

· 综述 ·

神经刺激技术对神经源性吞咽障碍治疗效果的 研究进展

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【摘要】 吞咽障碍主要是指由于各种因素导致食物不能有效安全地从口腔输送到胃, 其中神经源性吞咽障碍是指由于神经系统疾病导致的吞咽障碍。神经源性吞咽障碍可导致患者产生营养不良、吸入性肺炎、心理障碍甚至窒息死亡等严重后果。目前对于神经源性吞咽障碍的治疗主要以康复干预治疗为主, 其中神经刺激技术是临床应用较为广泛的一类, 目前神经刺激技术可选择的类别较多, 关于如何选择最合适的治疗方案尚没有明确的临床指南。现就临床常用的4种神经刺激技术在神经源性吞咽障碍患者中的康复疗效展开综述, 旨在为神经源性吞咽障碍患者提供可供参考的个体化康复措施选择。

【关键词】 吞咽障碍; 神经系统疾病; 神经刺激技术; 吞咽功能; 康复; 综述

Research progress on the effect of neurostimulation techniques in the treatment of neurogenic dysphagia

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【Abstract】 Dysphagia mainly refers to the inability that food cannot be safely and efficiently delivered from mouth to stomach due to various reasons. Dysphagia caused by neurological disorders is called neurogenic dysphagia. Neurogenic dysphagia can lead to serious consequences such as malnutrition, aspiration pneumonia, psychological disorders and even death by asphyxiation. At present, the treatment of neurogenic dysphagia is mainly based on rehabilitation intervention. Among them, neurostimulation technology is a more widely used category in clinical practice. There are many categories of neurostimulation technology which can be selected, and there is no clear clinical guideline on how to choose the most appropriate treatment plan. This paper reviews the rehabilitation efficacy of four neurostimulation techniques which are commonly used in clinical practice in patients with neurogenic dysphagia, aiming to provide a reference of individualized rehabilitation measures for patients with neurogenic dysphagia.

【Key words】 Deglutition disorders; Nervous system diseases; Neurostimulation techniques; Deglutition function; Rehabilitation; Review

吞咽是一种感觉及运动均参与的高度复合的神经肌肉运动, 涉及数对脑神经参与以及20对以上的肌肉协调控制, 同时也需要大脑皮层及脑干的协调, 才能安全有效地完成吞咽过程, 将食物顺利输送到胃^[1]。当吞咽过程中任何一个环节出现问题, 就会发生吞咽障碍, 临床上通常将吞咽障碍分为结构性和神经源性两大类, 结构性吞咽障碍主要是指吞咽通道发生结构性病理改变, 如头颈部肿瘤、慢性炎症以及肿瘤的化放疗术后等; 神经源性吞咽障碍是指

中枢和周围神经系统、神经肌肉传递或者肌肉疾病等引起广泛大脑皮质及脑干等部位病变引起^[2], 可见于脑卒中、肌萎缩侧索硬化症、多发性硬化症、痴呆、帕金森病和重症肌无力等疾病^[3]。吞咽障碍的发病率因病而异, 研究发现, 全世界每年因为各式各样疾病导致的神经源性吞咽障碍的患者达40万~80万^[4], 这一人数远远超过结构性吞咽障碍。神经源性吞咽障碍最终导致了患者多方面问题, 如因食物摄入量不足引起的营养不足, 因间歇置管引起的

生活质量下降以及因渗漏、误吸引起的吸入性肺炎等问题,对患者的身体、心理都造成了较为严重的伤害^[5]。

目前神经源性吞咽障碍的治疗主要依赖于康复干预,其核心是提高从口咽部到吞咽中枢的感觉反馈,增加吞咽相关肌肉的收缩,防止其萎缩,最终通过代偿性姿势来最大程度地改善吞咽功能,从而降低并发症的发生率,降低病死率^[6-7]。神经源性吞咽障碍康复干预治疗方式较多,有传统吞咽训练、针灸、神经发育疗法、球囊扩张术、神经刺激技术等。现对常用的神经刺激技术在神经源性吞咽困难患者中的应用进展进行综述,以期为患者选择个体化康复治疗措施提供可供参考建议。

