康复学报
Rehabilitation Medicine

·综 述·

运动想象脑机接口技术在脑卒中后运动功能康复中的应用

蒋咏春[1,2,3],尹浚骁[4],赵碧仪[1,3,5],王思晴[1,3],区培琳[1,3],李家雯[1,3],张燕妮[1,3],林 强[2,3*]

1 广州医科大学附属第五医院,广东 广州 510700;
2 中山大学附属第七医院,广东 深圳 518107;
3 广州医科大学第五临床学院,广东 广州 510700;
4 广州中医药大学针灸康复临床医学院,广东 广州 510006;
5 暨南大学中医学院,广东 广州 510632
* 通信作者:林强,E-mail:linqiang@sysush.com

收稿日期:2023-04-04;接受日期:2023-07-12
基金项目:广东省自然科学基金面上项目(2023A1515010586);广东省教育科学规划课题(2022GXJK299);
广州市卫生健康科技一般引导项目(20221A011109)
DOI:10.3724/SP.J.1329.2023.06013
开放科学(资源服务)标识码(OSID):

摘要 运动想象脑机接口(MI-BCI)技术通过识别运动想象产生的脑电信号来判断其运动意图,进而实现人脑与外部设备之间的通信与控制。MI-BCI技术在脑卒中后患者的运动功能康复应用中取得肯定疗效,对中、重度肢体运动功能障碍患者的康复也具有很大潜力。本研究总结了国内外MI-BCI技术在脑卒中后运动功能康复中的应用现状(MI-BCI技术的神经调控机制、临床康复应用及存在的问题和可能的解决途径3个方面),以期为MI-BCI技术的临床应用和相关设备研发提供理论支持。MI-BCI技术的神经调控机制主要包括"中枢-外周-中枢"闭环理论["中枢-外周"自上而下的中枢刺激模式(运动想象)与"外周-中枢"自下而上的感觉运动反馈(外置设备带动肢体运动)模式]、神经反馈和赫布理论;临床康复应用主要集中在脑卒中后上肢/下肢运动功能康复、大脑功能网络变化等方面。但MI-BCI技术在临床康复应用中仍存在表现力不佳、治疗剂量不明确、采集信号质量亟待提高、运动想象模式的类别较少和训练周期长等问题。下一步仍需开展MI-BCI技术联合其他中枢神经干预方式相关研究,增加运动想象模式类别等方式以改善MI-BCI技术的康复效果,并开发适用于各个时期脑卒中患者MI-BCI技术训练方案,为中枢神经系统疾病患者的肢体运动康复提供参考。
关键词 脑卒中;神经调控;运动功能康复;运动想象;脑机接口

运动想象(motor imagery,MI)是指在不产生实际动作的情况下,通过大脑想象动作的发生,从而激发与执行这个动作相似的神经元活动[1-2]。运动想象脑机接口(motor imagery brain-computer interface,MI-BCI)技术是指通过计算机采集想象肢体运动产生的脑电信号,将获取到的脑电信号进行预处理、特征提取、分类,进而转化为对外部设备的控制指令,并提供实时反馈[3],实现人脑与外部设备之间通信和控制[4]。近年来,MI-BCI技术在神经康复领域的应用逐渐增多,有研究显示MI-BCI技术在改善脑卒中患者运动功能障碍方面取得良好疗效[5],在中、重度肢体运动功能障碍患者的康复中也具有较大潜力[6]。但是,其相关机制尚不完全明确,且应用过程中还存在一些临床问题未能解决,极大地限制了MI-BCI技术在康复领域中的应用。本研究从MI-BCI技术的原理、神经调控机制、康复应用进展、

引用格式:蒋咏春,尹浚骁,赵碧仪,等. 运动想象脑机接口技术在脑卒中后运动功能康复中的应用[J]. 康复学报,2023,33(6):562-570.
JIANG Y C, YIN J X, ZHAO B Y, et al. Application of motor imagery brain-computer interface on patients with motor dysfunction after stroke [J]. Rehabil Med, 2023,33(6):562-570.
DOI:10.3724/SP.J.1329.2023.06013

存在的问题和可能的解决途径等方面进行阐述，以期为MI-BCI技术的临床应用和相关设备研发提供理论支持。

1 MI-BCI技术的神经调控机制

1.1 基于闭环理论的神经重塑机制

神经可塑性是指神经连接生成和修改的能力，既可以发生在功能与结构层面，也可以发生在突触、细胞和大脑网络结构水平。神经可塑性的触发是中枢神经系统疾病康复的基础。脑卒中患者中枢神经系统受损会导致肢体运动功能障碍。其康复治疗方案可分为中枢干预方式和外周干预方式。其中，中枢干预方式包括经颅磁刺激(transcranial magnetic stimulation，TMS)和经颅电刺激(transcranial electrical stimulation，TES)；外周干预方式包括运动疗法(kinesitherapy)、神经肌肉电刺激(neuromuscular electrical stimulation，NES)。中枢干预方式通过直接刺激或激活脑功能区，增强突触可塑性，从而促进相关脑区的功能恢复，提高肢体运动能力；外周干预方式通过强化感觉输入，将正确的运动模式反馈于中枢，促进功能恢复。也有研究尝试将中枢干预和外周干预2种方式进行整合，可以有效针对脑损伤后皮质功能改变的本质问题，以大脑的可塑性以及神经通路的重塑为基础，促进中枢重塑和外周控制，进而促进神经功能恢复。贾杰[7]提出“中枢-外周-中枢”闭环理论，阐明了MI-BCI系统是将“中枢-外周”自上而下的中枢刺激模式(运动想象)与“外周-中枢”自下而上的感觉运动反馈(外置设备带动肢体运动)相结合。MI-BCI系统借助外置设备重建中枢到外周的神经控制通路[8]，更加符合真实运动模式，理论上更有利于脑卒中后神经可塑性的触发[9-10]，在临床应用方面具有较大潜力。见图1。

