reports in which a BCI system was used in conjunction with visual feedback and actuated movement led to a substantial rehabilitative result.

When comparing the efficacy of BCI-based treatment with other rehabilitative methods by taking into consideration the results of randomized controlled trials, it is apparent that a significant improvement was reported for the majority of the groups, regardless of the method of intervention. From 5 groups in which participants in the experimental condition received BCI treatment with visual and actuated movement and the ones in the control condition underwent passive mechanotherapy, 50% reported significant increases in both groups, with a higher increase in motor function for the experimental group, 25% revealed a significant increase in both groups with no intergroup difference and 25% reported a significant increase for the control group only. Two groups compared a BCI-based intervention paired with electrical stimulation to passive electrical stimulation, both reporting a significant improvement for both groups, one with a higher improvement for the experimental group and the other with no intergroup difference (Jang et al., 2016; Li et al., 2014). Two studies evaluated the differences in improvement of motor function between patients who received a BCI-based treatment and patients who received physical therapy only. In one study, the experimental group received electrical stimulation as feedback and it was reported to have a higher increase in motor function, although both groups had a significant difference in scores (Kim et al., 2016). The second used a BCI system with actuated movement for patients in the experimental group and reported reported a significant increase in both groups, with higher scores for the experimental group. (Wu et al., 2020). Lastly, two studies used a BCI system paired with visual feedback for the experimental group. One administered only motor imagery training for the control condition and reported a significant increase in motor function for both, with higher improvements for the experimental group (Pichiorri et al., 2015). The second had three conditions, one control group receiving biofeedback and the other occupational therapy only and reported a significant improvement in the hand function of all patients (Rayegani et al., 2014). 80% the randomized controlled trials in which a sham-condition was used as an intervention for the control group reported a significant improvement in the experimental group only, regardless of the type of feedback offered through the BCI system. By evaluating the outcomes of the studies in which two experimental conditions were used, it becomes apparent that the application of tDCS did not influence the outcome measured upon completion of treatment, however, the groups that received it had higher scores at follow-up. Additionally, Ono et al. (2014) demonstrated an increase in motor function in the group that received proprioceptive feedback, but not in the one who received visual feedback. Lastly, Ono et al. (2018) had two groups, from which one received 14 days of therapy, while the other only one day and reported a significant improvement in both. Overall, out of 38 conditions in which physical therapy was provided, 89% were reported to have had a significant improvement.

Our meta-analysis results reveal a significant correlation between the addition of physical therapy to the rehabilitative treatment and improvement in motor function. No therapy method other than conventional therapy correlated with an improvement. The fact that our multiple comparisons did not lead to any significant result regarding the correlation between different BCI strategies and outcome indicates that the efficacy of these methods cannot be confirmed. Additionally, the sham-electrical stimulation condition has led to the decrease in motor function in some of the participants allocated to control groups, aspect which should be taken into consideration in future studies.

Generally, no significant adverse effects have been reported for the experimental groups, indicating that a BCI-based post stroke rehabilitation is safe to be administered to patients.

8. Related literature

A number of reviews and meta-analyses in regard to the use of BCI systems in post-stroke rehabilitation have been published. Frolov et al. (2018a) elaborated on post-stroke rehabilitation in which robotic devices, such as exoskeletons and orthoses, are used. They evaluated the use of such systems both in passive and BCI-based rehabilitation settings and concluded that both strategies can be effective, the improvement heavily relying on the patients' active involvement. Passive robot therapy, compared to a BCI-based strategy, can be perceived as unnatural by patients. The authors suggested that a goal-oriented movement linked to the patient's intent to perform it might yield better rehabilitative results. Monge-Pereira et al. (2017) conducted a systematic review of 13 articles in order to assess the intervention effects of BCI-based upper limb rehabilitation and concluded that BCI-based post stroke interventions might be beneficial for the improvement of motor function. However, they indicated that, based on their findings, BCI-based treatment added to physical practice might lead to better rehabilitation outcomes than BCI therapy alone. Cervera et al. (2018) conducted a meta-analysis on the results of 9 clinical trials in which BCI systems were used for upper limb rehabilitation and reported that BCI-based rehabilitation can lead to higher motor scores compared to other rehabilitative methods.