一、神经源性吞咽障碍的病理生理机制

正常吞咽过程起源于摄食后形成食团,食团入咽,该过程刺激舌咽、迷走神经等将感觉由脑干传入大脑皮质后,大脑皮质将运动信号传入皮质下行纤维,再传导至脑干,由脑干中延髓的“中枢模式发生器”整合信息后,协调口咽部、喉部、食管部位的肌肉收缩,最后食团通过食管完成整个吞咽过程^[8]。在此过程中,包括丘脑、红核、黑质、脑干网状结构等在内的锥体外系对于协调吞咽的随意精细运动、吞咽肌肉张力等至关重要^[9]。当神经源性疾病致使外周神经核团、延髓吞咽中枢、大脑皮质及皮质下纤维中任一位置调节受损或锥体外系损伤时,就会导致神经源性吞咽障碍。

二、神经刺激技术分类

(一)外周神经刺激

1. 咽部电刺激(pharyngeal electrical stimulation, PES):是一种经口或经鼻将导管放入咽腔,在局部施加电流刺激咽部黏膜的神经调控技术^[10]。其作用机制可能有两个:其一,在治疗过程中,PES刺激大脑吞咽运动皮质诱导其重组^[11];其二,PES增加了口咽、鼻咽部黏膜处舌咽神经及迷走神经的感觉传入,该部分的纤维直接与孤束核相连,上行传入到脑干及皮质下区域^[12],这两者共同作用提高了大脑吞咽感觉运动皮层的兴奋性,从而改善了吞咽功能。Suntrup-krueger等^[13]研究发现,PES还能促进唾液中的神经肽P物质分泌增加,增强了吞咽反射。Sasegbon等^[14]研究认为,相比其他频率而言,5 Hz频率能够刺激咽部黏膜的运动功能,更好地诱发大脑吞咽运动皮质区的兴奋性。

2. 神经肌肉电刺激(neuromuscular electrical stimulation, NMES):是通过低频脉冲电刺激舌

骨上相关部位,刺激包括二缩肌前腹在内的舌骨肌群收缩,提高吞咽相关肌群收缩力量,同时提高舌咽复合体的动度,改善吞咽功能的同时加强吞咽过程中的气道保护^[15];此外,NMES还可以通过促进吞咽反射的建立、增强局部感觉刺激等机制改善吞咽功能^[16]。80 Hz频率的NMES应用最为广泛^[17-18];研究中最常见的持续时间是700 μ s^[19-20];NMES的应用强度范围在7~28 mA^[17,21],随着疗程的进展,患者对电流的耐受性会增加^[15,22],因此在达到患者的痛阈之前,高强度NMES的效果更为显著^[23];电极位置建议优先放置于颈部前侧,以舌骨上或舌骨下区、甲状腺肌、咽外侧区等位置为代表^[24-26];NMES的治疗时间为20~60 min^[27],而30 min是常用的治疗时间^[28]。

(二)无创性脑刺激

1. 重复经颅磁刺激(repetitive transcranial magnetic stimulation, rTMS):是一种通过促进皮质和皮质下区域之间的功能连接变化,改变大脑皮层的皮质兴奋性,提高皮质可塑性的刺激技术^[29]。高频rTMS(> 1 Hz)产生兴奋性作用,而低频rTMS(\leq 1 Hz)则产生抑制性作用^[30]。Du等^[31]的研究通过对不同频率rTMS对脑梗死后吞咽障碍的影响发现,推荐将患侧10 Hz的rTMS用于脑梗死后吞咽障碍患者的康复治疗。除此以外,小脑在吞咽时可被激活,进而调节咽运动皮质对吞咽功能产生影响,Sasegbon等^[32]通过在小脑施加10 Hz的rTMS,发现咽部的兴奋性增加,改善了吞咽功能,这种方式尤其适用于伴有后颅窝区脑损害患者^[33]。此外,Liao等^[34]对rTMS治疗在卒中后吞咽困难的荟萃分析中发现,停止治疗4周后,rTMS组仍比非rTMS组患者保持更好的吞咽功能,表明rTMS对吞咽功能的改善具有持续性。Cheng等^[35]研究发现,通过rTMS对健康人咽运动皮质的预适应刺激,能够敏化咽运动皮质;然后在一个最佳时间间隔内实施条件刺激,这两者共同作用能够更强地诱导咽运动皮质的可塑性,效果优于传统的rTMS治疗。

