Efficacy of Brain–Computer Interface and the Impact of Its Design Characteristics on Poststroke Upper-limb Rehabilitation: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Abstract

Background. A number of recent randomized controlled trials reported the efficacy of brain–computer interface (BCI) for upper-limb stroke rehabilitation compared with other therapies. Despite the encouraging results reported, there is a significant variance in the reported outcomes. This paper aims to investigate the effectiveness of different BCI designs on poststroke upper-limb rehabilitation. *Methods.* The effect sizes of pooled and individual studies were assessed by computing Hedge's g values with a 95% confidence interval. Subgroup analyses were also performed to examine the impact of different BCI designs on the treatment effect. *Results.* The study included 12 clinical trials involving 298 patients. The analysis showed that the BCI yielded significant superior short-term and long-term efficacy in improving the upper-limb motor function compared to the control therapies (Hedge's $g = 0.73$ and 0.33, respectively). Based on our subgroup analyses, the BCI studies that used the intention of movement had a higher effect size compared to those used motor imagery (Hedge's $g = 1.21$ and 0.55, respectively). The BCI studies using band power features had a significantly higher effect size than those using filter bank common spatial patterns features (Hedge's $g = 1.25$ and -0.23, respectively). Finally, the studies that used functional electrical stimulation as the BCI feedback had the highest effect size compared to other devices (Hedge's $g = 1.2$). *Conclusion.* This meta-analysis confirmed the effectiveness of BCI for upper-limb rehabilitation. Our findings support the use of band power features, the intention of movement, and the functional electrical stimulation in future BCI designs for poststroke upper-limb rehabilitation.

Keywords

Introduction

As a novel rehabilitation method, BCI has attracted a lot of attention. A BCI records, analyzes, and decodes brain signals and translates them into commands for communication and control.[1,2] The BCI system for stroke rehabilitation usually consists of 6 stages, as shown in Figure 1:

1. *Signal acquisition*: A number of modalities for acquisition of brain signals are suitable for the BCI in stroke rehabilitation, namely electroencephalography (EEG), functional near-infrared spectroscopy (fNIRS), and magnetoencephalography (MEG). Due to its lower cost, higher temporal resolution, and portability, EEG is the most commonly used modality in BCI-based stroke rehabilitation.[3]

2. *Mental practice*: In the motor imagery (MI)-based BCI studies, the patients are instructed to imagine moving the impaired hand without any physical movements,

whereas in the intention of the movement (IM)-based BCI studies, the patients attempt to perform physical movement of the impaired hand if possible. The MI or IM produces brain waves, called movement-related cortical potentials (MRCPs) and event-related desynchronization/

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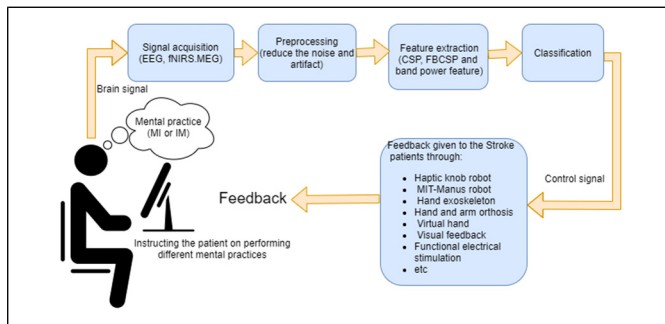[3]School of Computer Science and Engineering, Nanyang Technological University, Singapore.
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Figure 1. Components of brain–computer interface commonly used for upper-limb stroke rehabilitation.
Abbreviations: CSP, common spatial patterns; EEG, electroencephalography; FBCSP, filter bank common spatial patterns; fNIRS, functional near-infrared spectroscopy; IM, intention of movement; MI, motor imagery; MEG, magnetoencephalography.

synchronization (ERD/ERS).[4,5] MRCP and ERD/ERS are distinct movement-related brain patterns. MRCP is characterized as slow changes of the brain signals in the time domain. ERD and ERS are, respectively, described as a suppression and an enhancement in the power of the sensorimotor rhythms. For example, the power of beta rhythm (13-30 Hz) recorded over the sensorimotor regions has been shown to decrease before the motor task, reaches its minimum during the movement execution (ERD), and then recovers sharply after the end of the motor task (ERS).[6] In the application of upper-limb stroke rehabilitation, the BCI is used to detect either MRCP or ERD\ERS in brain signals when the patient performs the relevant mental practice.

3. *Preprocessing*: The recorded brain signals can be contaminated with artifacts caused by blinking, muscle activity, and other sources of noise. In the preprocessing stage, different spectral, temporal, and spatial algorithms are applied on the measured brain signals to reduce these artifacts. Among different preprocessing algorithms, the threshold-based artifact rejection, and 8 to 30 Hz band-pass filtering have been widely used in many BCI-based stroke rehabilitation studies.[7]

4. *Feature extraction*: In this step, to detect movement-related brain patterns, a set of informative, nonredundant, and distinctive characteristics, named features are extracted from the preprocessed brain signals. The previous BCI-based stroke rehabilitation studies have often used one of the following 3 types of features, namely, common spatial patterns (CSP) features,[8] filter bank CSP (FBCSP) features,[9,10] and band power features.[11–13] CSP is a feature extraction algorithm that assigns different weights to different EEG channels, such that the weighted sum of the powers of brain signals is maximized for one class and minimized for the other class.[14,15] In MI- and IM-based BCIs, the CSP features are the weighted sum of the powers of 8 to 30 Hz band-pass filtered brain signals, whereas FBCSP features are multiple CSP features extracted from a bank of brain signals filtered using different small band-pass filters.[16]

5. *Classification*: The extracted features are fed to a classifier to detect whether or not the recorded brain signals prominently represent the movement-related brain patterns associated with the performed mental practice. If the movement-related brain patterns are detected, a control signal is sent to an external device to provide the feedback.

