

·综述·

卒中后抑郁及其非药物治疗研究进展

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摘要 卒中是我国居民致死的首位病因,约30%的患者会出现卒中后抑郁(post-stroke depression, PSD)。卒中的严重程度,类型,病灶的体积、位置和侧别,生活环境,神经递质,神经炎症,神经内分泌功能紊乱,线粒体功能障碍等均参与了PSD的发生和发展。非药物治疗是PSD的主要治疗方法中的重要一类。本综述总结了心理治疗、非侵入性脑刺激、电针、深部脑刺激等常规非药物治疗方法的研究进展;重点分析了脑机接口技术的研究进展,并探讨其在PSD治疗中的潜在治疗价值及发展方向。研究PSD的病理生理机制并研发新的治疗方法,对改善患者预后有重要临床意义。

关键词 卒中;卒中后抑郁;非药物治疗;脑机接口

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Research Progress on Post-Stroke Depression and Its Non-Pharmacological Treatments LI Shengjie, XU Xinran, CHEN Danyang, LI Zhijun, LIU Na, CHEN Shiling, TANG Zhouping, TANG Yingxin.
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Abstract Stroke is the leading cause of death among residents in China, with approximately 30% of patients experiencing post-stroke depression (PSD). The severity and type of the stroke, as well as the volume, location, and lateralization of the cerebral lesion, living environment of patients, neurotransmitters, neuroinflammation, neuroendocrine dysfunction, and mitochondrial dysfunction are all implicated in the onset and progression of PSD. Non-pharmacological treatments represent a significant category within the primary treatment methods for PSD. This review summarizes the research progress on conventional non-pharmacological methods such as psychotherapy, non-invasive brain stimulation, electroacupuncture, and deep brain stimulation; it particularly highlights the progress in brain-computer interface technology and discusses its potential therapeutic value and future directions in the management of PSD. Investigating the pathophysiological mechanisms of PSD and developing innovative treatment strategies are of paramount clinical importance for enhancing patient outcomes.

Keywords stroke; post-stroke depression; non-pharmacological treatment; brain-computer interface

根据《中国脑卒中防治报告2021》,卒中是我国位居首位的过早死亡原因^[1];2019年的全球疾病负担研究数据显示,卒中是中国伤残调整生命年(disability-adjusted life years, DALYs)的第一大病因^[2]。卒中后,除了肢体运动、感觉、语言及认知障碍等常见并发症外,约30%的患者会出现卒中后抑郁(post-stroke depression, PSD),表现为快感缺失、抑郁及其他各种心理障碍^[3]。PSD可以发生在卒中后任何时期,第1年患病率最高,此后逐渐降低,但超过50%的患者被诊断为伴有持续性抑郁(持久的情绪低落)的轻度抑郁^[4]。PSD与患者的转归不良、病死率增高相关^[5]。及时诊断PSD,并给予有效治疗,有助于改善患者预后。

PSD的治疗主要分为药物治疗和非药物治疗。药物治疗主要包括:①5-羟色胺再摄取抑制剂(selective serotonin reuptake inhibitors, SSRIs),如氟西汀、帕罗西汀、舍曲林等;②去甲肾上腺素能和5-羟色胺能抗抑郁剂(noradrenaline and specific serotonergic antidepressants, NaSSAs),代表药物为

米氮平;③5-羟色胺和去甲肾上腺再摄取抑制剂(serotonin and noradrenaline reuptake inhibitors, SNRIs),如文拉法辛、度洛西汀等;④三环类抗抑郁药,如去甲替林、阿米替林、多塞平等;⑤抗炎药物(anti-inflammatory drugs),如阿司匹林、非甾体抗炎药、米诺环素等;⑥维生素D等^[6,7]。但各类药物有效性不稳定,均一定的副作用,患者依从度较低,且长期抗抑郁药物治疗可能成为卒中复发的隐患。非药物疗法具有安全、患者依从性好的独特优势,且随着科技的发展,更多的非药物疗法开始作为PSD的替代或重要辅助疗法。本研究即对近年来有关PSD的病理生理机制及其非药物疗法的研究进展综述如下。

1 卒中参数与PSD

研究认为卒中的严重程度,类型,病灶的体积、位置和侧别,生活环境等是导致发生PSD的最直接促进因素^[8]。大面积脑梗死、左半球损伤、前额叶皮质区域、基底节、边缘系统、丘脑的梗死更容易发生

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PSD^[9];白质疏松也与 PSD 有关^[10];个人和家族的精神疾病史,及缺乏社会支持的患者患 PSD 的风险增加^[11]。缺血性卒中和出血性卒中患者 PSD 的发生率未发现差异^[11]。

