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Review

Combining brain–computer interface and virtual reality for rehabilitation in neurological diseases: A narrative review

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ABSTRACT

Background: The traditional rehabilitation for neurological diseases lacks the active participation of patients, its process is monotonous and tedious, and the effects need to be improved. Therefore, a new type of rehabilitation technology with more active participation combining brain–computer interface (BCI) with virtual reality (VR) has developed rapidly in recent years and has been used in rehabilitation in neurological diseases.
Objectives: This narrative review analyzed and characterized the development and application of the new training system (BCI-VR) in rehabilitation of neurological diseases from the perspective of the BCI paradigm, to provide a pathway for future research in this field.
Methods: The review involved a search of the Web of Science-Science Citation Index/Social Sciences Citation Index and the China National Knowledge Infrastructure databases; 39 papers were selected. Advantages and challenges of BCI-VR – based neurological rehabilitation were analyzed in detail.
Results: Most BCI-VR studies included could be classified by 3 major BCI paradigms: motor imagery, P300, and steady-state visual-evoked potential. Integrating VR scenes into BCI systems could effectively promote the recovery process from nervous system injuries as compared with traditional methods.
Conclusion: As compared with rehabilitation based on traditional BCI, rehabilitation based on BCI-VR can provide better feedback information for patients and promote the recovery of brain function. By solving the challenges and continual development, the BCI-VR system can be broadly applied to the clinical treatment of various neurological diseases.

1. Introduction

Brain–computer interface (BCI) is a new external information exchange and control technology between the human brain and computer or other electronic devices that does not rely on conventional brain information output pathways (peripheral nerves and muscle tissues) [1]. It can help patients with severe motor dysfunction directly communicate with the real world.

BCI technology is often used to induce neuroplasticity in the brain and help patients regain motor function [2]. In particular, great progress has been made in helping disabled people control prosthetics [3], propel wheelchairs [4], drive vehicles [5], and even spell, type and play online games [6]. Some systematic reviews analyzed the effectiveness of BCI-based rehabilitative programs [7,8].

In recent years, with the increase and development of virtual reality (VR), numerous systematic reviews have examined the

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effectiveness of VR-based rehabilitative programs [7,8]. In addition, a new BCI technology has emerged recently: BCI based on VR, also known as BCI-VR [9]. This technology provides individuals with an immersive virtual reality stimulation environment, which makes them more engaged and has a stronger immersive experience, thus better controlling the BCI system and improving the effect of BCI [7]. The BCI-VR system can use the respective advantages of BCI and VR, so it has attractive broad application in the field of rehabilitation medicine, especially in the rehabilitation of patients with stroke [10], spinal cord injury (SCI) [11], attention deficit hyperactivity disorder (ADHD) [12], Alzheimer's disease (AD) and Parkinson's disease (PD) [13]. However, various problems arise in clinically applying the new technology to neurological diseases such as real-time capability, performance variability across training sessions and patients, and the user experience. Also, many questions need to be answered. For example, Which are the most-used BCI paradigms in studies coupling BCI and VR? What are the neurological diseases included in these new BCI studies? and What is the added value of coupling BCI-VR in terms of rehabilitation effectiveness, user experience, etc.?

No study has systematically reviewed the application and validity of rehabilitative programs based on BCI-VR and have not answered these questions. Therefore, we systematically reviewed the current status of the BCI-VR technology and its application in neurological rehabilitation. Also, we discuss the advantages and challenges of the BCI-VR system applied to neurological rehabilitation.

2. Literature search strategy and selection criterion

We searched the Web of Science-Science Citation Index/Social Sciences Citation Index (WOS-SCI/SSCI) database, the China National Knowledge Infrastructure (CNKI) database and additional records identified with other sources (Webpage, FTP server, etc.), focusing on studies that used BCI with VR scenes for neurological rehabilitation that were published from Jun, 2000 and August, 2018. The following search keywords and criteria were used: (motor imagery [MI] OR P300 OR steady-state visual evoked potential [SSVEP] OR brain-computer interface [BCI] OR electroencephalography [EEG]) AND virtual reality (VR) AND (rehabilitation OR training). DW, YF and YZ used the full technical terms as well as their acronyms for the search, with no restriction on study type or publication time. The most recent search was conducted on August 27, 2018. When searching the WOS-SCI/SSCI database, we excluded non-English publications.