6. *Feedback*: The patient is presented with feedback indicating whether the classification algorithm accurately interpreted their motor intention/imagination. The commonly used type of BCI feedback in stroke rehabilitation is kinesthetic, whereby following the detection of the movement-related brain patterns, the impaired hand is moved along a predefined trajectory. For instance, Ang et al[9] and Biasiucci et al,[17] respectively, used an Massachusetts Institute of Technology (MIT)–Manus robot and functional electrical stimulation (FES) in order to facilitate the movement of the impaired hand as the BCI feedback. The MIT-Manus robot is a wearable robot that has been extensively studied for providing individualized rehabilitation after stroke. During the intervention, the patient is instructed to move the affected arm towards a target. If needed, the robot facilitates the movement of the affected arm by providing assistive forces based on the patient's speed and the direction of the movement. Although rehabilitation with the MIT-Manus robot can be potentially effective,[18,19] if the patient does not engage well in generating voluntary attempts, the movements of the affected arm turn out to be completely passive. This leads to a great decrease in the possible benefits of the therapy.

To enhance neuroplasticity in the poststroke upper-limb rehabilitation, the BCI links the movement-related brain patterns (generated during either MI or the IM of the affected arm) with feedback such as robotic-based movements, neuromuscular stimulation, virtual reality, etc.[20] In other words, the BCI is coupled with the existing therapies to enhance their efficacy by making the rehabilitation more active.[21]

Recently, a number of randomized controlled trials (RCTs) have investigated the efficacy of the BCI for poststroke upper-limb rehabilitation, and compared the outcomes with those obtained from other existing therapies.[11,13,17,22] Despite the encouraging results in many of these RCTs, there is a significant variance in their reported BCI outcomes.[9,10,13,17] This issue might be due to the heterogeneity among their BCI study designs,[23] including differences in the performed mental practice, the extracted brain features, the type of feedback given to the patients, and the level of stroke chronicity in the participants. A meta-analysis conducted by Cervera et al[24] reported positive effects of the BCI on upper-limb stroke rehabilitation in a short term. Another meta-analysis conducted by Bai et al[25] considered the long-term efficacy of

the BCI on upper-limb stroke rehabilitation. However, given the considerable heterogeneity in the motor function improvement among the BCI RCTs, there is a need for an extensive meta-analysis to assess the impact of different BCI designs on the treatment efficacy.

This study conducts a systematic review and meta-analysis of the short-term and long-term effects of BCI on upper-limb rehabilitation after stroke. Importantly, we also study the impact of different BCI design characteristics on the efficacy of the poststroke upper-limb rehabilitation. The findings of this meta-analysis aim to improve future clinical trials by providing evidence-based information about different designs of the BCI used for rehabilitation.

Method

This study was conducted in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) checklist for systematic review and meta-analysis.[26] PRISMA aims to help researchers effectively report the findings of systematic reviews and meta-analyses.[27] The PRISMA checklist contains 27 items, which should be reported to ensure the transparency and completeness of the report. The 27 items are divided into 7 categories, including title, abstract, introduction, methods, results, discussion, and funding.

We systematically searched PubMed, Physiotherapy Evidence-Based Database (PEDro), and Cochrane Library for the studies that published up until 25 April 2020. Supplemental Appendix 1 provides the detailed electronic search strategy that we used. The identified studies were included in this meta-analysis only if they met the following inclusion criteria:

1. The study is written in English.
2. The study design is a randomized controlled trial of upper-limb BCI rehabilitation, in which the 2 groups (ie, the experimental group and the control) are all stroke patients;
3. The study reported the results of the Fugl-Mayer assessment for upper extremity (FMA-UE) before and after the intervention.

We chose the FMA-UE, because it is the most commonly used outcome measure in the upper-limb BCI rehabilitation studies.[28] The FMA-UE is widely used to evaluate and measure the upper-limb motor function impairment in patients after the stroke.[29] The FMA-UE score mainly ranges from a minimum of 0 (hemiplegia) to a maximum of 66 (normal motor function). We excluded studies without a control group, studies with healthy subjects, studies with a feedback mechanism not combined with BCI, or studies without FMA-UE. Two reviewers independently evaluated the eligibility of the included articles, and disagreements were resolved through consensus during a meeting.

We extracted the following details from each included studies: surname of the first author, year of the publication, aim of the study, brain imaging modality, number of participants, phase of the stroke (ie, chronic or subacute), length and frequency of the interventions, outcome measures, type of performed mental practice during the BCI intervention (ie, MI or IM), BCI feature extraction method, type of BCI feedback, and length of follow-up assessments after the intervention. The corresponding investigators were contacted if the included studies lacked some details.