2 PSD 的病理生理机制

2.1 神经递质

2.1.1 单胺类神经递质 单胺类神经递质主要包括去5-羟色胺(5-hydroxytryptamine, 5-HT)、去甲肾上腺素和多巴胺,是与 PSD 最密切相关的机制之一。中枢神经系统的单胺类核团位于脑干,从核团发出上行投射,分布在整个大脑,包括大脑皮质和边缘系统^[9]。当单胺类核团或其投射受到缺血或出血损害时,可能会导致相应路径受损、递质水平降低、生物活性降低、受体数量异常等,如出现左额皮质中 5-HT 水平降低,导致情绪低落和认知障碍;基底节受影响,导致情绪、认知、奖励和疲劳调节障碍;奖励系统失调,导致愉悦感降低^[12,13]等。

2.1.2 氨酸类神经递质 谷氨酸作为一种非必需氨基酸,是中枢神经系统中的主要兴奋性神经递质之一,占大脑中所有神经介质活动的 55%以上。卒中后,脑组织发生急性缺血缺氧,细胞受损,谷氨酸过量释放,广泛激活谷氨酸门控 N-甲基-D-天冬氨酸(N-methyl-D-aspartic acid, NMDA)离子通道,导致离子转运体功能障碍;同时,过量的谷氨酸释放加剧氧化应激和炎症,导致突触兴奋性毒性,小胶质细胞和星形胶质细胞清除谷氨酸能力受损^[14,15];兴奋性氨基酸转运体系统也受到损伤,过多的谷氨酸不能从突触间隙中清除;此外还有细胞内 Ca²⁺超载等一系列级联反应,进一步扩大谷氨酸的兴奋性毒性,最终导致更多神经元受损或死亡^[16],大大增加了精神障碍如 PSD 的发生^[17]。研究发现,在 PSD 患者的血液和脑组织中,尤其是额叶,谷氨酸及其代谢物的水平较高^[18,19],也有研究认为 PSD 患者的血液中的谷氨酸水平低于健康对照^[20,21],这可能与研究的纳入标准、检测时间等有关,但 PSD 的发生和发展必然伴随着谷氨酸水平的变化。最新血浆代谢组学相关通路分析研究显示,谷氨酸代谢可能参与 PSD 的发病机制^[22]。越来越多的动物研究证明血液谷氨酸清除剂可能是有前途的 PSD 新治疗方法^[17]。

2.2 神经炎症

卒中后,缺血缺氧导致三磷酸腺苷(adenosine triphosphate, ATP)生成障碍,引起神经细胞损伤和死亡。死亡细胞释放危险相关分子,与小胶质细胞表面的 toll 样受体结合,引发信号转导,促进局部炎症因子的释放^[23]。除了小胶质细胞外,中性粒细胞和巨噬细胞被进一步激活,放大炎症,降低了单胺类神经递质的产生和调节活动,甚至影响突触可塑性变化^[24]。抑郁症患者血清中的炎症细胞因子水平升高^[25],而抗抑郁药物,如 SSRIs 可以降低促炎细胞因子白细胞介素(interleukin, IL)-6、IL-1 β 、肿瘤坏死因子(tumor necrosis factor, TNF)- α 和干扰素- γ (interferon- γ , IFN- γ)的水平,或增加抗炎细胞因子,如 IL-10、IL-4、IL-13 的水平^[26]。此外,卒中也导致外周免疫细胞分泌促炎细胞因子,如 TNF- α 、IL-1 β 和 IL-6,这些细胞因子穿过受损的血脑屏障,进一步激活中枢神经系统中的小胶质细胞和星形胶质细胞,最终导致广泛

的神经炎症,促进 PSD 的形成^[27,28]。

2.3 神经内分泌功能紊乱

下丘脑-垂体-肾上腺(hypothalamic-pituitary-adrenal, HPA)轴是神经内分泌系统的重要组成部分。恐惧、抑郁、焦虑等精神障碍的形成与 HPA 轴的过度激活与有关^[29]。40% 的卒中患者存在 HPA 功能障碍^[30]。在卒中急性期的应激状态下,HPA 轴被过度激活,下丘脑神经元分泌更多的促皮质素释放激素(corticotropin releasing hormone, CRH),垂体释放更多的促肾上腺皮质激素(adrenocorticotrophic hormone, ACTH),然后 ACTH 诱导肾上腺皮质合成和分泌过多的糖皮质激素^[31],包括皮质醇。糖皮质激素的过度释放导致主要分布在隔区和海马的高亲和力糖皮质激素受体饱和,加剧了神经激素功能障碍^[32]。此外,糖皮质激素还可以通过神经递质途径影响预后。如血浆中升高的皮质醇与血液和海马中的脑源性神经营养因子(brain derived neurotrophic factor, BDNF)水平、认知、神经状态、功能反应和情绪状况呈负相关,也损害了海马神经发生^[33]。此外 HPA 系统的功能也与神经炎症、神经递质存在相互影响^[34],共同促进 PSD 发生。