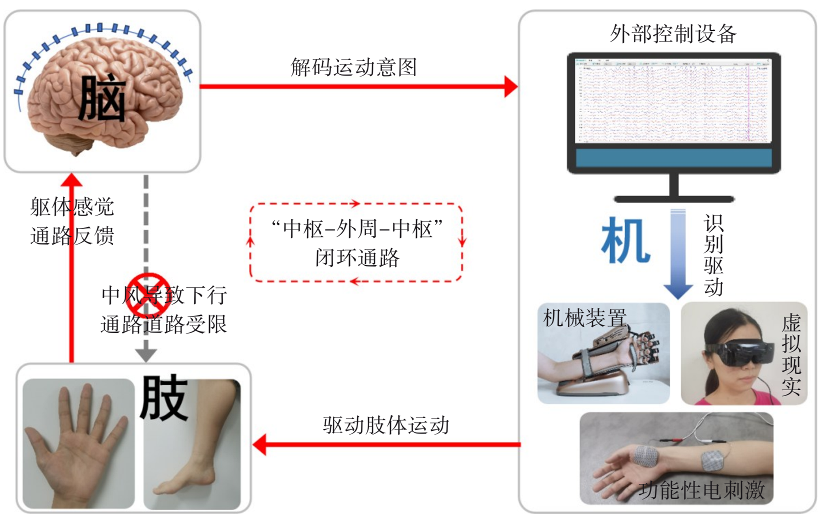

图1 基于“中枢-外周-中枢”闭环理论的MI-BCI康复系统

Figure 1 MI-BCI rehabilitation system based on the "central-peripheral-central" closed-loop theory

1.2 基于神经反馈和赫布理论的脑功能调控机制

1.2.1 神经反馈训练　神经反馈训练是指通过测量特定功能脑区的神经活动，将相关结果转化为视觉、听觉、触觉等形式实时反馈给患者[11]，同时加入奖励机制，有目的地帮助患者调节和训练脑神经活动，以改善对应的脑功能，达到修复受损功能的作用[12]。在MI-BCI训练过程中，患者执行特定动作的想象，采用计算机设备分析获取的脑电信号，若达到系统阈值就会驱动外置设备完成该动作，并将动作相关的视觉和本体感觉反馈至大脑。系统还会根据患者动作的完成程度给予鼓励或评分等信息反馈[13-15]。反复的神经反馈训练可促进正常运动神经回路的重复招募，加强受脑卒中影响的神经元连接，从而改善患者的肢体运动功能[7,16]。

1.2.2 赫布理论　赫布理论被认为是脑机接口系统在神经康复中的另一重要修复机制[13]，是指通过重复的学习或持续的刺激用以增加相关突触前神经元向突触后神经元的传递效能，从而引发经常同时放电的神经元形成的连接增强，有利于受损神经的重塑及功能恢复[13,17]。基于赫布理论，MI-BCI康复训练的过程通过计算机和外置设备，替代或弥补了由于中枢神经系统损伤造成中枢与外周神经之

间的控制中断，反复产生的感觉反馈与运动控制形成闭合的感觉-运动环路刺激有利于受损的中枢神经与外周神经的功能重建[13,18-20]，恢复受损的神经连接，从而促进受损功能康复[21]。

神经反馈是将患者产生的视觉、听觉、触觉等反馈给大脑，是利用"外周-中枢"自下而上的感觉运动反馈，从而有目的地帮助患者调节和训练脑神经活动。赫布理论是通过重复的学习或持续的刺激来增强相关神经元之间的连接，进而修复由于疾病引起的中枢对外周的控制中断。闭环理论是将"中枢-外周"自上而下的中枢刺激模式（运动想象）与"外周-中枢"自下而上的感觉运动反馈（外置设备带动肢体运动）相结合，形成一个完整的闭合链。闭环理论是神经反馈和赫布理论的有机统一。

2　MI-BCI技术的临床康复应用

2.1　MI-BCI技术在脑卒中后运动功能康复领域的应用

既往研究发现基于MI-BCI技术的神经康复训练能够改善脑卒中后患者的运动功能障碍[22-23]；MI-BCI技术与外部控制设备联合可改善脑卒中患者的运动功能障碍[23-26]。

2.1.1　MI-BCI技术在改善脑卒中上肢运动功能方面的应用　FROLOV等[27]采用多中心、随机对照研究，共纳入74例亚慢性期脑卒中患者，随机分为对照组和MI-BCI训练组，对照组接受常规物理治疗和上肢外骨骼设备驱动的手部运动训练，MI-BCI训练组接受常规物理治疗和基于上肢外骨骼驱动的MI-BCI系统训练。与对照组比较，MI-BCI训练组干预后Fugl-Meyer上肢运动功能评定量表（Fugl-Meyer assessment upper extremity scale，FMA-UE）、手臂动作调查测试（action research arm test，ARAT）评分明显更高，研究结果表明基于上肢外骨骼驱动的MI-BCI系统对治疗脑卒中后患者的运动功能障碍具有积极作用。为探究MI-BCI训练能否促进脑卒中患者运动功能恢复，VOURVOPOULOS等[28]纳入4例慢性期脑卒中患者，接受8次基于虚拟现实（virtual reality，VR）系统的MI-BCI上肢运动功能训练，90 min/次，研究结果显示，与治疗前比较，所有患者治疗后FMA-UE评分明显提高，表明基于BCI-VR系统的康复训练对于上肢运动功能的改善可能是有效的，但仍需要进行更大规模的临床试验，以确定其安全性和有效性。

2.1.2　MI-BCI技术在改善脑卒中下肢运动功能方面的应用　足下垂是导致脑卒中患者步态功能障碍的重要因素之一[29-30]。MCCRIMMON等[31]纳入9例慢性脑卒中下肢运动功能障碍患者进行为期4周的MI-BCI联合功能性电刺激（functional electrical stimulation，FES）足背屈训练，研究发现，5例患者治疗后十分钟步行测试（10-minute walking test，10MWT）和六分钟步行试验（6-minute walking test，6MWT）均明显提高，3例患者Fugl-Meyer下肢运动功能评定量表（Fugl-Meyer assessment lower extremity scale，FMA-LE）评分明显提高。