In this way, 519 articles were identified. Titles, abstracts and full texts were screened for studies that:

- involved neurological diseases that could treated by neurological rehabilitation, such as AD, ADHD, PD, stroke, SCI, and mild cognitive impairment;
- used cognition, language or exercise as training modalities;
- used one or more BCI paradigms, EEG signals, or BCI;
- included evaluation of training programs and reported training outcomes.

If one paper did not meet the first inclusion criterion, the paper was not screened for other inclusion criteria; if one paper did meet the first and second inclusion criteria, the paper was not screened for the remaining criteria etc. In the final 58 papers selected, 19 papers were excluded, including 5 pairs of same papers in two different databases, 6 conference abstracts without original paper, and 8 papers only using behavioral data for analysis. Finally, 39 articles were included in the review. Fig. 1 described the search strategy.

3. Research significance and current status of BCI and VR technology

The BCI system is a direct communication channel between the brain and external devices. This system is undoubtedly a great blessing for individuals who lose the ability to exercise due to disease, accident or natural disaster and has great significance for physical rehabilitation and improvement of life quality [14]. BCI aims to help users accurately control external devices such as prosthetics, wheelchairs, and keyboards to regain partial daily function without the participation of body parts [15]. VR technology can simulate a virtual yet immersive and realistic space or environment to provide users with visual, haptic, auditory and other sensory feedback [16]. As compared with traditional feedback such as color bars or arrows, VR feedback can be applied to BCI systems with more active, colorful, intuitive, direct, and real-time feedback [15]. VR technology can also make the training more engaging, shorten the training time, and improve the overall efficiency of BCI. That is helpful for disabled people to learn and adapt to the BCI system and to control the virtual or actual devices in the applications.

VR technology applied in rehabilitation medicine has had some success, including for stroke individuals with hemiplegia after rehabilitation training (upper and lower limbs) [17], PD rehabilitation [18], and wheelchair drivers [4]. The rehabilitation and training are more embodied in the recovery of motor function.

Fig. 2 shows the general workflow of the BCI-VR system.

At present, BCI-VR systems can be classified by the BCI paradigms used: (1) motor-imagery (MI) potential, event-related potential (such as P300), and SSVEP. The MI potential generates event-related desynchronization or event-related synchronization potential signals when imagining the movement of body parts [19]. P300 is the event-related potential response in an oddball paradigm with positive potential at latency of about 300 ms that can be used to identify the target that a subject attends to [20]. SSVEP is the steady-state response of the visual cortex when a subject is given visual stimuli that flicker at specific frequencies. These 3 BCI paradigms have been developed and widely used in real-world applications.

Starting in 2000, Bayliss et al. combined VR and BCI technology for the first time. In their study, the subject operated a car in a virtual environment to stop at a red light, and the red light was set to induce a P300 signal [21]. In 2005, Lalor et al. used BCI technology based on SSVEP to control a game in a VR environment [22]. In 2007, Leeb et al. created a BCI system to control a wheelchair to move forward or stop in a virtual environment [23]. In recent years, BCI-VR research and technology have been rapidly developed [24]. For example, SSVEP-based BCI has been used in stroke rehabilitation [25], to overcome the limitation of refresh frequency of a conventional monitor [26] and to improve user engagement [27]. MI-based BCI has been used in stroke rehabilitation [28] and paraplegia [29]. P300-based BCI has been used to train normal aging individuals [30], and people with autism [31].