2.4 线粒体功能障碍

线粒体在维持细胞能量平衡、调节凋亡以及控制氧化还原信号传导中扮演着至关重要的角色。线粒体功能失调与包括精神疾病在内的各种脑部疾病的发病机制有关^[35]。卒中导致的缺血再灌注会引起线粒体功能障碍,其特征包括线粒体氧化应激、Ca²⁺超载、铁代谢失调、线粒体 DNA 缺陷以及线粒体质量控制的破坏等^[36],进一步加剧线粒体生物功能失调,从而导致能量供应和代谢不足,细胞功能障碍^[36]。卒中后,线粒体应激作为一种适应性机制,旨在减少错误折叠蛋白的积累和整体蛋白质合成。当线粒体应激过于强烈时,会激活小胶质细胞等炎性细胞,导致神经炎症^[37]。此外,线粒体功能障碍还会导致线粒体通透性转换孔(mitochondrial permeability transition pore, mPTP)开放、线粒体自噬功能障碍和线粒体过度分裂,引发多种形式的细胞死亡,如自噬、细胞凋亡和铁死亡等^[38]。这些由线粒体功能障碍引起的级联反应最终导致了卒中后出现的各种并发症,包括痴呆、癫痫和精神障碍等。线粒体靶向的多功能纳米粒子,通过鼻腔给药,能有效减轻大脑中动脉栓塞模型大鼠脑组织的氧化应激、炎症,修复线粒体功能并减少细胞凋亡^[39]。

3 PSD 的非药物治疗

3.1 心理治疗

PSD 的心理治疗最主要的方式是认知行为疗法(cognitive behavioral therapy, CBT)。CBT 认为患者的心理困境的根源是不良的思维模式和无益行为,通过分析给予引导和纠正。荟萃分析发现 CBT 对改善 PSD 抑郁症状有一定的积极影响,但因为纳入研究的局限性,尚需更多研究以证实^[40]。

3.2 非侵入性脑刺激

非侵入性脑刺激是治疗重度抑郁症患者的有效方法,主要包括经颅直流电刺激(transcranial direct current stimulation,

tDCS) 和重复经颅磁刺激 (repetitive transcranial magnetic stimulation, rTMS), 但其对 PSD 的疗效仍需更多研究。tDCS 通过使用微弱的直流电来调节钠-钙依赖性通道和 NMDA 受体活性, 从而根据刺激的持续时间和极性增加或减少神经可塑性和兴奋性^[41]。Li 等^[42]的系统评价分析结果显示, tDCS 对改善 PSD 有作用, 但仍不清楚哪种刺激方案最好。Hao 等^[43]的研究也认为 tDCS 为治疗 PSD 提供了有希望的结果。rTMS 是用重复脉冲磁场作用于特定的中枢神经, 诱导刺激部位产生感应电流, 改变皮质兴奋性, 改善相关神经回路功能。高频刺激(5~20 Hz)增加皮质兴奋性, 而低频刺激(<1 Hz)降低皮质兴奋性。美国 FDA 已批准 rTMS 作为一种非侵入性的物理治疗技术。多项荟萃分析也显示, 在左侧背外侧前额叶皮质应用高频 rTMS 是 PSD 的有效治疗方案^[44]。最新有研究比较了 tDCS 和 rTMS 治疗 PSD 的疗效, 结果显示双侧 rTMS 和高频 rTMS 改善 PSD 的效果优于 tDCS^[45]。

3.3 电针

电针是通过对特定穴位的刺激治疗对卒中后患者进行康复的常规方法, 已在许多国际指南中被推荐用于 PSD 治疗^[46]。多项随机对照试验均发现电针治疗 PSD 有效且安全, 改善汉密尔顿抑郁量表(Hamilton depression scale, HAMD)-17、抑郁自评量表(self-rating depression scale, SDS) 和改良 Barthel 指数(modified Barthel index, mBI) 评分, 并调节 PSD 患者的神经炎症反应^[47,48]。动物实验研究显示, 电针改善 PSD 的机制可能与通过激活磷酸腺苷活化蛋白激酶(adenosine 5'-monophosphate-activated protein kinase, AMPK)介导的线粒体功能^[49]、激活大麻素受体-1(cannabinoid receptor 1, CB1R)促进线粒体生物发生^[50]等有关。

3.4 深部脑刺激(deep brain stimulation, DBS)