目前针对脑卒中后上肢运动功能障碍的MI-BCI训练研究大多采用FMA-UE、ARAT等功能量表评估作为主要结局指标；而针对脑卒中后下肢运动功能障碍的MI-BCI训练研究，大多采用FMA-LE、6MWT、10MWT等功能量表评估作为主要结局指标。与下肢运动功能研究比较，应用MI-BCI技术改善上肢运动功能障碍的研究更加成熟。可能的主要原因如下：① 大脑皮层中支配上肢运动功能的区域面积较大且位于中部，而支配下肢运动功能的区域面积较小且位于顶部及大脑皮层的内侧面，使上肢运动功能脑区的脑电信号采集较下肢更为容易；② 现有技术难以通过无创的方法对下肢运动学和动力学参数进行精准采集及解码[32]；③ 由于行走涉及多个肌肉运动的精确协调，致使为下肢运动设计适当的反馈机制非常困难[33]。

2.2　MI-BCI技术在脑功能调控方面的应用

既往研究表明，MI-BCI运动康复训练系统的靶点脑区主要包括初级运动皮层（primary motor cortex，M1）、辅助运动区（supplementary motor area，SMA）、运动前区（premotor area，PMA）和初级躯体感觉皮层（primary somatosensory cortex，S1）等。MI-BCI训练的运动想象阶段能够诱发mu节律和beta节律的事件相关去同步化（event-related desynchronization，ERD）[3,34-35]，MI-BCI系统正是通过放置在关键脑区的电极采集、获取相应的脑电信号，在上述的频域（mu/beta）中控制外部设备，完成外周肢体的运动活动。在健康人群的研究中，已有研究显示基于MI-BCI技术的运动想象过程能够激活M1皮层。LIN等[36]通过功能性近红外光谱技术（functional near-infrared spectroscopy，fNIRS）研究发现健康受试者非利手经过10次MI-BCI训练后对侧大脑M1区激活较训练前明显增加。脑卒中患者经过MI-BCI训练后，健侧SMA和中央前回（包括M1和PMA）的低频波动振幅（amplitude of low frequency fluctuation， ALFF)较训练前明显升高,同时发现ALFF指标越高,运动功能恢复越好[37]。

大脑执行运动或认知任务需要多个皮层区域的参与,这些区域相互连接并交换信息。有研究显示,MI-BCI训练可使大脑活动和连接重新正常化[37],增强脑区连通性,从而促进脑卒中后功能恢复[37-39]。VÁRKUTI等[40]研究发现脑卒中患者接受MI-BCI治疗后,额顶叶区域间的功能连接较治疗前有较大程度的增强;此外,SMA、患侧M1以及相关的视觉空间系统部分功能连接增加与个体上肢功能的改善相关。

综上,MI-BCI训练可能通过改善大脑功能网络变化,从而促进肢体运动功能的恢复。但目前该领域的研究对象多为健康人群,而对脑卒中患者的研究较少。虽然MI-BCI技术在健康人群中的应用研究结果可为脑卒中患者提供参考依据,但由于脑卒中患者大脑的异质性高[41-42]、脑结构受损导致脑激活模式改变[43-45],未来MI-BCI研究需要更多地关注脑卒中患者,深入探索MI-BCI训练对脑卒中患者大脑功能网络变化的影响。

3 MI-BCI技术临床康复应用中存在的问题及其解决途径

3.1 MI-BCI表现力不佳

既往研究发现,部分受试者虽然接受了BCI培训,但仍无法有效控制MI-BCI系统[46-47],常被称为BCI非响应者[48]。造成BCI非响应的原因有很多,多数研究从工科的角度分析认为是BCI信号采集方式的问题,从临床角度的归纳总结还不深入。有研究认为,造成BCI非响应的主要临床因素之一为受损脑区致运动皮质本身激活不足和受损脑区致感觉皮层对运动皮层的易化作用减退。① 虽然MI-BCI训练可以促进损伤脑区激活,但由于神经元活动与脑损伤程度、运动任务的复杂性有关[49],当脑区严重受损时,由于病灶本身和瘫痪肢体废用[50],患侧脑区皮层激活不足或激活阈值较高,导致BCI设备对脑电信号和运动意图的识别率降低,无法有效控制外接设备[51]。② 根据半球间抑制(interhemispheric inhibition,IHI)理论,健侧脑区对于受损严重的患侧脑区抑制作用会进一步限制患侧运动皮质兴奋性促发[52-54],使得神经元募集差,难以控制BCI外置设备,最终导致训练效力不佳[55]。③ 患者脑损伤后多伴有不同程度的感知觉功能减退和神经通路改变,导致其外周感觉输入减少,感觉皮层的激活减少,对于运动皮层的易化作用减退[56-57],导致MI-BCI训练后运动功能的重塑效果不理想。④ 此外,运动想象能力[58-60]、认知功能、运动想象任务的复杂程度[60]等因素可能也会影响MI-BCI的表现力。

联合其他中枢干预方式,可能为改善MI-BCI表现力不佳提供新思路。HONG等[61]研究发现,与单纯MI-BCI训练比较,脑卒中患者进行MI-BCI训练前先给予经颅直流电刺激(transcranial direct current stimulation,tDCS)(将tDCS阳极放置在大脑患侧M1区,阴极放置在健侧M1区),其同侧皮质脊髓束和双侧胼胝体的白质完整性明显增加,提示tDCS联合MI-BCI训练可更好地促进神经可塑性。TUCHAN等[62]研究发现,感觉阈值体感电刺激(sensory threshold somatosensory electrical stimulation,st-SES)可以调节感觉运动皮层的活动,激活感觉轴突以传递本体感觉信号,促进手部运动功能的恢复。MI结合st-SES训练可增强低BCI表现受试者感觉运动区域的激活和额顶网络之间的皮质连接,不同MI任务之间的分类精度也显著提高[63-64]。但是MI-BCI技术最佳的中枢干预方式、干预时间、干预靶点脑区、干预效果尚无定论,仍需进一步研究。