The PEDro scale is commonly used to measure the methodological quality of a clinical trial by considering 11 criteria (ie, eligibility criteria specified, random allocation, concealed allocation, baseline comparability, blinded subjects, blinded therapist, blinded assessor, adequate follow-up, intention to treat analysis, between-group statistical comparison for at least 1 key outcome, point and variability measures).[30] The PEDro score is a score ranging from 0 to 10, which represents the total number of criteria, excluding the first one that has been satisfied in the clinical trial. A clinical trial with a score from 6 to 10 is considered as high quality, 4 to 5 as fair quality, and ≤3 as poor quality. In this study, 2 reviewers independently applied the PEDro scale to assess the methodological quality of the included studies. In the case of disagreement, a third reviewer was consulted and an agreement was reached.
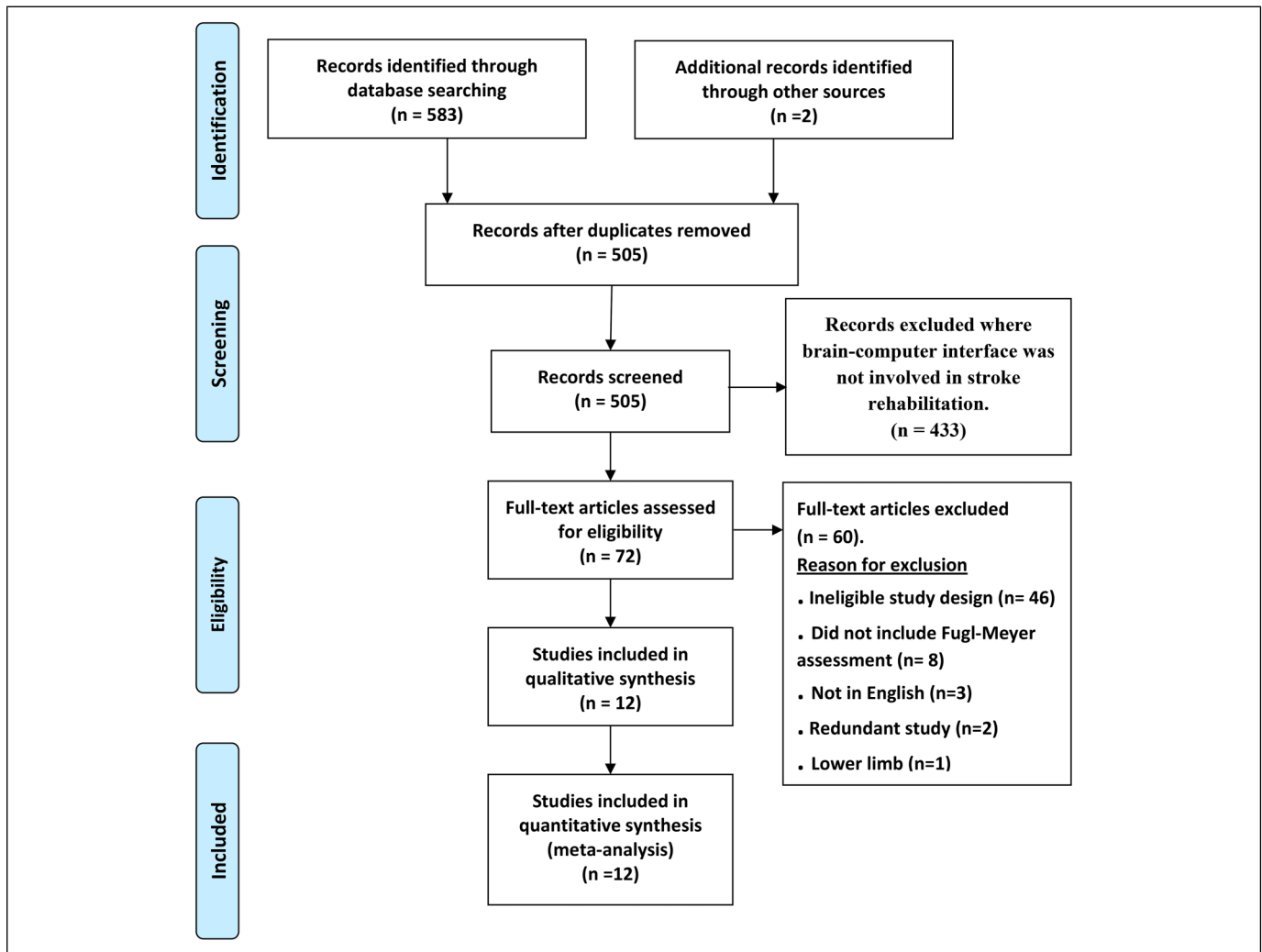
We conducted the meta-analysis using Comprehensive Meta-Analysis (CMA) version 3.0 software.[31] CMA is a tool to perform meta-analysis, create forest plots, calculate effect sizes, and much more. We calculated the effect sizes for the pooled and individual studies using Hedge's equation with correction for small studies.[32] Due to considerable variations in characteristics of the included studies, random-effects models were used to estimate the pooled effect sizes and their 95% confidence intervals (CIs).[33] In addition, we performed subgroup analyses to investigate the impact of different BCI design characteristics (ie, performed mental practice, extracted BCI features, type of the given BCI feedback, and the stroke phase) on treatment efficacy.

We used the Higgins' I^2 statistic to assess heterogeneity across the included studies.[34] Generally, $I^2 > 50\%$ could be considered as substantial heterogeneity. Finally, the probability of publication bias in our meta-analysis was assessed by plotting the funnel plot and applying Egger's regression test.[35,36]

Results

Literature Search and Characteristics of the Selected Studies

Figure 2 shows the flowchart of the search strategy and the selection steps taken in this review. We initially identified 585 articles, 12 of which met the inclusion criteria. The study by Ang et al[37] had 2 control groups, 1 control group used the standard arm therapy and the second control group used the haptic knob. Thus, we combined the 2 control groups into a single control group as recommended by the Cochrane handbook for systematic reviews of interventions.[38] Table 1 provides the main characteristics of the included studies.

Figure 2. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flowchart illustrating the process for the selection of the included studies in this meta-analysis.

Supplemental Table S1 presents the PEDro scores for the 12 included studies. It can be seen that according to the PEDro scores, none of the selected studies are considered to have low methodological quality.

Supplemental Table S2 presents the mean and standard deviation of the changes in FMA-UE scores between the pre and postintervention in the selected studies, while the Supplemental Table S3 shows the mean and standard deviation of the changes in FMA-UE scores between the preintervention and the follow-up session.

Short-term and Long-term Efficacy of BCI

The pooled results showed that according to the short-term assessments immediately after finishing the intervention, the BCI is significantly more effective than the control interventions in post-stroke upper-limb rehabilitation (Hedge's $g = 0.73$; $P = .006$) (Figure 3A). In 9 out of 12 studies, the BCI resulted in higher improvements in FMA-UE, compared to the control