4. Research status of BCI-VR for neurological rehabilitation

With the advances in both BCI and VR technology, BCI-VR system-based rehabilitation training for neurological diseases has received increasing attention. For example, in 2011, Jiang et al. developed a VR game that converted the attention state of subjects into game control to train patients with ADHD and improve their attention time span [12]. In 2013, Zheng et al. proposed an experimental study on virtual-navigation tasks to help patients with SCI improve their navigation ability. The participants

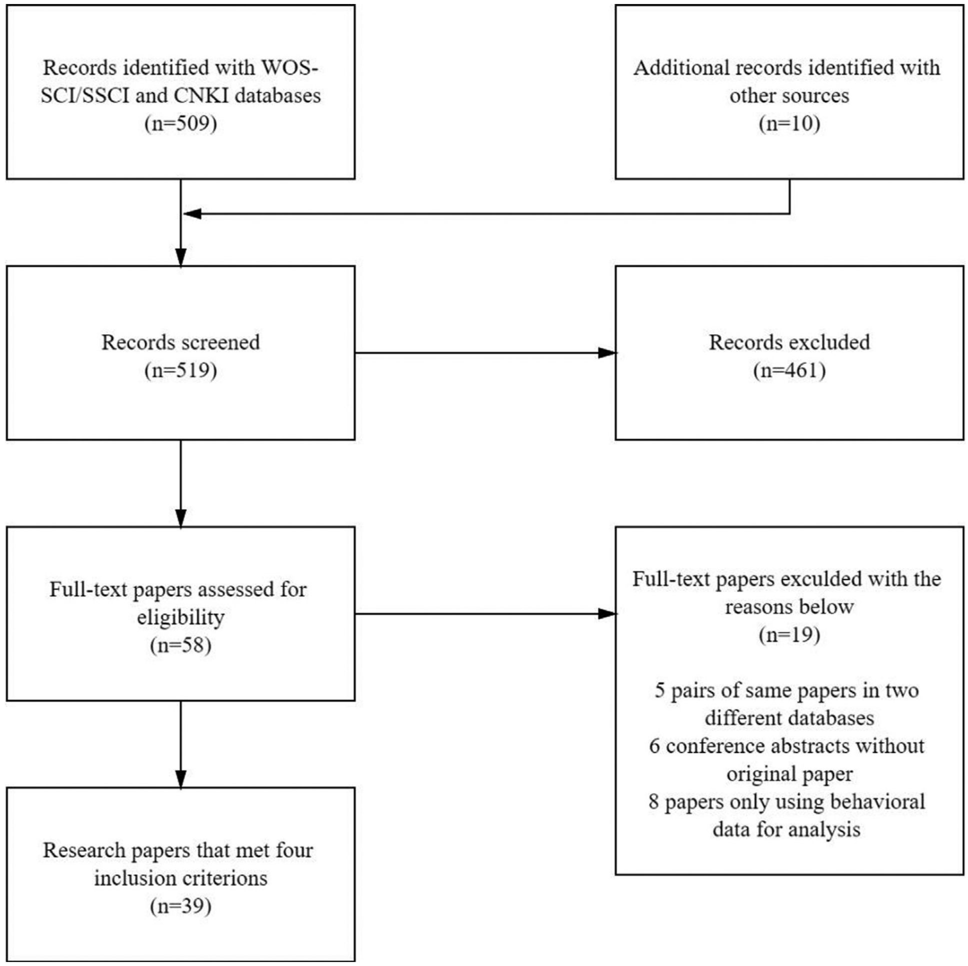

Fig. 1. Flow chart of the search strategy.

performed navigation tasks in a VR environment with MI, and the accuracy of walking direction judgment was about 67.5% [32]. In 2015, Luu et al. used a BCI-VR system for gait rehabilitation of individuals with stroke [33]. In 2017, Alchalabi et al. designed a VR game using wireless wearable BCI devices to improve the concentration ability of individuals with ADHD and ADD [34]. Fernandez-Caballero et al. also proposed to use BCI and VR technology to seek non-drug treatment for individuals with schizophrenia [35]. In 2018, Lupu et al. used an MI-based BCI and VR system for rehabilitation of individuals with stroke. According to the instruction of virtual therapists, individuals controlled virtual characters in VR scenes by using MI. Motor function was significantly improved as compared with conventional rehabilitation [36].