3.2 MI-BCI技术的治疗剂量不明确

MI-BCI技术的治疗剂量包括治疗疗程、治疗频率、治疗持续时间、治疗强度等。YOUNG等[65]研究发现,MI-BCI疗程和强度会影响神经系统的改善。MI-BCI训练时间过长会引起患者疲劳和情绪的变化[66-67]。部分研究以健康人为受试对象,对脑卒中患者选择合适的治疗剂量有一定借鉴意义。LIN等[36]研究发现,与低频MI-BCI训练组(30 min/次,1次/2 d)比较,高频MI-BCI训练组(30 min/次,1次/d)在5次MI-BCI训练后可见更加明显的M1皮质响应。明确MI-BCI训练的持续时间、频率和强度如何影响中枢神经系统的可塑性和临床功能,对于制定MI-BCI康复计划至关重要。未来还需要更多有关脑卒中患者MI-BCI训练强度、疗程的临床研究,以进一步提高MI-BCI技术治疗的有效性。

3.3 MI-BCI信号质量亟待提高

MI-BCI作为一种非侵入式的脑机接口技术,虽然具备安全、无创的优点,但其通过固定在头皮上的穿戴设备对大脑信息进行提取和解码,脑电信号的强度和空间分辨率会由于颅骨和颅内容物对信号传输的削弱作用而有所降低,且易受肌电信号、高频噪声等因素干扰,难以精准确定发出信号的脑区或者相应神经元活动,采集的信号质量不高,从

而影响MI-BCI技术治疗效果。因此,准确读取大脑信号,提高信号采集质量是MI-BCI技术亟待解决的关键问题。与单一模态MI-BCI系统比较,联合其他神经成像方式的多模态脑机接口系统,能够优势互补,以获得更加精准的脑电信号,如功能性磁共振成像技术(functional magnetic resonance imaging,fMRI)以其高空间分辨率,与MI-BCI系统联合应用可提高MI-BCI信号读取度;ZICH等[58]将运动想象期间的脑电图(electroencephalogram,EEG)与fMRI联合,从干扰心电图(electrocardiogram,ECG)和磁共振成像(magnetic resonance imaging,MRI)梯度的伪影中校正EEG信号,对脑电图进行实时反馈,可有效提高EEG的读取度和时空分辨率。此外,fNIRS-BCI系统因其时空分辨率适中、不受电磁干扰的影响、操作简单方便、受试者头部运动对其影响较小等优点,在神经康复领域的应用越来越多。YIN等[68]研究发现使用EEG-fNIRS结合的多模态BCI可以解决单一模态的信号质量低的局限性,有效识别受试者的运动意图,提高MI-BCI信号采集质量。

联合fMRI或fNIRS等其他神经成像方式的多模态脑机接口系统能够提高信号采集质量,可在一定程度上缓解MI-BCI系统无法精准定位患者运动想象过程中所激活脑区位置的困境,提高系统驱动外部设备运动的准确性,增强MI-BCI技术的治疗效果。但目前该领域的研究尚不完善,如何提高MI-BCI信号采集质量以提高脑卒中患者MI-BCI治疗效果仍需进一步探讨。

3.4 MI-BCI运动想象模式的类别较少

目前,基于脑电图的运动想象模式类别较少,临床领域的研究主要集中在双手或手与脚之间的二分类运动想象任务,致使指令集的数量较为受限。运动想象是通过对肢体运动的心理模拟,从而诱发感觉运动皮层的神经元活动,不同于基于稳态视觉诱发电位(steady-state visual evoked potential,SSVEP)和P300范式的脑机接口系统,能够通过给予受试者不同刺激实现各种不同类型的指令。MI-BCI系统需要受试者自行调节感觉运动节律(sensorimotor rhythms,SMR)中的mu节律和beta节律完成想象任务,故灵活转换各种运动想象任务对于受试者而言较为困难。不同BCI范式相结合的串行混合脑机接口系统可能是增加运动想象指令集数量的新方法。如SSVEP和MI信号串联融合的多模态脑机接口系统,能够通过调整简单指令的执行顺序完成复杂操作。在该类BCI系统中,受试者每个时刻只需进行一个任务,丰富指令集不会增加受试者的训练负担[69]。因此,基于串联融合策略的多模态脑机接口系统可能有助于弥补MI-BCI系统运动想象目标指令受限的缺陷。

3.5 MI-BCI训练周期长

为使受试者更好地控制MI-BCI系统,受试者在信号校准阶段需要学习如何通过转换MI任务模式对脑电信号进行调整[70]。运动想象训练有助于在执行不同运动想象任务时产生独特且稳定的脑电信号,增强MI-EEG的特异性。因此,受试者在训练前期需要耗费大量时间学习如何控制大脑节律。由于时间、环境、自身状态等因素对脑电信号的影响较大[71],因此初学受试者在不同时间执行同一运动想象任务的信号存在差异性,提供准确的EEG特征将受影响,从而导致错误反馈。为实现脑电信号分类的高精准性,需要获取足够的脑电数据以形成个性化的信号分类器。但长时间的校准训练及频繁发生的错误反馈易使受试者感到疲劳和沮丧,从而产生抵触情绪,无法获得良好的训练体验[72-73]。因此,缩短运动想象阶段的训练时间是MI-BCI系统的关键问题之一。有学者认为基于不同EEG范式相结合的多模态脑机接口系统可为提高运动想象训练效果提供新思路。YU等[74]提出了一种联合MI和SSVEP的多模态脑机接口系统,可提取受试者基于MI和SSVEP混合特征的相关脑电信号,结果表明同时执行视觉反馈任务和运动想象任务能够有效提高MI-BCI系统的准确性,为运动想象训练提供连续的正向反馈,有利于维持受试者对当下任务的兴趣和注意力,提高训练效果,缩短训练时间。但目前针对该领域的研究较为缺乏,未来研究仍需要开发更多MI-BCI系统的优化治疗方案以满足脑卒中患者的训练需求。