DBS 是一种神经调控技术, 通过定位将电极精准置入特定的脑区或核团, 给予特定频率和强度的电刺激调节神经功能, 被广泛应用于难治性抑郁症^[51]、强迫症^[52]、帕金森病及其相关情绪和认知功能障碍^[53]等。神经化学传递的变化是 DBS 抗抑郁治疗的重要机制^[54]: 腹内侧前额叶皮质 DBS 可诱导血清素 5-HT 释放并增加 5-HT1B 受体表达, 其抗抑郁样作用可能由前额叶投射到中缝的直接调节所介导; 腺苷能和谷氨酸能传递也可能发挥作用; 内侧前脑束 DBS 增加多巴胺水平并降低 D2 受体表达, 而伏隔核和外侧缰核刺激则增加不同大脑区域的儿茶酚胺水平; 底丘脑核 DBS 减少血清素能传递, 减轻抑郁样反应, 其中一些效应由 5HT1A 受体介导。动物实验研究还显示, 伏隔核 DBS 可促进 BDNF 表达, 从而改变多巴胺能通路中的功能连接和代谢特征, 改善抑郁情绪^[55]; 还可通过激活 BDNF/TrkB 信号通路及其下游 ERK1/2 活性^[56]等。DBS 因为其一定的创伤性, 目前应用于 PSD 的研究尚不多, 但随着技术的更新发展, DBS 也是 PSD 治疗的潜在有效方法。

3.5 脑机接口(brain-computer interface, BCI)

BCI 是指绕过外周神经与肌肉的正常输出通道, 人脑与外部设备(计算机、机器人等)直接连接的通讯控制系统, 目前主要

有侵入式、半侵入式和非侵入式 3 大类^[57]。BCI 可以通过不同的脑功能测量技术获得输入信息, 有脑电图(如事件相关脑电图 P300、运动想象、稳态视觉诱发电位等), 皮质脑电图, 功能磁共振, 功能性近红外光谱等^[58]。随着技术发展, 出现了多模态 BCI, 即使用不同种类的传感器, 将脑电信号与其他生理信号(如眼动、心电、视频和音频等)多模态信号进行同步采集和处理的 BCI 系统, 以实现更加精准的信号识别与功能调控^[59]。

虽然 BCI 技术仍有待进一步研发, 但其在抑郁症的诊断和治疗方面已经展现出现较大潜力。重度抑郁症可以通过先进的神经计算和传统的机器学习技术进行评估。有研究开发了一种 BCI 系统, 基于脑电图监测的残差神经网络(ResNet), 用于对抑郁症进行分类(分类器)和对抑郁严重程度进行评分(回归)。研究发现, 从 β 带提取的信号对抑郁症的分类和严重程度评分准确度更高; 当抑郁症状加重时, 主要表现为增加的 δ 失活伴随着强烈的 β 激活。该模型基于脑电信号构建了一个由拓扑依赖性、量化语义抑郁症状和临床特征构成的精神疾病诊断模型, 可以用于抑郁症分类和抑郁严重程度评分的辅助诊断^[60]。受限于技术, BCI 直接用于抑郁症的相关治疗研究目前尚不多。有研究通过刺激参数的动态调整, 再现感觉输入在大脑中引起的强烈起始和偏移瞬态, 通过这种训练编码构建仿生皮质内微刺激(intracortical microstimulation, ICMS)。动物实验评估结果显示, 动态幅度的调整会引起明显的起始和偏移瞬态, 减少神经钙活动的抑制, 并通过减少神经元的募集来减少总电荷注入, 降低 BCI 中的感觉反馈; 动态频率的调整只在小部分神经元中引起明显的起始和偏移瞬变, 但也通过降低激活率来减少招募的神经元的抑制^[61]。2021 年 7 月, Synchron 公司的经血管植入式脑机接口产品“Stentrode”获得美国 FDA 的 IDE 批准。Stentrode 是一种由尼钛合金制成的支架, 上面添加了一组铂电极。通过血管穿刺将 Stentrode 经颈静脉入颅, 嵌入到目标脑区附近的静脉中, 植入在胸部的接收设备将神经信号传输到解码器, 再通过机器学习算法将脑信号转化为数字控制指令。Stentrode 提供了一种无需破坏颅骨即可获取大脑特定部分高质量信号的方法。SWITCH 研究^[62]是对 Stentrode 进行的一项单中心、前瞻性的首次人体研究。该研究评估了 5 例患有严重双侧上肢瘫痪(4 例患肌萎缩侧索硬化症、1 例患原发性侧索硬化症)的患者, 并进行了 12 个月的随访。该研究于 2019 年 5 月 27 日开始, 随访于 2022 年 1 月 9 日完成。研究的主要安全终点是与设备相关的严重不良事件导致的增加死亡率或永久残疾, 次要终点包括血管闭塞和设备迁移。结果显示, 没有发生严重不良事件、血管闭塞或设备移位。SWITCH 研究提供了 Stentrode 应用于 BCI 的临床安全性的早期证据。随着技术的不断升级, BCI 是 PSD 治疗的未来发展方向。