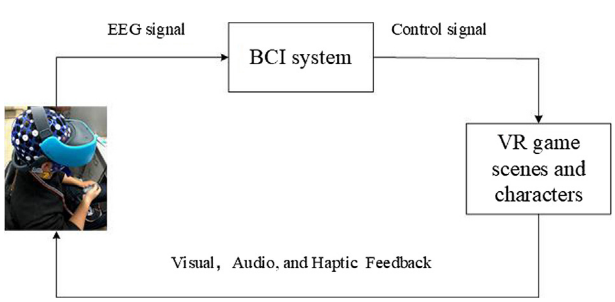

Fig. 2. Workflow of brain – computer interface – virtual reality (BCI-VR) system. EEG: electroencephalography.

5. Results of review

For this review of 39 studies of BCI-VR, Fig. 3 shows the distribution of use of the 3 BCI paradigms (MI, P300, and SSVEP) in

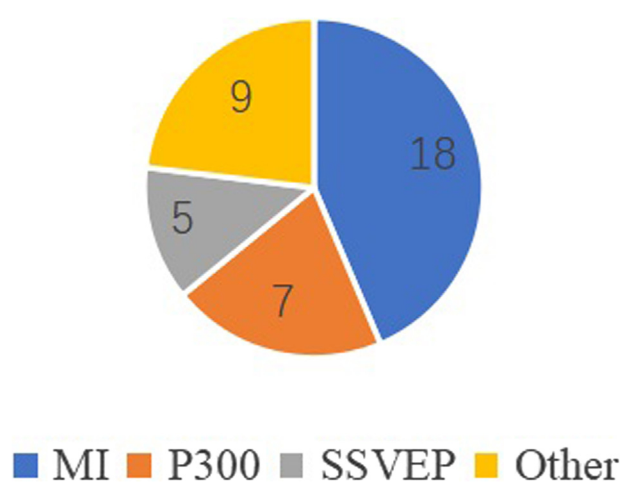

Fig. 3. Distribution of BCI paradigms. Data are numbers.

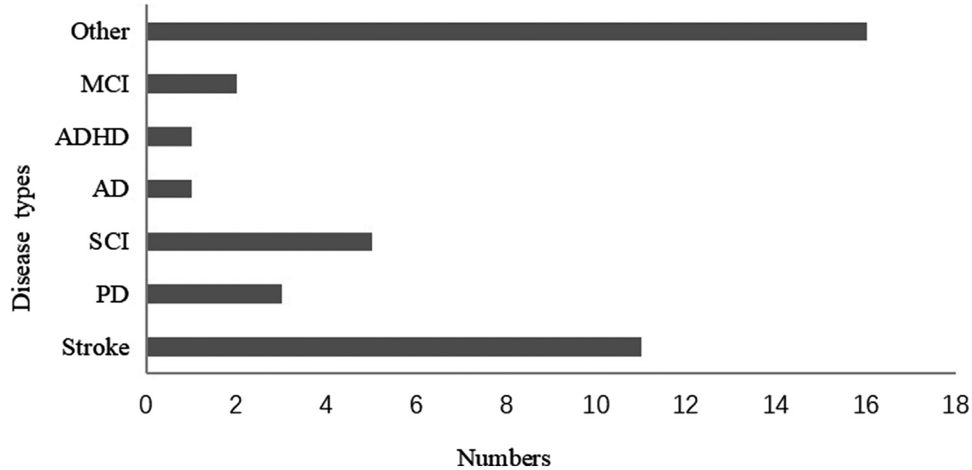

Fig. 4. Distribution of the literature studying different diseases with BCI paradigms.

these studies. Fig. 4 shows the number of studies that used BCI-VR systems for rehabilitation training in individuals with AD, ADHD, PD, stroke, SCI, mild cognitive impairment, etc. The Table 1 describes the 39 studies, including some of the BCI-VR systems for neuro-rehabilitation with details of the BCI paradigms used, virtual scenes used, and targeted patients.