interventions (Ang et al,[37] Biasiucci et al,[17] Frolov et al,[39] Kim et al,[40] Li et al,[8] Mihara et al,[12] Pichiorri et al,[41] Ramos-Murguialday et al,[11] and Wu et al[13]). The highest BCI intervention effect size was reported by Wu et al[13] (Hedge's $g = 3.48$; $P < .001$). In 6 studies, namely Biasiucci et al,[17] Kim et al,[40] Mihara et al,[12] Pichiorri et al,[41] Ramos-Murguialday et al,[11] and Wu et al,[13] the effect size was significantly favoring BCI. There was substantial heterogeneity among the included studies ($I^2 = 77.12\%$; $Q = 48.077$; $df = 11$; $P = .000$).
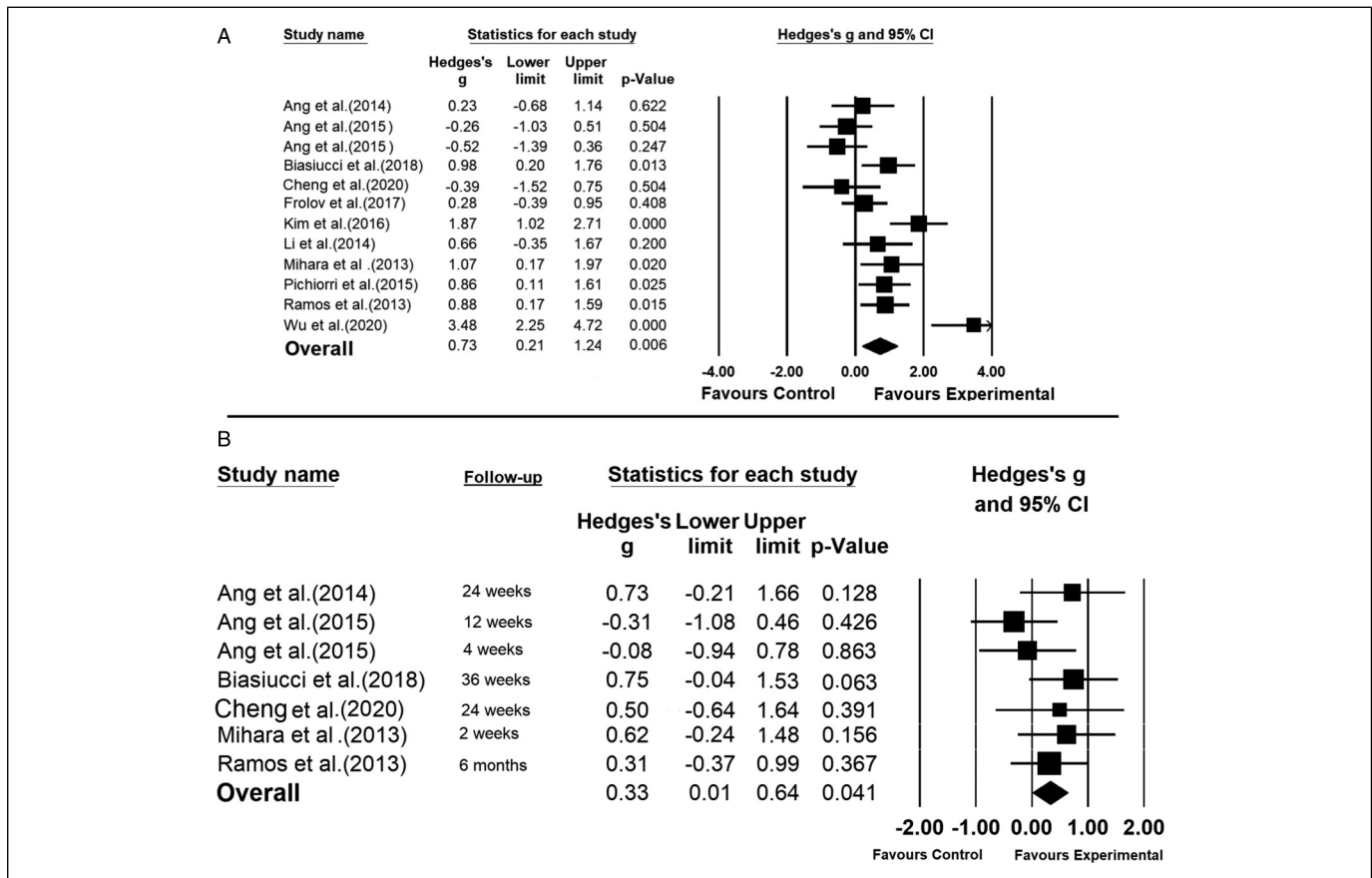
There is no evidence that the short-term effects of BCI are subject to publication bias. As shown in Supplemental Figure 1, the included studies have a relatively symmetric distribution across the overall effect size in the funnel plot. Moreover, the P value for Egger's test is not significant ($P = .3795$).

The overall effect size, shown in Figure 3B, indicates the effectiveness of the BCI intervention in long term (Hedge's $g = 0.33$; $P = .041$) with no heterogeneity among the included studies ($I^2 = 0.000\%$; $Q = 5.839$; $df = 6$; $P = .442$). Specifically, in 5 out of 7 studies, the FMA-UE changes between the follow-up

Table I. Main Characteristics of the Included Studies.

Study	EG/CG	BCI modality	Experimental intervention	Control intervention	Intervention period	Feature	Stroke phase	MI/IM	Outcome measures	Follow-up (weeks)
Ang et al[37]	6/8 HK/7 SAT	EEG	BCI-HK 1 h BCI + 30 min TAAM	HK:1 h HK + 30 min TAAM; SAT:1.5 h TAAM	6 weeks, 18 sessions	FBCSP	Chronic	MI	FMA-UE	24
Ang et al[9]	11/14	EEG	BCI-MIT-Manus robot 1.5 h 136 repetitions	MIT-Manus robot 1.5 h 1040 repetitions	4 weeks, 12 sessions	FBCSP	Chronic	MI	FMA-UE	12
Ang et al.[10]	10/9	EEG	20 min tDCS + 1 h BCI-MIT-Manus robot	20 min sham tDCS + 1 h sham BCI	2 weeks, 10 sessions	FBCSP	Chronic	MI	FMA-UE	4
Biasiucci et al[17]	14/13	EEG	BCI-FES 1 h	Sham BCI-FES 1 h	5 weeks, 10 sessions	Band power	Chronic	IM	FMA-UE, ESS, MRC, MAS	36
Cheng et al[42]	5/5	EEG	BCI-assisted soft robotic glove 90 min + 30 min SAT	Soft robotic glove 90 min + 30 min SAT	6 weeks, 18 sessions	FBCSP	Chronic	MI	FMA-UE, ARAT	24
Frolov et al[39]	36/11	EEG	BCI-exoskeleton 30 min + SPT	Sham BCI 30 min	2 weeks, 10 sessions	Band power	Chronic	MI	FMA-UE, ARAT	N/A
Kim et al[40]	15/15	EEG	BCI-FES 30 min + 30 min AOT	AOT 30 min	4 weeks, 12 sessions BCI. 20 sessions AOT	Band power	Chronic	IM	FMA-UE, MAL, MBI	N/A
Li et al[8]	7ne/7nc	EEG	BCI-FES 1–1.5 h + CON	FES 20 min + CON	8 weeks, 24 sessions BCI/FES and 40 sessions CON	CSP	Subacute	MI	FMA-UE, ARAT	N/A
Mihara et al[12]	10/10	fNIRS	BCI-visual feedback 20 min + 120 min NDT	Sham BCI 20 min + 120 min NDT	2 weeks, 6 sessions BCI/Sham, 14 sessions NDT	Band power	Subacute	MI	FMA-UE, ARAT, MAL	2
Pichiorri et al[41]	14/14	EEG	BCI-virtual hand 1 h	MI, 1 h	4 weeks, 12 sessions	Band power	Subacute	MI	FMA-UE	N/A
Ramos-Murguialday et al[11]	16/16	EEG	BCI-orthosis 1 h + 1 h BPT	Sham BCI-orthosis 1 h + 1 h BPT	4 weeks, 20 sessions	Band power	Chronic	IM	FMA-UE GAS, MAL	26
Wu et al[13]	14/11	EEG	BCI-exoskeleton 1 h + 1 h routine training	Routine training 2 h	4 weeks, 20 sessions	Band power	Subacute	MI	FMA-UE ARAT, WMFT	N/A