4 小 结

基于“中枢-外周-中枢”闭环理论的MI-BCI训练通过自上而下的中枢刺激模式与自下而上的感觉运动反馈相结合,形成感觉-运动闭环。此外,患者通过反复训练并给予鼓励等信息反馈,增强神经元间的连接,可诱导大脑重塑性。因此,MI-BCI训练理论上更有利于患者的肢体功能重建,临床应用更具潜力。但是,MI-BCI技术在临床康复中的应用仍存在一些困难。首先,脑卒中患者由于脑损伤致患侧脑区皮层激活不足或激活阈值调高,BCI设备

对于脑电信号和运动意图的识别率降低,无法有效控制外接设备,导致中枢到外周的通路薄弱。其次,脑卒中患者感知觉功能减退,其外周感觉输入和感觉皮层的激活减少,对于运动皮层的易化作用减退,导致外周到中枢通路薄弱。MI-BCI技术联合其他中枢神经干预方式,增加运动想象模式类别方式可改善其康复效果。但未来仍需要更多相关临床研究,开发适用于各个时期脑卒中患者MI-BCI训练方案,为中枢神经系统疾病患者的肢体运动康复提供新方向。

参考文献

[1] RUFFINO C, GAVEAU J, PAPAXANTHIS C, et al. An acute session of motor imagery training induces use-dependent plasticity [J]. Sci Rep, 2019, 9(1): 20002.

[2] SZAMEITAT A J, SHEN S, STERR A. Motor imagery of complex everyday movements. An fMRI study [J]. NeuroImage, 2007, 34(2): 702-713.

[3] SINGH A, HUSSAIN A A, LAL S, et al. A comprehensive review on critical issues and possible solutions of motor imagery based electroencephalography brain-computer interface [J]. Sensors, 2021, 21(6): 2173.

[4] FUMANAL-IDOCIN J, WANG Y K, LIN C T, et al. Motor-imagery-based brain-computer interface using signal derivation and aggregation functions [J]. IEEE Trans Cybern, 2022, 52(8): 7944-7955.

[5] 何艳,张通. 脑机接口技术在慢性脑卒中患者上肢康复中的研究进展[J]. 中国康复理论与实践,2021,27(3):277-281.
HE Y, ZHANG T. Advance in application of brain-computer interface for upper limb rehabilitation for patients with chronic stroke (review) [J]. Chin J Rehabil Theory Pract, 2021, 27(3): 277-281.

[6] PICHIORRI F, MORONE G, PETTI M, et al. Brain-computer interface boosts motor imagery practice during stroke recovery [J]. Ann Neurol, 2015, 77(5): 851-865.

[7] 贾杰. "中枢-外周-中枢"闭环康复:脑卒中后手功能康复新理念[J]. 中国康复医学杂志,2016,31(11):1180-1182.
JIA J. "central-peripheral-central" closed-loop rehabilitation: a new concept of hand function rehabilitation after stroke [J]. Chin J Rehabil Med, 2016, 31(11): 1180-1182.

[8] WIERZGAŁA P, ZAPAŁA D, WOJCIK G M, et al. Most popular signal processing methods in motor-imagery BCI: a review and meta-analysis [J]. Front Neuroinform, 2018, 12: 78.

[9] NIERHAUS T, VIDAURRE C, SANNELLI C, et al. Immediate brain plasticity after one hour of brain-computer interface (BCI) [J]. J Physiol, 2021, 599(9): 2435-2451.

[10] WANG Z P, CHEN L, YI W B, et al. Enhancement of cortical activation for motor imagery during BCI-FES training [C]//2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC). Honolulu, HI, USA: IEEE, 2018: 2527-2530.

[11] 王萌亚,王仲朋,陈龙,等. 卒中后运动神经反馈康复训练研究进展与前景[J]. 中国生物医学工程学报,2019,38(6):742-752.
WANG M Y, WANG Z P, CHEN L, et al. Research progress and prospects of motor neurofeedback rehabilitation training after stroke [J]. Chin J Biomed Eng, 2019, 38(6): 742-752.

[12] SITARAM R, ROS T, STOECKEL L, et al. Closed-loop brain training: the science of neurofeedback [J]. Nat Rev Neurosci, 2017, 18(2): 86-100.

[13] MANE R, CHOUHAN T, GUAN C T. BCI for stroke rehabilitation: motor and beyond [J]. J Neural Eng, 2020, 17(4): 041001.

[14] WANG Z P, CAO C, CHEN L, et al. Multimodal neural response and effect assessment during a BCI-based neurofeedback training after stroke [J]. Front Neurosci, 2022, 16: 884420.

[15] SPYCHALA N, DEBENER S, BONGARTZ E, et al. Exploring self-paced embodiable neurofeedback for post-stroke motor rehabilitation [J]. Front Hum Neurosci, 2019, 13: 461.

[16] VARGAS P, SITARAM R, SEPÚLVEDA P, et al. Weighted neurofeedback facilitates greater self-regulation of functional connectivity between the primary motor area and cerebellum [J]. J Neural Eng, 2021, 18(5): 1-14.

[17] 陈树耿,贾杰. 脑机接口在脑卒中手功能康复中的应用进展[J]. 中国康复理论与实践,2017,23(1):23-26.
CHEN S G, JIA J. Application of brain-computer interface in rehabilitation of hand function after stroke (review) [J]. Chin J Rehabil Theory Pract, 2017, 23(1): 23-26.

[18] TING W K C, FADUL F A R, FECTEAU S, et al. Neurostimulation for stroke rehabilitation [J]. Front Neurosci, 2021, 15: 649459.

[19] DOBKIN B H. Brain-computer interface technology as a tool to augment plasticity and outcomes for neurological rehabilitation [J]. J Physiol, 2007, 579(3): 637-642.

[20] BIRBAUMER N, COHEN L G. Brain-computer interfaces: communication and restoration of movement in paralysis [J]. J Physiol, 2007, 579(Pt 3): 621-636.