The following describes the application of the 3 BCI-VR paradigms, namely MI-VR, P300-VR and SSVEP-VR, to the rehabilitation of individuals with neurological diseases.

5.1. MI-VR system for rehabilitation training

In the past decade, MI-based BCI has attracted great attention for neuro-rehabilitation. In 2012, Ortner et al. suggested that MI can be a common strategy for motor rehabilitation of individuals with stroke [39]. Other scholars have provided further evidence that individuals with neurological diseases can use MI-based BCI paradigms to imagine and control virtual or actual devices in VR scenes for repeatedly performing movements, thereby inducing neural plasticity and promoting recovery of the injured motor-nerve pathway. For example, in 2007, Leeb et al. invited a patient with total paralysis to use a MI-based BCI to move a wheelchair in a VR experiment. This was the first demonstration that a quadriplegic patient could control a virtual device [23]. In the 2010 study by Prasad et al., 5 individuals with chronic hemiplegic stroke underwent a 6-week MI course of exercises to train the left- and right-hand handshakes. The researchers used the task classifier based on MI-based BCI to evaluate the performance of neural feedback, and the final classification accuracy was 60% to 75%. Although the accuracy was not high, it did not hinder the positive recovery trend [60]. In 2012, Ortner et al. used the MI-BCI system to train individuals with stroke in VR scenes by imagining the movements of the left and right hands and optimized a classification algorithm that reduced the average classification error to 9.6% [39]. Therefore, MI provides a solid foundation for BCI development and application, and the fusion of MI-based BCI and VR systems improves the effectiveness of rehabilitation training for individuals with neurological diseases, especially motor impairment.

As MI-VR systems for neuro-rehabilitation advance, challenges in development and application also emerge. For example, in VR feedback, subjects sometimes have difficulty focusing on targets while neglecting the immersive, virtual environment that can be distracting. Also, using the MI-VR systems is not stable over the course of experiments. Both factors reduce the effectiveness of rehabilitation training. To find a reliable solution, researchers conducted experiments across different BCI feedback and VR platforms. For example, Vourvopoulos et al. developed the NeuRow [42], a new multiplatform prototype that provides multimodal feedback in VR environments by using state-of-the-art head-mounted displays to improve attention. NeuRow also provides a comprehensive approach to MI-driven BCI by combining an immersive VR environment, sensory stimulation and MI. During the experimental training, the participants relied on only MI-BCI to control virtual hands in the system. They performed MI in a random order, and the rowing motion of the virtual hands was visual feedback to their corresponding hands, as was the vibration and tactile feedback.

5.2. P300-VR system for rehabilitation training

P300-based BCI can detect targets that users attend to by eliciting P300 brain responses to an oddball visual stimulant and has been used in individuals with paralysis for communication or controlling external devices. To explore whether VR devices can achieve similar accuracy as traditional displays, Kathner et al. [52] asked 18 subjects to use 3 different display methods for online spelling tasks. The first display was a 5-by-5 matrix of a conventional thin film transistor. The second was the same 5-by-5 display but in a VR scene that covered the subject's field of view. The third was also in a VR environment, but only a single letter in the 5-by-5 matrix filled the subject's field of view at one time. The empirical results showed comparable online spelling accuracy (96%, 96%, and 94%, respectively). Therefore, VR devices could achieve similar accuracy as traditional flat-panel displays and could perform fast P300-BCI communication in VR devices. In 2016, De Tommaso et al. constructed a VR environment similar to the daily house environment and instructed participants to use a P300-BCI to perform a virtual pathfinding task by searching the corresponding house according to the change of light color in the house [30]. Considering that the P300-BCI system is convenient to use, cost-effective, and with reliable performance, more research groups have been integrating such systems with VR technology for a more immersive experience for rehabilitation of neurological diseases.