4 总结

本文对 PSD 的病理生理机制研究进展进行综述, 卒中的严重程度, 类型, 病灶的体积、位置和侧别, 生活环境, 神经递质, 神经炎症, 神经内分泌功能紊乱, 线粒体功能障碍等均参与了 PSD

的发生和发展。关于PSD的治疗,本综述重点关注非药物治疗。总结了心理治疗、非侵入性脑刺激、电针、DBS等常规治疗方法的研究进展;重点分析了BCI技术的研究进展,并探讨其在PSD治疗中的潜在治疗价值及发展方向。卒中是我国居民致死的首位病因,PSD是卒中后的常见并发症。研究PSD的病理生理机制并研发新的治疗方法,对改善患者预后有重要临床意义。

参考文献

- [1]《中国脑卒中防治报告2021》编写组.《中国脑卒中防治报告2021》概要[J].中国脑血管病杂志,2023,20(11): 783-793.
- [2] GBD 2019 Stroke Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019[J]. Lancet Neurol, 2021, 20(10): 795-820.
- [3] Sewell K, Tse T, Donnan GA, et al. Screening for post-stroke depression: who, when and how[J]? Med J Aust, 2021, 215(7): 305-307.
- [4] Lan Y, Pan C, Qiu X, et al. Nomogram for Persistent Post-Stroke Depression and Decision Curve Analysis[J]. Clin Interv Aging, 2022, 17: 393-403.
- [5] Li LJ, Yao XM, Guan BY, et al. Persistent depression is a predictor of quality of life in stroke survivors: results from a 5-year follow-up study of a Chinese cohort[J]. Chin Med J, 2019, 132(18): 2206-2212.
- [6] 王莉迪,李桂兰,曹鹏远,等.卒中后抑郁的药物治疗[J].国际脑血管病杂志,2023,31(11): 846-851.
- [7] Zhan Q, Kong F. Mechanisms associated with post-stroke depression and pharmacologic therapy[J]. Front Neurol, 2023, 14: 1274709.
- [8] Zhang E, Liao P. Brain-derived neurotrophic factor and post-stroke depression[J]. J Neurosci Res, 2020, 98(3): 537-548.
- [9] Medeiros GC, Roy D, Kontos N, et al. Post-stroke depression: A 2020 updated review[J]. Gen Hosp Psychiatry, 2020, 66: 70-80.
- [10] Carnes-Vendrell A, Deus J, Molina-Seguin J, et al. Depression and Apathy After Transient Ischemic Attack or Minor Stroke: Prevalence, Evolution and Predictors[J]. Sci Rep, 2019, 9(1): 16248.
- [11] Shi Y, Yang D, Zeng Y, et al. Risk Factors for Post-stroke Depression: A Meta-analysis[J]. Front Aging Neurosci, 2017, 9: 218.
- [12] Robinson RG, Jorge RE. Post-Stroke Depression: A Review[J]. Am J Psychiatry, 2016, 173(3): 221-231.
- [13] Guo J, Wang J, Sun W, et al. The advances of post-stroke depression: 2021 update[J]. J Neurol, 2022, 269(3): 1236-1249.
- [14] Tomasetti C, Iasevoli F, Buonaguro EF, et al. Treating the Synapse in Major Psychiatric Disorders: The Role of Postsynaptic Density Network in Dopamine-Glutamate Interplay and Psychopharmacologic Drugs Molecular Actions[J]. Int J Mol Sci, 2017, 18(1): 135.
- [15] Haroon E, Miller AH, Sanacora G. Inflammation, Glutamate, and Glia: A Trio of Trouble in Mood Disorders[J]. Neuropsychopharmacology, 2017, 42(1): 193-215.
- [16] Suzuki H, Kawakita F, Asada R, et al. Old but Still Hot Target, Glutamate-Mediated Neurotoxicity in Stroke[J]. Transl Stroke Res, 2022, 13(2): 216-217.
- [17] Gruenbaum BF, Kutz R, Zlotnik A, et al. Blood glutamate scavenging as a novel glutamate-based therapeutic approach for post-stroke depression [J]. Ther Adv Psychopharmacol, 2020, 10: 2045125320903951.
- [18] Cheng SY, Zhao YD, Li J, et al. Plasma levels of glutamate during stroke is associated with development of post-stroke depression[J]. Psychoneuroendocrinology, 2014, 47: 126-135.
- [19] Wang X, Li YH, Li MH, et al. Glutamate level detection by magnetic resonance spectroscopy in patients with post-stroke depression[J]. Eur Arch Psychiatry Clin Neurosci, 2012, 262(1): 33-38.
- [20] Zhang XH, Zhang X, Liu XW, et al. Examining the Role of GLU/GABA to GLN Metabolic Cycle in the Pathogenesis of Post-Stroke Depressive Disorder and Insomnia[J]. Neuropsychiatr Dis Treat, 2023, 19: 2833-2840.
- [21] Geng LY, Qian FY, Qian JF, et al. The combination of plasma glutamate and physical impairment after acute stroke as a potential indicator for the early-onset post-stroke depression[J]. J Psychosom Res, 2017, 96: 35-41.