[21] REMSIK A, YOUNG B, VERMILYEA R, et al. A review of the progression and future implications of brain-computer interface therapies for restoration of distal upper extremity motor function after stroke [J]. Expert Rev Med Devices, 2016, 13(5): 445-454.

[22] MATTIA D, PICHIORRI F, COLAMARINO E, et al. The Promotoer, a brain-computer interface-assisted intervention to promote upper limb functional motor recovery after stroke: a study protocol for a randomized controlled trial to test early and long-term efficacy and to identify determinants of response [J]. BMC Neurol, 2020, 20(1): 254.

[23] KHAN M A, DAS R, IVERSEN H K, et al. Review on motor imagery based BCI systems for upper limb post-stroke neurorehabilitation: from designing to application [J]. Comput Biol Med, 2020, 123: 103843.

[24] BAI Z F, FONG K N K, ZHANG J J, et al. Immediate and long-term effects of BCI-based rehabilitation of the upper extremity after stroke: a systematic review and meta-analysis [J]. J Neuroeng Rehabil, 2020, 17(1): 57.

[25] LEE S H, KIM S S, LEE B H. Action observation training and brain-computer interface controlled functional electrical stimulation enhance upper extremity performance and cortical activation

in patients with stroke: a randomized controlled trial [J]. Physiother Theory Pract, 2022, 38(9): 1126-1134.
[26] LI C, WEI J Y, HUANG X Q, et al. Effects of a brain-computer interface-operated lower limb rehabilitation robot on motor function recovery in patients with stroke [J]. J Healthc Eng, 2021, 2021: 4710044.
[27] FROLOV A A, MOKIENKO O, LYUKMANOV R, et al. Post-stroke rehabilitation training with a motor-imagery-based brain-computer interface (BCI)-controlled hand exoskeleton: a randomized controlled multicenter trial [J]. Front Neurosci, 2017, 11: 400.
[28] VOURVOPOULOS A, PARDO O M, LEFEBVRE S, et al. Effects of a brain-computer interface with virtual reality (VR) neurofeedback: a pilot study in chronic stroke patients [J]. Front Hum Neurosci, 2019, 13: 210.
[29] ALNAJJAR F, ZAIER R, KHALID S, et al. Trends and technologies in rehabilitation of foot drop: a systematic review [J]. Expert Rev Med Devices, 2021, 18(1): 31-46.
[30] PRENTON S, HOLLANDS K L, KENNEY L P J, et al. Functional electrical stimulation and ankle foot orthoses provide equivalent therapeutic effects on foot drop: a meta-analysis providing direction for future research [J]. J Rehabil Med, 2018, 50(2): 129-139.
[31] MCCRIMMON C M, KING C E, WANG P T, et al. Brain-controlled functional electrical stimulation therapy for gait rehabilitation after stroke: a safety study [J]. J Neuroeng Rehabil, 2015, 12: 57.
[32] MANE R, WU Z Z, WANG D. Poststroke motor, cognitive and speech rehabilitation with brain-computer interface: a perspective review [J]. Stroke Vasc Neurol, 2022, 7(6): 541-549.
[33] LENNON O, TONELLATO M, DEL FELICE A, et al. A systematic review establishing the current state-of-the-art, the limitations, and the DESIRED checklist in studies of direct neural interfacing with robotic gait devices in stroke rehabilitation [J]. Front Neurosci, 2020, 14: 578.
[34] TAKEMI M, MAEDA T, MASAKADO Y, et al. Muscle-selective disinhibition of corticomotor representations using a motor imagery-based brain-computer interface [J]. NeuroImage, 2018, 183: 597-605.
[35] LI F L, PENG W J, JIANG Y L, et al. The dynamic brain networks of motor imagery: time-varying causality analysis of scalp EEG [J]. Int J Neural Syst, 2019, 29(1): 1850016.
[36] LIN Q, ZHANG Y N, ZHANG Y J, et al. The frequency effect of the motor imagery brain computer interface training on cortical response in healthy subjects: a randomized clinical trial of functional near-infrared spectroscopy study [J]. Front Neurosci, 2022, 16: 810553.
[37] HU M J, CHENG H J, JI F, et al. Brain functional changes in stroke following rehabilitation using brain-computer interface-assisted motor imagery with and without tDCS: a pilot study [J]. Front Hum Neurosci, 2021, 15: 692304.
[38] WANG Y H, LUO J J, GUO Y Z, et al. Changes in EEG brain connectivity caused by short-term BCI neurofeedback-rehabilitation training: a case study [J]. Front Hum Neurosci, 2021, 15: 627100.
[39] 吴琼,任诗媛,乐赞,等. 脑机接口综合康复训练对亚急性期脑卒中疗效的静息态功能磁共振研究[J]. 中国康复理论与实践,2020,26(1):77-84.
WU Q, REN S Y, YUE Z, et al. Brain-computer interface and comprehensive training for stroke: a resting state functional magnetic resonance imaging study [J]. Chin J Rehabil Theory Pract, 2020, 26(1): 77-84.
[40] VÁRKUTI B, GUAN C T, PAN Y Z, et al. Resting state changes in functional connectivity correlate with movement recovery for BCI and robot-assisted upper-extremity training after stroke [J]. Neurorehabil Neural Repair, 2013, 27(1): 53-62.
[41] MESCHIA J F. Addressing the heterogeneity of the ischemic stroke phenotype in human genetics research [J]. Stroke, 2002, 33(12): 2770-2774.
[42] KHAN W, EGOROVA N, KHLIF M S, et al. Three-tissue compositional analysis reveals *in-vivo* microstructural heterogeneity of white matter hyperintensities following stroke [J]. NeuroImage, 2020, 218: 116869.
[43] GREFKES C, FINK G R. Noninvasive brain stimulation after stroke: it is time for large randomized controlled trials! [J]. Curr Opin Neurol, 2016, 29(6): 714-720.
[44] REHME A K, EICKHOFF S B, ROTTSCHY C, et al. Activation likelihood estimation meta-analysis of motor-related neural activity after stroke [J]. NeuroImage, 2012, 59(3): 2771-2782.
[45] LIM S B, ENG J J. Increased sensorimotor cortex activation with decreased motor performance during functional upper extremity tasks poststroke [J]. J Neurol Phys Ther, 2019, 43(3): 141-150.
[46] JEUNET C, N'KAOUA B, SUBRAMANIAN S, et al. Predicting mental imagery-based BCI performance from personality, cognitive profile and neurophysiological patterns [J]. PLoS One, 2015, 10(12): e0143962.
[47] LEEUWIS N, PAAS A, ALIMARDANI M. Vividness of visual imagery and personality impact motor-imagery brain computer interfaces [J]. Front Hum Neurosci, 2021, 15: 634748.
[48] YAO L, SHENG X J, MRACHACZ-KERSTING N, et al. Performance of brain-computer interfacing based on tactile selective sensation and motor imagery [J]. IEEE Trans Neural Syst Rehabil Eng, 2018, 26(1): 60-68.
[49] HOYER E H, CELNIK P A. Understanding and enhancing motor recovery after stroke using transcranial magnetic stimulation [J]. Restor Neurol Neurosci, 2011, 29(6): 395-409.
[50] PAGGIARO A, BIRBAUMER N, CAVINATO M, et al. Magnetoencephalography in stroke recovery and rehabilitation [J]. Front Neurol, 2016, 7: 35.
[51] THOMPSON M C. Critiquing the concept of BCI illiteracy [J]. Sci Eng Ethics, 2019, 25(4): 1217-1233.
[52] BODDINGTON L J, REYNOLDS J N J. Targeting interhemispheric inhibition with neuromodulation to enhance stroke rehabilitation [J]. Brain Stimul, 2017, 10(2): 214-222.
[53] CASULA E P, PELLICCIARI M C, BONNÌ S, et al. Evidence for interhemispheric imbalance in stroke patients as revealed by combining transcranial magnetic stimulation and electroencephalogra-