Rohani et al. proposed a novel BCI system using P300 and VR by designing virtual scenes that vividly mimicked the daily life environment, attempting to help children with ADHD improve attention [50]. The BCI system was embedded into an immersive 3D virtual reality classroom. By using the P300 paradigm in

Table 1
Summary of 39 studies of brain–computer interface–virtual reality (BCI-VR) for rehabilitation in neurological diseases.

Reference	BCI paradigm	Virtual reality scene and action	Other auxiliary tools	Diseases	Number of subjects	Evaluation of rehabilitation	System reliability (average classification accuracy)
Coogan (2018) [7]	MI	Controlling virtual character movement in virtual scenes	Hand controller	–	31	–	–
Achanccaray (2017) [11]	MI	Controlling the virtual hand to bend and straighten	–	Stroke	8	Adaptive neuro-fuzzy inference system	89%
Ma (2017) [15]	MI	Controlling virtual character movement in virtual scenes	Role controller component	–	4	SVM	82.19%
Badia (2013) [28]	MI	Controlling the virtual arm to intercept the incoming sphere	–	Stroke	9	Sensory motor rhythm	85%
Zheng (2013) [32]	MI	Performing navigation tasks in a virtual environment	–	Stroke or spinal cord injury	1	Filter bank common spatial pattern	67.5%
Lupu (2018) [36]	MI	Carrying out the corresponding movement according to the instructions in the virtual environment	–	Stroke	3	LDA	85%
Zhang (2017) [37]	MI	Controlling virtual character for hand movements	–	Stroke	5	SVM	78%
Ma (2007) [38]	MI	Controlling virtual character movement in virtual scenes	–	Nerve injury	3	LDA	97%
Ortner (2012) [39]	MI	Controlling left and right hands in virtual scenes	–	Stroke	3	LDA	90.4%
Vourvopoulos (2015) [40]	MI	Controlling the left and right hands in the virtual scene to open the garage door	–	Stroke	9	LDA	65.6%
Tan (2016) [41]	MI	Virtual scene controls, and the feedback of human eyes to control the relaxation and contraction of the arms	Dual-arm robot	Stroke	1	SVM	–
Vourvopoulos (2016) [42]	MI	Controlling virtual hands for rowing in virtual scenes	Hand controller	Nerve injury	13	LDA	70.7%
Ortner (2012) [43]	MI	Controlling left and right hands in virtual scenes	–	Stroke	3	LDA	80.82%
Rinderknecht (2012) [44]	MI	Feedback the information of arm motion in virtual reality	Rehabilitation equipment	Stroke	10	–	93%
Triponyuwasin, (2014) [45]	MI	Game in a virtual scene	Rehabilitation equipment	Stroke	3	LDA	62%
Munoz (2014) [46]	MI	Controlling left and right hands in virtual game scenes	–	Stroke	8	LDA, SVM	96.7%
Vourvopoulos, (2016) [47]	MI	Controlling the opening of the virtual garage door	–	Stroke	9	LDA	–
Lotte (2013) [48]	MI	Controlling virtual character movement in virtual scenes	–	Disability	7	–	90%
Kong (2015) [9]	P300	Operating a virtual vehicle in a virtual environment	–	Disability	–	–	93.5%
De Tommaso (2016) [30]	P300	Navigating in a virtual room to find the target location	–	Alzheimer's disease	22	one-way ANOVA	90%
Amaral (2017) [31]	P300	Random flicker of objects in virtual environment	–	Autism spectrum disorder	17	Naïve Bayesian	80%
Tarnanas (2012) [49]	P300	Navigating tasks in a virtual museum	–	Mild cognitive impairment	50	KNN	87%
Rohani (2014) [50]	P300	Identifying pictures in a virtual classroom	–	Attention deficit hyperactivity disorder	5	SVM	70%
Tidoni (2017) [51]	P300	Playing games with virtual character in a virtual scene	Robot	Spinal cord injury	21	LDA	89%
Kathner (2015) [52]	P300	Online sequence spelling in virtual environment	–	Paralysis	18	Stepwise linear discriminant analysis	80.5%
Zhang (2015) [17]	SSVEP	Controlling virtual character movement in virtual scenes	Lower limb robot	Stroke	3	Canonical correlation analysis	81.4%
Koo (2015) [27]	SSEVP	Playing maze games in virtual environment	–	Neuro-muscular defect	3	–	–
Legeny (2011) [53]	SSVEP	Navigating in a virtual scene	–	Mild cognitive impairment	1	LDA	91%
Zeng (2017) [54]	SSVEP	Mole game in a virtual scene	Ankle rehabilitation robot	Stroke	5	Information transfer rate	90%
Hu (2017) [55]	SSVEP	Controlling virtual character for hand movements	–	Stroke	1	Probabilistic neural network	95%
White (2016) [4]	–	Performing navigation tasks in a virtual environment	–	Alzheimer's disease	1	–	–