- [22] Wen L, Yan C, Zheng W, et al. Metabolic Alterations and Related Biological Functions of Post-Stroke Depression in Ischemic Stroke Patients [J]. Neuropsychiatr Dis Treat, 2023, 19: 1555-1564.
- [23] Wen H, Weymann KB, Wood L, et al. Inflammatory Signaling in Post-Stroke Fatigue and Depression[J]. Eur Neurol, 2018, 80(3-4): 138-148.
- [24] Fang M, Zhong L, Jin X, et al. Effect of Inflammation on the Process of Stroke Rehabilitation and Poststroke Depression[J]. Front Psychiatry, 2019, 10: 184.
- [25] Oglodek E. Changes in the Serum Levels of Cytokines: IL-1 β , IL-4, IL-8 and IL-10 in Depression with and without Posttraumatic Stress Disorder[J]. Brain Sci, 2022, 12(3): 387.
- [26] Wang L, Wang R, Liu L, et al. Effects of SSRIs on peripheral inflammatory markers in patients with major depressive disorder: A systematic review and meta-analysis[J]. Brain Behav Immun, 2019, 79: 24-38.
- [27] Zheng L, Li XY, Huang FZ, et al. Effect of electroacupuncture on relieving central post-stroke pain by inhibiting autophagy in the hippocampus[J]. Brain Res, 2020, 1733: 146680.
- [28] Shi K, Tian DC, Li ZG, et al. Global brain inflammation in stroke[J]. Lancet Neurol, 2019, 8(11): 1058-1066.
- [29] Liu J, Meng T, Wang C, et al. Natural products for the treatment of depression: Insights into signal pathways influencing the hypothalamic-pituitary-adrenal axis[J]. Medicine (Baltimore), 2023, 102(44): e35862.
- [30] Xu T, Pu S, Ni Y, et al. Elevated plasma macrophage migration inhibitor factor as a risk factor for the development of post-stroke depression in ischemic stroke[J]. J Neuroimmunol, 2018, 320: 58-63.
- [31] Chen XG, Shi SY, Hu L, et al. Longitudinal changes in the hypothalamic-pituitary-adrenal axis and sympathetic nervous system are related to the prognosis of stroke[J]. Front Neurol, 2022, 13: 946593.
- [32] Zhou L, Wang T, Yu Y, et al. The etiology of poststroke-depression: a hypothesis involving HPA axis[J]. Biomed Pharmacother, 2022, 151: 113146.
- [33] Casas S, Perez AF, Mattiazzi M, et al. Potential Biomarkers with Plasma Cortisol, Brain-derived Neurotrophic Factor and Nitrites in Patients with Acute Ischemic Stroke[J]. Curr Neurovasc Res, 2017, 14(4): 338-346.
- [34] Kim S, Park ES, Chen PR, et al. Dysregulated Hypothalamic-Pituitary-Adrenal Axis Is Associated With Increased Inflammation and Worse Outcomes After Ischemic Stroke in Diabetic Mice [J]. Front Immunol, 2022, 13: 864858.
- [35] Clemente-Suárez VJ, Redondo-Flórez L, Beltrán-Velasco AI, et al. Mitochondria and Brain Disease: A Comprehensive Review of Pathological Mechanisms and Therapeutic Opportunities[J]. Biomedicines, 2023, 11(9): 2488.
- [36] She R, Liu D, Liao J, et al. Mitochondrial dysfunctions induce PANoptosis and ferroptosis in cerebral ischemia/reperfusion injury: from pathology to therapeutic potential[J]. Front Cell Neurosci, 2023, 17: 1191629.
- [37] Gao L, Peng L, Wang J, et al. Mitochondrial stress: a key role of neuroinflammation in stroke[J]. J Neuroinflammation, 2024, 21(1): 44.
- [38] Farzaei MH, Ramezani-Aliakbari F, Ramezani-Aliakbari M, et al. Regulatory effects of trimetazidine in cardiac ischemia/reperfusion injury [J]. Naunyn Schmiedebergs Arch Pharmacol, 2023, 396(8): 1633-1646.
- [39] Zhang Y, Zhang H, Zhao F, et al. Mitochondrial-targeted and ROS-responsive nanocarrier via nose-to-brain pathway for ischemic stroke treatment[J]. Acta Pharm Sin B, 2023, 13(12): 5107-5120.
- [40] Wang SB, Wang YY, Zhang QE, et al. Cognitive behavioral therapy for post-stroke depression: A meta-analysis[J]. J Affect Disord, 2018, 235: 589-596.
- [41] Lefaucheur JP, Antal A, Ayache SS, et al. Evidence-based guidelines on the therapeutic use of transcranial direct current stimulation (tDCS)[J]. Clin Neurophysiol, 2017, 128(1): 56-92.