2. 经颅直流电刺激(transcranial direct current stimulation, tDCS):是一种通过持续而微弱的直流电刺激大脑局部,使得局部神经元膜电位发生改变,调节目标脑区的皮质兴奋性,从而改善相关脑功能的无创性脑刺激技术^[36]。阴极tDCS通过刺激降低皮质兴奋性起到抑制作用,而阳极tDCS则通过刺激增加皮质兴奋性起到兴奋作用。tDCS对皮质兴奋性的作用受电流强度、极性及时长的影响。一般

来说,阳极电极放置于患侧咽皮质运动区,阴极电极放置于健侧眶上区,电流强度以低于2 mA为宜^[37]。He等^[38]通过对卒中后吞咽障碍的荟萃分析发现,高强度tDCS(1.6~2 mA)与低强度tDCS(1~1.5 mA)对比,前者对卒中后吞咽困难的治疗效果更佳。双侧tDCS可调节大脑运动感觉皮质网络内和网络之间的局部神经元活动及神经元之间的连通性,因此双侧tDCS效果优于单侧tDCS^[39]。目前tDCS对于吞咽障碍的作用持续时间有长有短,尚无确切时间。但有研究发现,阳极tDCS作用于初级运动皮质(M1区)持续时间大于26 min后,皮质兴奋性反而降低^[40]。Li等^[41]研究发现双侧使用阳极tDCS效果优于单侧阳极tDCS。Feng等^[42]研究发现tDCS在慢性脑卒中患者中更为常用。此外,tDCS还可增加局部脑血液循环^[43]。

(三)配对关联刺激(paired associative stimulation, PAS)

PAS是一种将外周神经刺激技术与无创性脑刺激技术相结合的康复治疗手段,其将两种技术通过特定的时间间隔分开实施,能够强烈诱导咽运动皮质的兴奋性^[44]。Zhang等^[45]研究表明,对于卒中后吞咽障碍的患者而言,NMES联合rTMS治疗效果优于单独使用rTMS或NMES。郑秀琴等^[46]研究表明,高频rTMS联合NMES能显著改善帕金森病患者的吞咽困难。

三、神经刺激技术之间的疗效对比分析

(一)外周神经刺激技术的疗效对比分析

NMES以其最易使用、费用低为特点,在脑卒中后吞咽障碍中使用颇为广泛,在其他神经疾病引起的吞咽障碍中研究较少^[47]。研究发现,NMES联合传统吞咽训练是改善卒中后吞咽障碍最常用的康复治疗方法^[16,26]。而PES需要经口或经鼻插入导管,使用过程可能会给患者带来不适,同时通过经口或经鼻的咽部定位具有一定难度,因此在临床使用具有一定的局限性^[12],实用性不如NMES。然而,对于病情严重需床旁康复的患者而言,PES以便携性、可反复使用的特点,对该类患者更为适用。研究表明,PES用于治疗卒中后吞咽障碍患者,不仅可以改善其吞咽困难,还能够提高气管切开患者的气管封管率、留置鼻饲管进食患者的拔管成功率^[48-49]。还有研究发现,PES对多发性硬化症相关性吞咽障碍改善有效^[12,50]。