Table 1 (*Continued*)

Reference	BCI paradigm	Virtual reality scene and action	Other auxiliary tools	Diseases	Number of subjects	Evaluation of rehabilitation	System reliability (average classification accuracy)
Jiang (2011) [12]	–	Controlling a plate of fruit in a virtual environment	–	Attention deficit hyperactivity disorder	10	–	–
Luu (2015) [33]	–	Controlling virtual character movement in virtual scenes	–	Spinal cord injury and stroke	2	–	–
Alchalcabi (2017) [34]	–	Controlling virtual character movement in virtual scenes	Keyboard	Attention deficit hyperactivity disorder	4	–	–
Fernandezcaballero (2017) [35]	–	Socializing in a virtual environment	–	Schizophrenia	–	–	–
Zhu (2011) [56]	–	Watching the scene in the virtual environment	–	Autism spectrum disorder	–	–	–
Wang (2012) [57]	–	Sports training combined with rehabilitation robot in virtual environment	Rehabilitation robot	–	4	–	–
Fan (2015) [58]	–	Operating a virtual vehicle in a virtual environment	–	Autism spectrum disorder	16	KNN	80%
Luu (2016) [59]	–	Visual training in virtual environment	Treadmill	Stroke	4	–	–

LDA: latent dirichlet allocation; SVM: support vector machine; KNN: K-nearest neighbor.

2 feedback games, the changes in attention could be better detected, and the average error was < 30%. This system shows promise for use of the P300-BCI system in a VR environment for rehabilitation of children with ADHD.

5.3. SSVEP-VR system for rehabilitation training

As compared with the 2 other BCI paradigms, SSVEP-based BCI usually has the advantages of higher information transmission rate, more convenient use, and less training time [9]. Koo et al. designed a VR maze game and explored whether visual stimulation in VR devices could improve the system performance and user experience of SSVEP-BCI [27]. The objective of the game was to make continuous selections and guide a ball to a specified destination in a 3D space by using the SSVEP signals induced by visual stimuli on the adjacent cells in the maze. The mean information transmission rate in VR was 10% higher than that in traditional displays. The above research demonstrated that combining a SSVEP-based BCI system and VR environment could be appropriate and effective.

However, one limitation of the SSVEP-VR system is that users have to receive flicker stimulation. For patients with neurological diseases, long-term and high-amplitude flicker stimulation could cause discomfort and even aggravate the disease. To reduce the effect of flicker stimulation, Legeny et al. combined SSVEP stimulation with the VR environment skillfully by making it close to nature [53]. The authors integrated flashing stimuli into virtual objects as part of the VR scene in a more transparent and ecological way, for example, by embedding the flickering stimulus on the wings of a flying butterfly in a virtual forest and providing feedback via the antenna of the butterfly. Integration of SSVEP-based BCI and VR can reduce the discomfort of flicker stimulation but also provide subjects with a richer interface and achieve more effective control, greatly improving the practicability of the BCI system for rehabilitation in cognitive impairment.