- T1-weighted MRI in patients with hemiballism-hemicoreia caused by non-ketotic hyperglycemia: report of seven new cases and a review of literature[J]. *J Neurol*, 2001, 248(9): 750-755.
- [6] Madu AE, Oliver L. Non-ketotic hyperglycinaemia: case report and review of medical literature[J]. *J Matern Fetal Neonatal Med*, 2013, 26(5): 537-539.
- [7] Aquino JH, Spitz M, Pereira JS. Hemichorea-Hemiballismus as the First Sign of Type 1b Diabetes During Adolescence and Its Recurrence in the Setting of Infection[J]. *J Child Neurol*, 2015, 30(10): 1362-1365.
- [8] Oh SH, Lee KY, Im JH, et al. Chorea associated with non-ketotic hyperglycemia and hyperintensity basal ganglia lesion on T1-weighted brain MRI study: a meta-analysis of 53 cases including four present cases [J]. *J Neurol Sci*, 2002, 200(1-2): 57-62.
- [9] Shafran I, Greenberg G, Grossman E, et al. Diabetic striatopathy-Does it exist in non-Asian subjects[J]? *Eur J Intern Med*, 2016, 35: 51-54.
- [10] Chang X, Hong W, Yu H, et al. Chorea associated with nonketotic hyperglycemia: A case report with atypical imaging changes[J]. *Medicine*, 2017, 96(45): e8602.
- [11] Ryan C, Ahlskog JE, Savica R. Hyperglycemic chorea/ballism ascertained over 15 years at a referral medical center[J]. *Parkinsonism Relat Disord*, 2018, 48: 97-100.
- [12] Abe Y, Yamamoto T, Soeda T, et al. Diabetic striatal disease: clinical presentation, neuroimaging, and pathology[J]. *Intern Med*, 2009, 48(13): 1135-1141.
- [13] Lin JJ. Ipsilateral putamen hyperintensity on T1-weighted MRI in non-ketotic hyperglycemia with hemiballism-hemicoreia: a case report[J]. *Parkinsonism Relat Disord*, 2001, 7(4): 319-321.
- [14] Chang KH, Tsou JC, Chen ST, et al. Temporal features of magnetic resonance imaging and spectroscopy in non-ketotic hyperglycemic chorea-ballism patients[J]. *Eur J Neurol*, 2010, 17(4): 589-593.
- [15] Johari B, Hanafiah M, Shahizon AM, et al. Unilateral striatal CT and MRI changes secondary to non-ketotic hyperglycaemia[J]. *BMJ Case Rep*, 2014, 2014, bcr2014204053.
- [16] Cervantes-Arriaga A, Arrambide G, Rodríguez-Violante M. A prospective series of patients with hyperglycaemia-associated movement disorders[J]. *J Clin Neurosci*, 2011, 18(10): 1329-1332.
- [17] D'souza M, Sharma R, Jaimini A, et al. 18F-fluorodeoxyglucose positron emission tomography/computed tomography in a case of non-ketotic hyperglycemia[J]. *Indian J Nucl Med*, 2014, 29(4): 254-256.
- [18] Wang JH, Wu T, Deng BQ, et al. Hemichorea-hemiballismus associated with nonketotic hyperglycemia: a possible role of inflammation [J]. *J Neurol Sci*, 2009, 284(1-2): 198-202.
- [19] Lee P, Kek P, Soh A. Hyperglycemia-associated Hemichorea-hemiballism: The Spectrum of Clinical Presentation[J]. *Intern Med*, 2015, 54(15): 1881-1884.