Bai et al. (2020) conducted a systematic review on 33 studies and a meta-analysis on 12 studies using BCI systems for upper limb rehabilitation. The subgroup analyses are in line with our findings, although the authors did not differentiate between the types of intervention administered to the control groups. The authors indicated that BCI used in conjunction with electrical stimulation is more effective that other types of feedback, an aspect which was also apparent in our analysis. From our dataset only two out of eleven studies in which this type of system was used reported no improvement in motor function. Additionally, their analysis showed that the interventions with BCI systems paired with visual feedback and the ones paired with automated movements did not have significantly different effects compared to the control interventions. Our review also reveals the fact that all randomized controlled trials reported significant improvements for both experimental and control groups. As opposed to selecting only randomized controlled trials based on a quality assessment, we used for our analysis all studies in which BCI-based systems were used for post stroke rehabilitation of upper and lower limbs, including the single group design studies and case reports. Additionally, we took into consideration the fact that multiple feedback modalities have been used within one BCI system and we also evaluated the clinical outcomes of all different control conditions.

Lastly, Bai et al. (2020) conclude that post-stroke hemiparetic upper extremity can be improved through BCI therapy, whose effects are significant and immediate. Our findings indicate that BCI therapy can be effective in enhancing patients' motor function. However, we did not find strong evidence to suggest that it is more effective than other rehabilitative
strategies.

9. Limitations

The available data is insufficient to properly evaluate the efficacy of BCI systems in poststroke rehabilitation or to evaluate the patient characteristics that might influence the outcome of the procedure. The conducted research is affected by the fact that not all necessary data for the analysis is disclosed. A few recurrent problems related to the reporting of results have been identified: (1) inconsistencies between the information included in the article and the information given in the supplementary material; (2) inconsistencies between the information given within one supplementary material; (3) no clear statement regarding whether or not recently published studies are a continuation of an earlier research, thus sharing a partially common sample; (4) no clear statement regarding case studies and whether or not the data of the patient was also analysed as part of a larger sample. Due to the fact that participant details are not given, it is not possible to be certain that one participant has not been included in the analysis twice, once as part of an experimental group and a second time as a case study or whether there is overlap between the samples of different studies.

Another limitation of this research is the fact that, without discarding most of the studies, every approach to evaluating and categorizing the results is faulty. Because different assessment scales are used, there is no method of properly comparing the outcomes across all studies. In case a duplicate has been included in our sample, the results of our analysis should not be affected.

10. Discussion

Post-stroke rehabilitation, as stated, is a complex process that requires the active involvement of both health specialists and patients. Determining whether a rehabilitative strategy leads to significant improvements is not a trivial endeavour due to the difficulty in establishing a minimal clinically important difference, partly because the patients' subjective experience plays a significant role in how the disability and the outcome of the therapy are experienced. When conducting research in the field of BCI-based post-stroke rehabilitation, it is needed to take into consideration a series of specific factors. Firstly, the novelty of the method can greatly influence patients' expectations and beliefs regarding the effectiveness of the treatment. The advanced age of most post-stroke patients plays a role in their acceptance of a technologically-based rehabilitation method and performance affecting factors, such as fear or incompetence, computer anxiety or distrust in the system can hinder the rehabilitation process. We recommend that future research also takes into consideration the patients' subjective experience while using a BCI system by taking factors such as motivation and expectations into consideration, besides using standardized questionnaires to measure fatigue and pain levels. Additionally, given the fact that the recovery process does not end when the rehabilitative intervention does, it would be recommended to include follow-up sessions that are not limited to the evaluation of the motor function, but also inquire whether, posttreatment, patients experience any changes in the way the affected limb and its movements are perceived, if they further experience kinaesthetic sensations and if they are more inclined to include the affected limb in daily activities.