Abbreviations: AOT, action observational training; ARAT, action research arm test; BCI, brain–computer Interface; BPT, behavioral physical therapy; CG, control group; CON, conventional therapy; CSP, common spatial pattern; EG, experimental group; EES, European stroke scale score; GAS, goal attainment scale; FBCSP, filter bank common spatial pattern; fNIRS, functional near-infrared spectroscopy; FES, functional electrical stimulation; FMA-UE, Fugl-Meyer assessment upper extremity; IM, intention of movement; HK, haptic knob; MAL, motor activity long; MAS, modified Ashworth scale; MBI, modified Barthel index; MI, motor imagery; MRC, medical research council; N/A, not available; NDT, neurodevelopmental treatment; SAT, standard activity therapy; SPT, standard physical therapy; TAAM, therapist-assisted arm mobilization; tDCS, transcranial direct-current stimulation; WMFT, Wolf motor function test.

Figure 3. Evaluating effects of brain–computer interface, compared to control interventions, in improving upper-limb motor functions after stroke: (A) assessed immediately after finishing the intervention and (B) assessed in the follow-up session a number of weeks after finishing the intervention.

session and the preintervention were in favor of the BCI group. According to the funnel plot shown in Supplemental Figure 2, and the Egger's test ($P = .541$), there is no evidence of publication bias in the outcome of analyzing the long-term efficacy of the BCI.
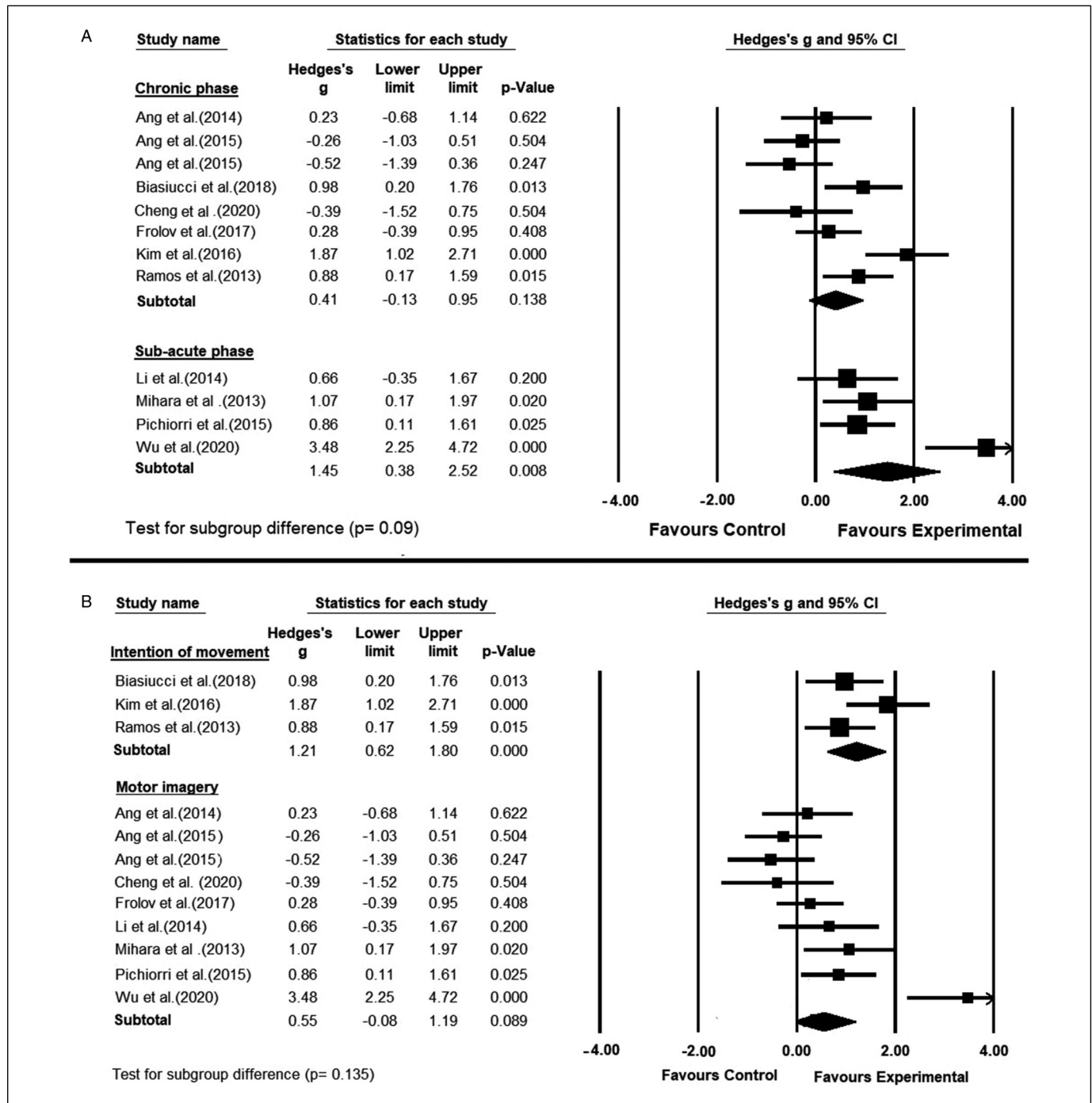
Chronic Versus Subacute