phy [J]. Hum Brain Mapp, 2021, 42(5): 1343-1358.

[54] GREFKES C, FINK G R. Disruption of motor network connectivity post-stroke and its noninvasive neuromodulation [J]. Curr Opin Neurol, 2012, 25(6): 670-675.

[55] DODD K C, NAIR V A, PRABHAKARAN V. Role of the contralesional *vs.* ipsilesional hemisphere in stroke recovery [J]. Front Hum Neurosci, 2017, 11: 469.

[56] PUNDIK S, SCOCO A, SKELLY M, et al. Greater cortical thickness is associated with enhanced sensory function after arm rehabilitation in chronic stroke [J]. Neurorehabil Neural Repair, 2018, 32(6/7): 590-601.

[57] HARRISON T C, SILASI G, BOYD J D, et al. Displacement of sensory maps and disorganization of motor cortex after targeted stroke in mice [J]. Stroke, 2013, 44(8): 2300-2306.

[58] ZICH C, DEBENER S, KRANCZIOCH C, et al. Real-time EEG feedback during simultaneous EEG-fMRI identifies the cortical signature of motor imagery [J]. NeuroImage, 2015, 114: 438-447.

[59] PILLETTE L, LOTTE F, N'KAOUA B, et al. Why we should systematically assess, control and report somatosensory impairments in BCI-based motor rehabilitation after stroke studies? [J]. Neuroimage Clin, 2020, 28: 102417.

[60] 左词立,毛盈,刘倩倩,等.不同复杂度汉字模式下运动想象脑机接口性能研究[J].生物医学工程学杂志,2021,38(3):417-424,454.
ZUO C L, MAO Y, LIU Q Q, et al. Research on performance of motor-imagery-based brain-computer interface in different complexity of Chinese character patterns [J]. J Biomed Eng, 2021, 38(3): 417-424, 454.

[61] HONG X, LU Z K, TEH I, et al. Brain plasticity following MI-BCI training combined with tDCS in a randomized trial in chronic subcortical stroke subjects: a preliminary study [J]. Sci Rep, 2017, 7(1): 9222.

[62] TU-CHAN A P, NATRAJ N, GODLOVE J, et al. Effects of somatosensory electrical stimulation on motor function and cortical oscillations [J]. J Neuroeng Rehabil, 2017, 14(1): 113.

[63] CHEN L, ZHANG L, WANG Z P, et al. The effects of sensory threshold somatosensory electrical stimulation on users with different MI-BCI performance [J]. Front Neurosci, 2022, 16: 909434.

[64] ZHANG L, CHEN L, WANG Z P, et al. Enhancing visual-guided motor imagery performance via sensory threshold somatosensory electrical stimulation training [J]. IEEE Trans Biomed Eng, 2022, 70(2): 756-765.

[65] YOUNG B M, NIGOGOSYAN Z, WALTON L M, et al. Dose-response relationships using brain-computer interface technology impact stroke rehabilitation [J]. Front Hum Neurosci, 2015, 9: 361.

[66] 王仲朋,陈龙,何峰,等.面向康复与辅助应用的脑-机接口趋势与展望[J].仪器仪表学报,2017,38(6):1307-1318.
WANG Z P, CHEN L, HE F, et al. Development trend and prospect of BCI technology facing rehabilitation and assisting applications [J]. Chin J Sci Instrum, 2017, 38(6): 1307-1318.

[67] SREEDHARAN S, SITARAM R, PAUL J S, et al. Brain-computer interfaces for neurorehabilitation [J]. Crit Rev Biomed Eng, 2013, 41(3): 269-279.

[68] YIN X X, XU B L, JIANG C H, et al. A hybrid BCI based on EEG and fNIRS signals improves the performance of decoding motor imagery of both force and speed of hand clenching [J]. J Neural Eng, 2015, 12(3): 036004.