The effectiveness of a BCI-based treatment, compared to other rehabilitation methods, cannot be accurately inferred from the conducted controlled trials for a number of reasons. Firstly, in more than half of the published studies, BCI-therapy is not investigated as a sole method, but as an add-on to usual care, which includes movement therapy. It is hence difficult to attribute the rehabilitation outcome to one form of therapy or another. Secondly, selection and history biases and inequalities in the intensity of the treatment affect the interpretation of results. Another aspect that should be taken into consideration when designing randomized controlled trials is that sham-conditions have contributed to the decrease in the motor function in some of the patients allocated to control groups. Lastly, in order to create a suitable setting for comparing different rehabilitation methods, it is recommended to apply an equally intensive intervention to participants from both groups. Based on patient reports, it is apparent that BCI-based interventions might benefit from the development of more engaging game scenarios and feedback modalities that have the potential to increase the patients' motivation and attention, while positive reinforcement and continuous guidance from therapists might help reduce the system-related anxiety.

By taking all studies into consideration, it can be stated that a BCI-based rehabilitation has the potential to yield positive results and that it generally has positive outcomes when paired with physical therapy. However, our meta-analysis results did not show any significant correlations between BCI-based interventions and significant increase in motor function. Therefore, there is currently not enough evidence to prove the efficacy of BCI-based poststroke rehabilitation over other standard intervention methods.

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Zusammenfassung

Hintergrund: Motorische Beeinträchtigungen nach Schlaganfällen haben negative Folgen für die Lebensqualität der Patienten. Brain Computer Interfaces (BCIs) wurden als neuartiger Ansatz zur Neurorehabilitation vorgeschlagen, der Werkzeuge für eine Therapie bereitstellt, mit der eine aktivitätsabhängige Plastizität des Gehirns induziert werden kann.

Ziel: In der vorliegenden Arbeit wird die Wirksamkeit von BCIs im Falle einer Widerherstellung der motorischen Funktionen nach einem Schlaganfall bewertet. Ebenfalls werden die Bedingungen untersucht, unter denen eine BCI-basierte Rehabilitation erfolgreich ist.

Methoden: Die systematische Übersichtsarbeit trägt die vorhanden Studien zusammen, in denen BCI-Systeme für die Rehabilitation der oberen und unteren Gliedmaßen nach einem Schlaganfall verwendet worden sind. Durch die Literaturrecherche wurden 532 wissenschaftliche Publikationen, welche die Schlüsselwörter "Gehirn-Computer-Schnittstelle", "Schlaganfall" und "Schlaganfall-Rehabilitation" nutzen, identifiziert; 59 davon sind in die von uns unternommene Analyse einbezogen worden. Die ausgewählten Studien unterliegen den folgenden Kriterien: Studien über Schlaganfallpatienten mit Hemiplegie oder Hemiparese, die sich einer Rehabilitation der oberen oder unteren Gliedmaßen unterziehen; Studien, die auf Elektroenzephalographie (EEG) oder Magnetoenzephalographie (MEG) -basierten BCI-Interventionen aufbauen, unabhängig von den verwendeten kognitiven Strategien oder den damit verbundenen Feedbackmodalitäten; Studien, in denen klinische Bewertungsergebnisse bezüglich der motorischen Funktion für die Ausgangswerte und das Ergebnis im Falle einer Gruppe angegeben werden, unabhängig von den verwendeten standardisierten Bewertungsmaßnahmen. Daten aus diesen Studien wurden extrahiert, operationalisiert und in einer Metaanalyse weiter analysiert.

Ergebnisse: Die Analyse wurde mit Gruppendaten von insgesamt 763 Patienten durchgeführt, die in 65 Versuchs- und 18 Kontrollgruppen unterteilt waren. Obwohl zahlreiche Studien eine moderate bis signifikante Verbesserung der motorischen Funktion der Patienten berichteten, fanden wir keine eindeutigen Hinweise, dass die BCI-Rehabilitation im Vergleich zu anderen Rehabilitationsmethoden einen zusätzlichen positiven Einfluss auf die motorische Rehabilitation hat.

Schlussfolgerung: Um die Wirksamkeit einer BCI-basierten Rehabilitation nach einem Schlaganfall und die Vorteile der Ergänzung standatisierter Methoden durch diese Therapieform besser einzuschätzen zu können, sind weitere Studien erforderlich. Die BCI-Rehabilitation kann möglicherweise besonders für Patienten, die keine residuale Bewegung aufweisen und für andere Interventionsmethoden nicht in Frage kommen, geeignet sein.