Eight studies recruited stroke patients in the chronic phase (>6 months from stroke onset)[9–11,17,37,39,40,42] and the remaining 4 studies recruited stroke patients in the subacute phase (1-6 months from stroke onset).[8,12,13,41] For both groups, the pooled effect size on motor recovery was in favor of BCI compared to the control interventions. However, the pooled effect size was higher for the patients in the subacute phase than those in the chronic group (Hedge's $g = 1.45$; $P = .008$ vs Hedge's $g = 0.41$; $P = .138$) (Figure 4A). The observed effect sizes tended to be significantly different between the 2 subgroups ($P = .09$). Furthermore, still a substantial heterogeneity was observed between the studies in the subacute phase ($I^2 = 80.17\%$; $Q = 15.128$; df $= 3$; $P = .002$) as well as in the chronic phase ($I^2 = 71.634\%$; $Q = 24.577$; df $= 7$; $P = .001$).

MI Versus IM

In the included studies, the performed BCI mental practices were different (Figure 4B). Nine studies instructed the BCI group to imagine the movement of the affected hand,[8–10,12,13,37,39,41,42] whereas 3 studies asked the BCI group to attempt moving the affected hand.[11,17,40] The effect size on motor function recovery was higher for the studies using the IM (Hedge's $g = 1.21$; $P < .001$) compared with those using the MI (Hedge's $g = 0.55$; $P = .089$). However, the difference between the 2 subgroups was not statistically significant ($P = .135$). The heterogeneity among the studies using the IM was moderate ($I^2 = 42.38\%$; $Q = 3.471$; df $= 2$; $P = .176$), whereas there was a substantial heterogeneity among the MI studies ($I^2 = 78.348\%$; $Q = 37.01$; df $= 8$; $P = .000$).

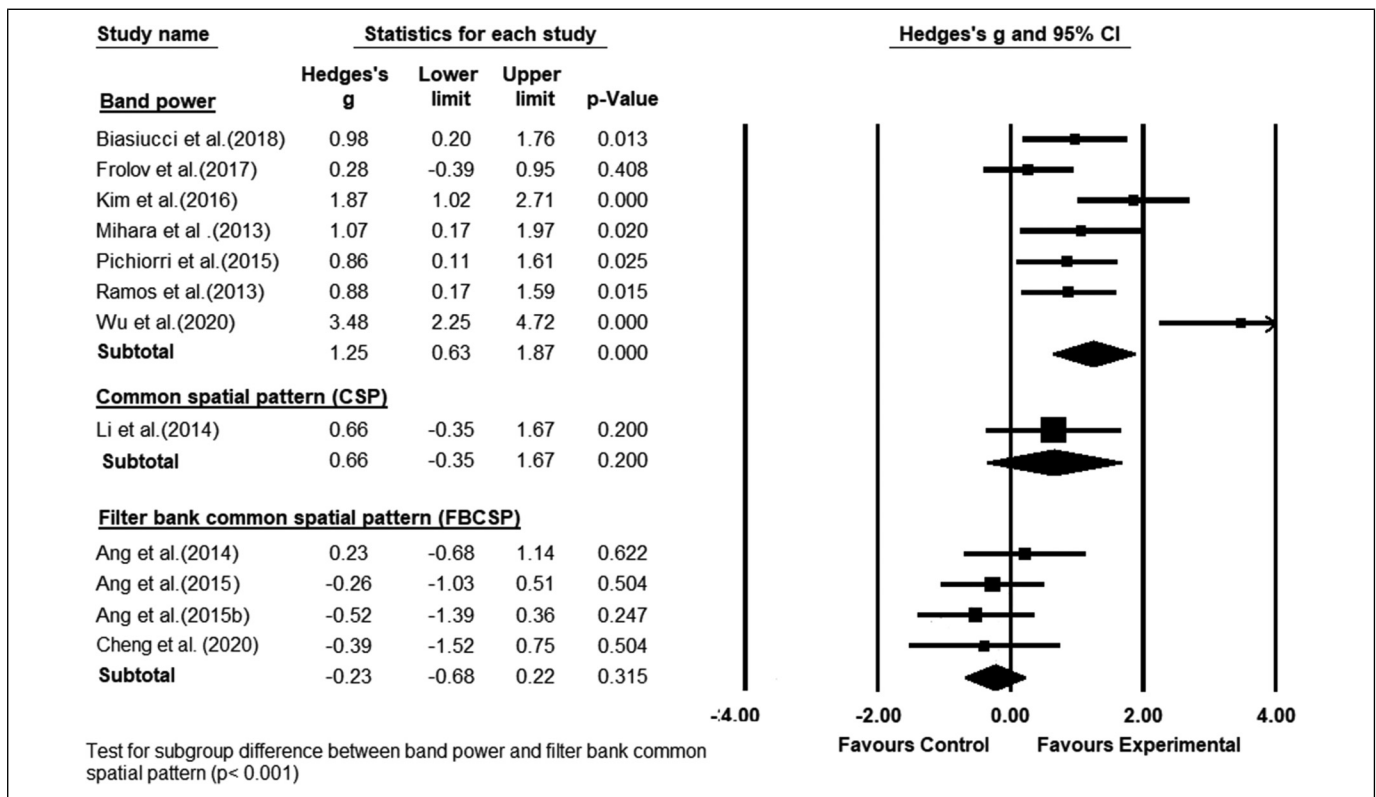## BCI Classification Features

The included studies were also different in BCI features that they used. Seven studies used the band power features to detect movement-related brain patterns in BCI.[11–13,17,39–41] The CSP features were used only in 1 study [8] and the FBCSP

Figure 4. (A) A subgroup meta-analysis comparing the efficacy of brain–computer interface in improving upper-limb motor functions, between 2 different phases of stroke. (B) A subgroup meta-analysis comparing the efficacy of brain–computer interfaces with different mental practices on poststroke upper-limb motor recovery; (ie, motor imagery vs intention of movement).

features were used in 4 studies.[9,10,37,42] The group of studies that used band power features had the highest significant effect size on motor function recovery in favor of the BCI intervention (Hedge's $g = 1.25$; $P < .001$) (Figure 5), with substantial heterogeneity among the studies ($I^2 = 75.208\%$; $Q = 24.201$; df $= 6$; $P = .000$). Conversely, the effect size on motor function recovery was in favor of the control group in the studies using the FBCSP features in the BCI (Hedge's $g = -0.23$; $P = .315$) with no heterogeneity. The difference between the studies with the band power features and the studies with the FBCSP features was statistically significant ($P < .001$).