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- [42] Li Y, Li HP, Wu MX, et al. Effects of transcranial direct current stimulation for post-stroke depression: A systematic review and meta-analysis[J]. *Clin Neurophysiol*, 2022, 142: 1-10.
- [43] Hao W, Liu Y, Gao Y, et al. Transcranial direct current stimulation for the treatment of post-stroke depression: A systematic review[J]. *Front Neurol*, 2022, 13: 955209.
- [44] Wang T, Liu X, Wu X, et al. High-frequency rTMS of the left dorsolateral prefrontal cortex for post-stroke depression: A systematic review and meta-analysis[J]. *Clin Neurophysiol*, 2023, 157: 130-141.
- [45] Yanyu S, Ying L, Kexin L, et al. Non-invasive brain stimulation for treating post-stroke depression: A network meta-analysis[J]. *Int J Geriatr Psychiatry*, 2023, 38(6): e5941.
- [46] Birch S, Robinson N. Acupuncture as a post-stroke treatment option: A narrative review of clinical guideline recommendations[J]. *Phytomedicine*, 2022, 104: 154297.
- [47] Cai W, Ma W, Li YJ, et al. Efficacy and safety of electroacupuncture for post-stroke depression: a randomized controlled trial[J]. *Acupunct Med*, 2022, 40(5): 434-442.
- [48] Ma F, Cao G, Lu L, et al. Electroacupuncture versus Escitalopram for mild to moderate Post-Stroke Depression: A randomized non-inferiority trial[J]. *Front Psychiatry*, 2024, 15: 1332107.
- [49] Ding Z, Gao J, Feng Y, et al. Electroacupuncture Ameliorates Depression-Like Behaviors in Post-Stroke Rats via Activating AMPK-Mediated Mitochondrial Function[J]. *Neuropsychiatr Dis Treat*, 2023, 19: 2657-2671.
- [50] Hu G, Zhou C, Wang J, et al. Electroacupuncture treatment ameliorates depressive-like behavior and cognitive dysfunction via CB1R dependent mitochondria biogenesis after experimental global cerebral ischemic stroke[J]. *Front Cell Neurosci*, 2023, 17: 1135227.
- [51] van Rheede JJ, Alagapan S, Denison TJ, et al. Cortical signatures of sleep are altered following effective deep brain stimulation for depression [J]. *Transl Psychiatry*, 2024, 14(1): 103.
- [52] Meyer GM, Hollunder B, Li N, et al. Deep Brain Stimulation for Obsessive-Compulsive Disorder: Optimal Stimulation Sites[J]. *Biol Psychiatry*, 2023; S0006-3223(23)01785-7.
- [53] Dong W, Qiu C, Lu Y, et al. Effect of deep brain stimulation compared with drug therapy alone on the progression of Parkinson's disease[J]. *Front Neurosci*, 2024, 17: 1330752.
- [54] Campos ACP, Pople C, Silk E, et al. Neurochemical mechanisms of deep brain stimulation for depression in animal models[J]. *Eur Neuropsychopharmacol*, 2023, 68: 11-26.
- [55] Li SJ, Lo YC, Tseng HY, et al. Nucleus accumbens deep brain stimulation improves depressive-like behaviors through BDNF-mediated alterations in brain functional connectivity of dopaminergic pathway[J]. *Neurobiol Stress*, 2023, 26: 100566.
- [56] Liu F, Huang S, Guo D, et al. Deep brain stimulation of ventromedial prefrontal cortex reverses depressive-like behaviors via BDNF/TrkB signaling pathway in rats[J]. *Life Sci*, 2023, 334: 122222.
- [57] Selvam A, Aggarwal T, Mukherjee M, et al. Humans and robots: Friends of the future? A bird's eye view of biomanufacturing industry 5.0 [J]. *Biotechnol Adv*, 2023, 68: 108237.
- [58] 刘昊宸, 白宇璇, 徐雅萱, 等. 脑机接口及测量脑功能技术的发展现状和应用前景[J]. 中华生物医学工程杂志, 2023, 29(2): 220-228.
- [59] 吕宝粮, 郑伟龙. 情感脑-机接口//高上凯、吕宝粮、张丽清. 脑-计算机交互研究前沿[M]. 上海: 上海交通大学出版社, 2021.
- [60] Kang C, Novak D, Yao X, et al. Classifying and Scoring Major Depressive Disorders by Residual Neural Networks on Specific Frequencies and Brain Regions[J]. *IEEE Trans Neural Syst Rehabil Eng*, 2023, 31: 2964-2973.
- [61] Hughes C, Kozai T. Dynamic amplitude modulation of microstimulation evokes biomimetic onset and offset transients and reduces depression of evoked calcium responses in sensory cortices[J]. *Brain Stimul*, 2023, 16(3): 939-965.
- [62] Mitchell P, Lee SCM, Yoo PE, et al. Assessment of safety of a fully implanted endovascular brain-computer interface for severe paralysis in 4 patients: the Stentrode with thought-controlled digital switch (SWITCH) study[J]. *JAMA Neurol*, 2023, 80: 270-278.