To further expand the usefulness of the SSVEP-VR system, researchers aim to improve the system by adding more command outputs to interact with the real world and applying it to rehabilitation training for individuals with stroke. For example, an assistant robot can be integrated with the SSVEP-VR system to help individuals with stroke speed up the recovery and improvement of their limb movement. Zhang et al. proposed a brain-driven lower-limb rehabilitation training system [17] that combined VR, BCI and robotics. In this system, a robot and a virtual person carried out corresponding motion behaviors simultaneously, and the individual could realize multiple commands such as left turn, right turn and acceleration. By using this system, the person achieved better rehabilitation training effect with the assistance of the robot. In 2017, Zeng et al. built an information transmission loop between the brain and the ankle-joint assist robot by using an SSVEP paradigm in a VR environment to help patients with weak ability of ankle movement to actively carry out robot-aided rehabilitation [54]. The lowest and highest success rates for individuals controlling the rehabilitation robot with the SSVEP paradigm was 80% and 100% respectively, which verified the feasibility of the scheme.

6. Discussion

As the number of patients with neurological diseases has increased over the past decades, new rehabilitation techniques that facilitate recovery and improve brain – body links are needed. The BCI and VR technology provide a new and promising way of rehabilitation for neurological diseases.

As compared with the simple BCI system, the BCI-VR system does not need too many external devices for the rehabilitation environment because VR can better replace various complex real rehabilitation environments and provide individuals with a rich rehabilitation environment and real experience. In addition, with the rich and vivid information and feedback that VR offers, individuals can now carry out the training process in a small physical space while increasing their enthusiasm and engagement for more active training given a virtual yet immersive environment. By combining both BCI and VR techniques, the neurorehabilitation process can improve performance and reduce learning and training time. The BCI-VR systems might play an increasingly important role in the development and application of neural engineering and rehabilitation medicine.

However, when using the BCI-VR system for rehabilitation, there are still some challenges.

The current information transfer rate of BCI system is not ideal. Although previous studies have shown that a BCI system can achieve relatively fast communication in the context of head-mounted VR devices [7,10–12], future BCI-VR systems need to consider actual needs such as the fluency of the VR user experience and more interaction methods and command numbers between users and VR, so the first priority is to significantly improve the transmission rate of EEG signals.

EEG signals in the BCI system are weak and susceptible to external interference such as motor, electromyography and electrooculography interference. Especially when the individual carries out a lot of movements in the virtual scene, the EEG signal is greatly disturbed by the external environment. Therefore, future research needs to improve the preprocessing performance of EEG signals in the BCI-VR system in real time.

In the BCI-VR system based on an MI paradigm, subjects need much motor imagination training before formally using the system, and the effect of training and the accuracy of brain control in the BCI-VR system vary in each individual. At the same time, the accuracy of brain control in the virtual scene needs to be improved. In the future, the accuracy and generalization performance of the analysis algorithm of EEG needs improvement.

In the BCI-VR system based on P300 and SSVEP paradigms, individuals are in a passive state, and they need to carefully check the stimuli in the VR scene to control the virtual role, which affects the interaction experience between the individual and the virtual role. Therefore, we need to explore a more natural brain–machine interaction mode based on P300 or SSVEP to improve the practical use of the BCI-VR system.

Therefore, with the continuous development of BCI, VR and BCI-VR technology, we need to overcome the above challenges and contribute to a deeper application of BCI-VR technology in rehabilitation of neurological diseases.

7. Conclusion

This narrative review analyzed and characterized the rehabilitation of neurological diseases with 3 major BCI paradigms — MI, P300 and SSVEP-based BCI — with specific focus on using VR as feedback modality. As compared with traditional rehabilitation methods, BCI-VR systems could increase the enthusiasm of the individual in training, increase the fun of training and thus shorten the training cycle, provide more effective feedback, and promote recovery of brain function. However, combining BCI and VR has just started, and there is still a long way to go before it can be effectively used in rehabilitation of individuals with neurological diseases.

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Disclosure of interest

The authors declare that they have no competing interest.

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