Figure 5. A subgroup meta-analysis comparing the efficacy of brain–computer interface, grouped based on different classification features, on poststroke upper-limb motor recovery.

Only 1 study used the CSP features in their BCI model, yielding the effect size in favor of the BCI group (Hedge's $g = 0.66$; $P = .2$).

Type of BCI Feedback

The type of BCI feedback used to move the affected hand was different across the studies. As can be seen in Figure 6, functional electrical stimulation (FES) was used in 3 studies,[8,17,40] a hand exoskeleton robot was used in 2 studies.[13,39] The MIT-Manus robot was used in 2 studies,[9,10] and haptic knob, an assisted soft robotic glove, and orthosis (hand and arm) robot were used in 1 each.[11,37,42] One study provided only visual feedback to the patients.[12] Finally, the study conducted by Pichiorri et al[41] used a virtual hand to provide the BCI feedback to the patients.
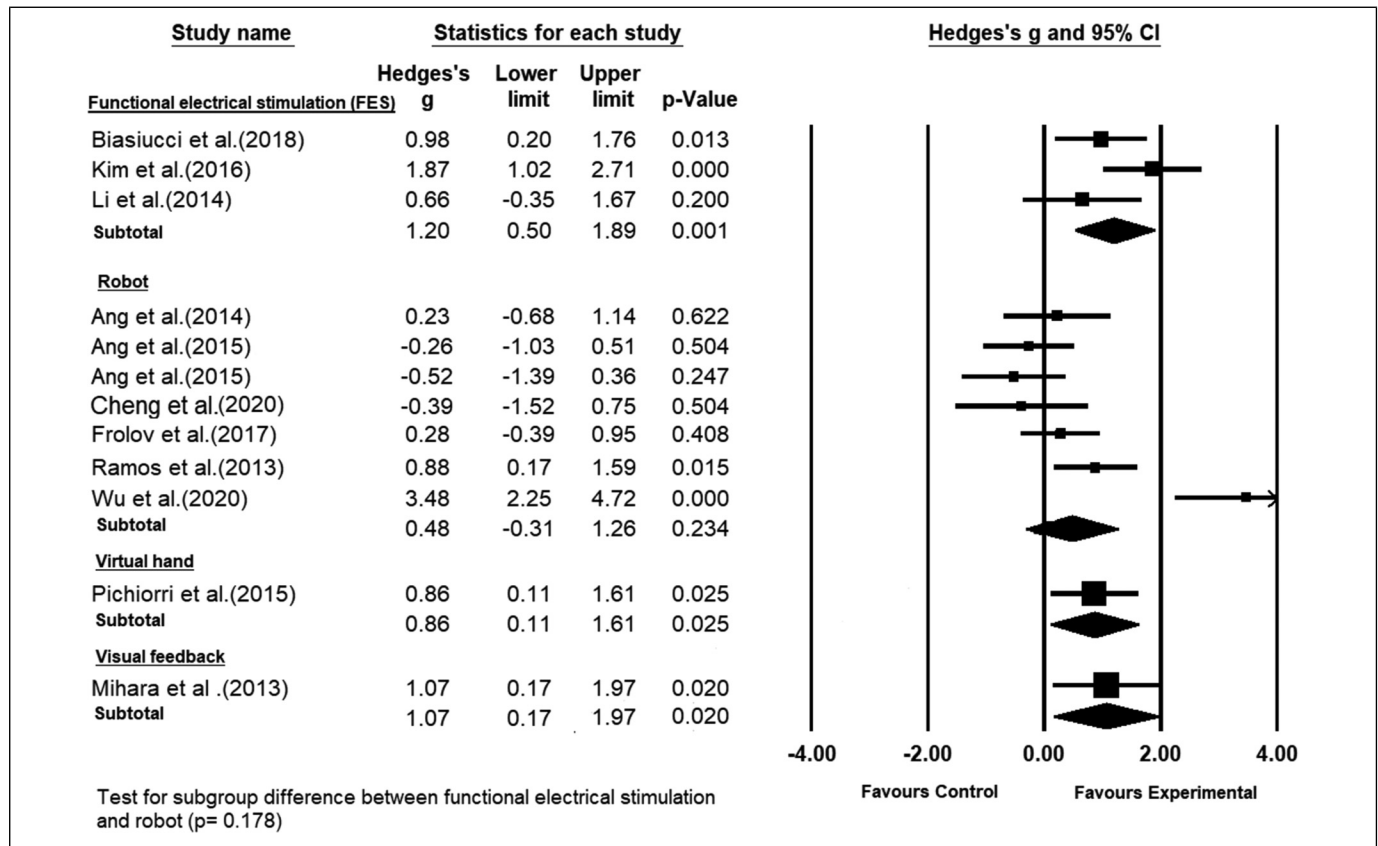
Compared to the control interventions, the highest statistically significant effect size on upper extremity recovery was obtained by the group of studies that used FES as the BCI feedback (Hedge's $g = 1.2$; $P = .001$), with moderate heterogeneity among the studies ($I^2 = 47.369\%$; $Q = 3.8$; df = 2; $P = .15$). However, the effect size of the group studies with the FES-based feedback was not significantly higher than the effect sizes of the other groups of studies with the other types of BCI feedback.

Discussion

This study was conducted according to the recommendations of the PRISMA checklist for meta-analyses and systematic reviews.[26] Our meta-analysis studied changes in the FMA-UE scores between pre and postintervention, and showed that BCI had a significantly higher effect size in improving upper extremity functions following stroke, when compared with control therapies. These findings are consistent with the results of the previous meta-analysis,[24] and support the short-term efficacy of BCI. Importantly, our study analyzed 12 randomized controlled trials involving 298 stroke patients, while the previous study[24] covered 9 randomized controlled trials with 235 stroke patients.