[69] 迟新一,崔红岩,陈小刚.结合稳态视觉诱发电位的多模态脑机接口研究进展[J].中国生物医学工程学报,2022,41(2):204-213.
CHI X Y, CUI H Y, CHEN X G. Advances in multi-modal brain-computer interface combined with steady-state visual evoked potential [J]. Chin J Biomed Eng, 2022, 41(2): 204-213.

[70] JEUNET C, JAHANPOUR E, LOTTE F. Why standard brain-computer interface (BCI) training protocols should be changed: an experimental study [J]. J Neural Eng, 2016, 13(3): 036024.

[71] ISLAM M K, RASTEGARNIA A, YANG Z. Methods for artifact detection and removal from scalp EEG: a review [J]. Neurophysiol Clin, 2016, 46(4/5): 287-305.

[72] GUO N, WANG X J, DUANMU D H, et al. SSVEP-based brain computer interface controlled soft robotic glove for post-stroke hand function rehabilitation [J]. IEEE Trans Neural Syst Rehabil Eng, 2022, 30: 1737-1744.

[73] ZIADEH H, GULYAS D, NIELSEN L D, et al. Mine works better: examining the influence of embodiment in virtual reality on the sense of agency during a binary motor imagery task with a brain-computer interface [J]. Front Psychol, 2021, 12: 806424.

[74] YU T Y, XIAO J, WANG F Y, et al. Enhanced motor imagery training using a hybrid BCI with feedback [J]. IEEE Trans Biomed Eng, 2015, 62(7): 1706-1717.

Application of Motor Imagery Brain−Computer Interface on Patients with Motor Dysfunction after Stroke

JIANG Yongchun[1,2,3], YIN Junxiao[4], ZHAO Biyi[1,3,5], WANG Siqing[1,3], OU Peilin[1,3], LI Jiawen[1,3], ZHANG Yanni[1,3], LIN Qiang[2,3*]
[1] *The Fifth Affiliated Hospital of Guangzhou Medical University, Guangzhou, Guangdong 510700, China;*
[2] *The Seventh Affiliated Hospital of Sun Yat−sen University, Shenzhen, Guangdong 518107, China;*
[3] *School of Fifth Clinical College, Guangzhou Medical University, Guangzhou, Guangdong 510700, China;*
[4] *Clinical Medical College of Acupuncture Moxibustion and Rehabilitation, Guangzhou University of Chinese Medicine, Guangzhou, Guangdong 510006, China;*
[5] *School of Traditional Chinese Medicine, Jinan University, Guangzhou, Guangdong 510632, China*
*Correspondence: LIN Qiang, E-mail: linqiang@sysush.com

ABSTRACT Motor imagery brain-computer interface (MI-BCI) technology determines the motor intention by recognizing the electroencephalogram (EEG) signals generated by motor imagery and then realizes the communication and control between the human brain and external devices. MI-BCI technology had achieved a positive effect in the application of motor function rehabilitation of patients after stroke, which has excellent potential for rehabilitating patients with moderate and severe limb motor dysfunctions. This paper summarizes the domestic and international research status evidence (neuroregulatory mechanism, clinical rehabilitation application, existing problems and possible solutions) of MI-BCI technology in motor function rehabilitation after stroke to provide theoretical support for the clinical application of MI-BCI technology and the development of related equipment. The neural regulation mechanisms of MI-BCI technology mainly include the "central-peripheral-central" closed-loop theory [the top-down central stimulation mode of "central-periphery" (motor imagery) and the down-top sensorimotor feedback mode of "peripheral-central" (limb movement driven by external devices)], neurofeedback and Hebb theory. The clinical rehabilitation application mainly focuses on rehabilitating upper/lower limb motor function and the changes in brain functional networks after stroke. However, there are still some problems in applying MI-BCI technology in clinical rehabilitation, such as poor performance, unclear treatment dose, the quality of collected signals needing to be improved, few categories of motor imagery, and long training cycle. The future study is needed to conduct research on MI-BCI technology combined with other central nervous system intervention, improve the rehabilitation effect of MI-BCI technology by increasing the categories of motor imagery modalities, develop MI-BCI training programs for stroke patients in all periods, and provide a reference for limb movement rehabilitation of patients with central nervous system diseases.
KEY WORDS stroke; neural regulation; motor functional rehabilitation; motor imagery; brain-computer interface
DOI:10.3724/SP.J.1329.2023.06013

（上接第 553 页）

Conception on the Teaching of "Rehabilitation Pharmacology" Based on Rehabilitation Pharmacy Services in Rehabilitation Majors

WANG Yulu, XU Wei, WANG Yinghao, LIN Ya, NAN Lihong, CHEN Yan, LIN Yu*
School of Pharmacy, Fujian University of Traditional Chinese Medicine, Fuzhou, Fujian 350122, China
*Correspondence: LIN Yu, E-mail: yulam@163.com

ABSTRACT Rehabilitation medicine is an important part of modern medicine, and rehabilitation medicine services are mostly provided for populations with diseases and functional disorders. It is necessary to comprehensively use rehabilitation treatment, functional exercise and drug treatment. However, the current existing training program for rehabilitation medicine related professionals does not pay enough attention to prioritize the "rehabilitation pharmacology" course, and there are relatively few inadequate "rehabilitation pharmacology" textbooks suitable for the training of rehabilitation medicine talents professionals. This study elaborates from three aspects: the course overview of "rehabilitation pharmacology" (the relationship between pharmacology and rehabilitation pharmacy, the concept and orientation of rehabilitation pharmacology and the necessity of rehabilitation pharmacology courses), the designing of "rehabilitation pharmacology" course teaching and practice (basic characteristics of course teaching, teaching content design, selection of teaching materials and teaching method design) and the teaching prospect of "rehabilitation pharmacology", in order to provide reference for colleges and universities to develop "rehabilitation pharmacology" courses based on rehabilitation pharmacy services in rehabilitation medicine related majors.
KEY WORDS rehabilitation pharmacology; rehabilitation pharmacy services; rehabilitation education; course design
DOI:10.3724/SP.J.1329.2023.06011