(二)无创性脑刺激技术的疗效对比分析

1.作用机制、特点对比分析:研究发现,吞咽功

能可以通过调节大脑咽运动皮质中舌骨上肌群的运动“热点”兴奋性来实现,分别在患侧与健侧施加无创性脑刺激技术、双侧同时应用无创性脑刺激技术,均能改善吞咽功能,但双侧刺激能更好地改善吞咽功能,这可能与吞咽功能同时受双侧大脑半球支配有关^[51-53]。就单侧使用无创性脑刺激技术来看,患侧兴奋性刺激对rTMS更有效,而对侧兴奋性刺激对tDCS更为有效^[54]。从使用性来看,tDCS是一种安全、便捷、易于使用的技术,但其在治疗过程中需要大面积纱布覆盖在头颅表面,准确定位刺激区域相对较难,因此对吞咽功能的改善效果不如rTMS,相对于rTMS来说,对于因病情不稳定需在床旁进行康复治疗患者,tDCS更为适用^[55]。

2.不同疾病对比分析:tDCS用于治疗神经源性疾病所致吞咽障碍,如卒中、帕金森病、多发性硬化等均取得积极效果^[56-58]。有研究表明,帕金森病的强直以及运动迟缓等症状会使患者口腔运送能力差,食物渗漏入气管,增加误吸风险。而rTMS作用于大脑初级运动皮质区(M1)不但能够改善帕金森病患者的吞咽功能,而且能够同时改善其运动症状^[59]。与卒中不同的是,帕金森病后吞咽障碍的病变部位是双侧的、广泛的、不固定的和进行性的^[58]。Huang等^[60]通过功能性磁共振动态监测研究发现,高频rTMS治疗后,帕金森病吞咽障碍患者的海马旁回、尾状核、丘脑的脑激活较治疗前增加,表明rTMS不仅能够通过刺激神经递质释放改变尾状核相关多巴胺水平的动态平衡,还能够改善其主观吞咽感觉,进而改善帕金森病患者的吞咽功能。

(三)不同神经刺激技术之间对比

对于神经系统相关疾病而言,无创性脑刺激技术被广泛用于脑卒中后吞咽障碍患者的康复治疗,Cheng等^[54]分析rTMS、tDCS、PES对卒中后吞咽困难的研究发现,rTMS效果最好,PES、tDCS次之。相关研究对神经刺激技术作用于卒中后吞咽困难的疗效进行Meta分析,发现rTMS、tDCS、NMES和PES均能改善吞咽功能,而rTMS可能是最有效的方法^[55,61]。

四、总结与展望

对于神经源性吞咽障碍患者而言,选择合适的康复治疗方法对其恢复至关重要。神经刺激技术以简便、安全、不良反应小等特点,通过改变大脑皮质兴奋性、刺激外周感觉输入、促进吞咽反射建立等作用,广泛用于神经源性吞咽障碍患者的康复干预。近来多项研究表明神经刺激技术对于神经源性吞咽障碍具有良好的效果,但不同研究之间的结果差异

较大。在临床工作中,如何将药物、传统吞咽训练、针灸、神经发育疗法、球囊扩张术等与神经刺激技术相结合,如何确定神经刺激技术的最佳治疗时机、最佳治疗时长,如何评估神经刺激技术对吞咽障碍患者的短期及长期影响,为神经源性吞咽困难患者寻找最佳、具体化、个体化康复治疗方,目前仍需要探索。

利益冲突 文章所有作者共同认可文章无相关利益冲突

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· 消息 ·

欢迎订阅2023年《神经疾病与精神卫生》杂志

《神经疾病与精神卫生》杂志是神经、精神科学及精神卫生领域的学术性期刊,国内外公开发行人,2006年被中国科学技术信息研究所收录为中国科技论文统计源期刊(中国科技核心期刊)。本刊坚持党的出版方针和卫生工作方针,遵循学科发展规律,以提高杂志质量、扩大社会效益为使命,及时反映科学研究的重大进展,更好地促进国内外学术交流。主要读者对象为广大神经科学、精神科学及精神卫生领域中从事基础、临床医学、教学、科研的工作者及学生。报道内容包括相关各学科领先的教学、科研成果及临床诊疗经验。主要栏目有专家论坛(述评)、论著、学术交流、短篇报道、综述、病例报告、会议纪要、国内外学术动态等。

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