We also analyzed the results of 7 out of 12 included studies that reported the FMA-UE scores of the patients in a follow-up session held a number of weeks after the cession of the intervention. Our results showed that the BCI effects in restoring upper extremity functions are persistent over long term with a pooled effect size significantly better than the control interventions. As an example, the upper-limb improvements were almost maintained at 36 weeks after the intervention in the study conducted by Biasiucci et al.[17] However, the recent meta-analysis conducted by Bai et al[25] did not observe long-term efficacy of BCI compared to conventional therapies. The reason might be because they considered a smaller number of randomized clinical

Figure 6. A subgroup meta-analysis comparing the efficacy of brain–computer interface, grouped based on different types of feedbacks, on poststroke upper-limb recovery.

trials (5 studies). In addition, we combined the 2 control groups in the study conducted by Ang et al[37] to create a single control group,[38] whereas Bai et al[25] selected the haptic knob group and excluded the standard arm therapy group.

Interestingly, the most recent randomized controlled trial conducted by Wu et al[13] showed the highest effect size in improving upper extremity functions in favor of BCI (ie, Hedge's $g = 3.48$).[13] As can be seen in Figure 3A, the BCI effect size of this study is much larger than the effect sizes of the other included studies. In this study, unlike the other studies, the MI instruction was given to the patients by displaying a video of a hand using different tools. Then, the patients were asked to repeat the presented hand movement using mental imagery. The authors emphasized that the given instruction played an important role in the observed motor function recovery, possibly by linking the brain's visual and motor system.

Our subgroup meta-analysis showed that for both subacute and chronic patients, BCI is more effective than conventional therapies in improving upper-limb function (see Figure 4A). Our results also showed that the BCI studies performing intention/attempting of movement of the impaired hand, often followed by real movement if available, achieved a higher overall effect size than those that performed only MI (although not statistically significant). As a possible reason, we would argue that intending to move rather than just imaging the movement may lead to higher activity in neural circuits and better patient engagement and attention.[43,44] Blokland et al[45] showed that for both groups of paralyzed and healthy participants, the accuracy of the BCI system that focused on the IM was significantly higher than that of MI. Moreover, among healthy participants, the IM and motor execution had more similar brain spectral responses and BCI performance than the results of MI. Considering the evidence provided here, future BCI-based stroke rehabilitation studies are encouraged to focus on intending rather than imagining of moving impaired hands. Further studies are required to confirm this observation.

Our subgroup meta-analysis grouped the included studies according to the BCI features that they used, further revealing that the use of band power features yielded the highest effect size in favor of the BCI compared to the control interventions. Indeed, the BCI studies using the band power features achieved a significantly greater upper-limb motor function recovery than those using the FBCSP features ($P < .001$). Previous studies on healthy and stroke participants suggested that FBCSP could lead to a higher BCI accuracy than the band power features. In addition, some studies have reported that there is a correlation between the BCI accuracy and motor function improvement

after a BCI intervention.[44,46] Thus, someone may initially assume that using FBCSP should produce a higher BCI effect size on motor recovery. However, the long-term effectiveness of BCI for stroke rehabilitation greatly involves human learning. The results of our meta-analysis suggest that in long term the use of band power features potentially helps patients better learn to self-regulate their brain patterns, leading to more motor recovery as compared to more complex features such as FBCSP. In FBCSP, the patients may not easily find a connection between their mental practice and what they observe as the output BCI.

The randomized control trials that coupled the BCI with FES had the largest significant effect size in restoring upper-limb function. This improvement may be due to the positive impact of FES on cortical excitability as reported by several studies.[47,48]

In the study conducted by Ang et al,[9] the effect size was in favor of the control group. This may be due to the relatively small number of training repetitions in the BCI group compared to the control group (136 vs 1040 repetitions). In addition to the number of training repetitions, the use of MI and FBCSP may have contributed to the negative results, as discussed in this study. Another study by the same research group also showed an effect size in favor of the control group.[10] This finding might be because of the short period of the rehabilitation intervention (2 weeks). Interestingly, this study reported a slight improvement in the BCI outcomes at the follow-up session held 4 weeks postintervention. However, it would be difficult to distinguish if this observed slight improvement was as a result of the BCI intervention or the transcranial direct current stimulation (tDCS). Typically, a longer intervention, such as 6 weeks of rehabilitation with 3 sessions per week is recommended.[49]

Limitations

In this meta-analysis, we observed large variations in the BCI intervention effect sizes across the included clinical trials. As discussed previously, these variations can be potentially due to differences in the BCI design, including differences in the BCI feedback, performed mental practices, extracted classification features, and the phase of the stroke in the participants, among others. This finding further confirms that there is a need to optimize the BCI design for upper-limb stroke rehabilitation in order to maximize the potential motor function improvement in patients.

Only 12 randomized clinical trials (298 patients) were available to analyze in this study. Hence, more studies with a larger number of patients are required to increase the reliability and generalizability of the results. Moreover, in order to have a reliable subgroup meta-analysis, it has been recommended to have at least 5 clinical trials in each subgroup.[50] In some of our subgroup analyses, this condition was not met. Moreover, we did not consider the variations among the included clinical trials in terms of the intensity of BCI intervention (see Table 1).

Conclusion

This study showed that BCI has significant immediate and long-term effects in improving upper-limb motor functions after stroke, compared to conventional therapies. Our results support using "intention of movement of the impaired hand" as the BCI mental practice, the band power features as the BCI classification features, and the functional electrical stimulation as the BCI feedback in future BCI-based stroke rehabilitation studies.

Author Contributions

SM and MA contributed to the study concept and design, independently searching and evaluating study eligibility, extracting the data and drafting the manuscript. The statistical analysis was performed by SM, and the research was supervised by MA. KKA, KPSN, and KSP all contributed significantly to the interpretation of the findings and the writing of the manuscript. The manuscript was revised by all authors, and they all gave their approval to the final version.

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Supplemental material

Supplemental material for this article is available online.

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