

脑卒中患者空间注意障碍的认知康复研究进展

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注意是人脑的高级认知功能之一,是指人们可以选择性地集中关注(外部或内部环境中的)某一刺激、动作、想法或事件等,并“忽视”同时出现的其他“无关信息”的能力。空间注意是指人们可以主动或被动地关注某一空间范围内的“信息”能力。这些空间信息可以来源于视觉、听觉、触觉、本体感觉等多种不同感觉通路,也可体现在涉及空间位置或空间规划的运动过程中^[1]。

注意障碍在脑卒中患者中较为常见,其中空间注意障碍,尤其是半侧(病灶对侧)空间忽视是最常见的注意障碍之一,也是迄今为止被研究最多的脑卒中后注意障碍类型^[2-3]。虽然注意障碍在脑卒中后数周、数月内可有自发改善,但仍有部分患者会遗留某种程度的注意缺陷^[2-4]。空间注意障碍可造成患者日常生活和工作能力的显著下降,导致意外跌倒等安全隐患,并且和患者的不良预后有一定相关关系^[2-5]。因此,寻找针对脑卒中患者空间注意障碍的有效治疗和康复训练方案,是神经病学、康复医学等多学科共同关注的问题。其中,认知康复训练是被关注和研究较多的一种治疗途径,并且已有一些积极的发现。本文拟对成年脑卒中患者空间注意障碍的认知康复做一简要综述,报道如下。

脑卒中患者空间注意障碍的表现及其相关神经机制

作为脑卒中后常见的认知功能障碍,表现形式、相关心理和神经机制受到了众多研究者关注。其中,空间注意障碍的半侧(病灶对侧)空间忽视现象受到的关注最多。

一、半侧空间忽视

半侧空间忽视(偏侧忽视)通常见于单侧脑损伤,其核心是患者将注意力指向病灶对侧空间范围的能力受损^[6]。半侧空间忽视的临床表现可因脑损伤部位、范围、严重程度和病程不同而有所差异。典型表现为患者在无明显偏盲或偏身感觉障碍的情况下,更多地忽视(更少地注意到)出现在病灶对侧空间的感觉刺激,尤其当双侧感觉刺激同时存在时更为明显^[6];此外,患者对位于病灶对侧空间感觉刺激的加工速度也有下降^[7],且空间搜索能力受损^[8]。患者的这种半侧空间忽视是非感觉通道特异的,不仅局限于视觉刺激,也可累及其他感觉通路,且在进行运动时^[9]也可有异常表现,但对于不同范畴的感觉对象(如一般物品、面孔等),半侧空间忽视的效应程度会有差异^[6]。

存在半侧空间忽视的患者在多种空间注意测验(如线段中分测验、图形或文字划消测验)上的表现可出现明显异常,例如,线段中分偏向病灶同侧、更少地划消病灶对侧的图形等^[5];患者在进行图形临摹或回忆(如临摹图画或画钟等)时,也可表现出对一侧图形的明显忽视。这些异常结果表明,半侧空间忽视同时累及了患者的整体空间注意,以及基于对象的空间记忆;还累及了患者对即时呈现感觉信息的注意、想象和回忆。

通过对脑损伤患者的病灶分析发现,造成半侧空间忽视的损伤部位主要位于右半球,包括腹侧额叶、后部顶叶、颞顶联合区皮质及其相关白质纤维;这一范围与主要位于右半球的腹侧额顶叶注意通路有较多重合^[10-11]。

二、其他空间注意障碍

除半侧空间忽视外,脑卒中患者一般的视觉空间注意能力、空间注意分布、空间注意精细度(提取空间感觉刺激信息细节的能力)也可受影响,表现为患者对视觉刺激的注意度下降^[4]、更易忽视空间刺激的细节(病灶对侧的细节可能更明显)^[6],辨别不连续图像的整体特征障碍^[12],抑制不相关刺激的障碍^[13]等。

通过对脑卒中患者病灶位置,及其选择性空间注意障碍、空间定向障碍等神经机制的研究发现,以上功能异常可能主要和右侧顶叶区域损伤或结构、功能异常有关,相关脑区包括角回^[14]、顶内沟^[15]、顶叶后部区域^[16]、颞顶交界区^[15-17]、右侧颞上回^[14]、枕叶外侧、额叶视区^[18]、丘脑后结节^[19]等。还有研究发现,脑卒中患者未被病灶累及的左侧顶叶相关白质纤维结构也存在异常,且和患者的空间注意障碍有关^[20]。此外,脑卒中患者在执行以目标物为导向的任务时,与目标相关的空间注意受损,可能和背侧注意网络的异常、额顶叶功能连接异常有关^[15,21-22]。

脑卒中患者空间注意障碍的认知康复现状

脑卒中后注意障碍受到广泛关注后,即有研究者对利用认知/行为训练方法治疗这一障碍进行了探索。但相比于脑卒中后注意障碍的临床表现和机制研究,其认知/行为治疗的研究尚显较为零散,其研究所用的干预方案不一,得到的研究结果比较初步,仍有很大的探索和发展空间。其中多数研究关注了半侧空间忽视通过调整感觉输入模式、给予运动反馈信息、进行认知训练等方法,探索出了一些改善脑卒中患者半侧空间忽视的方法,取得了一些初步成果。

一些早期研究调查了视觉空间搜索/浏览训练及相关注意功能训练是否可改善患者脑卒中后空间忽视症状^[23-24]。结果发现相比于其他认知训练对照组(如阅读、计算等),视觉空间搜索/浏览及相关注意训练对患者半侧空间忽视的改善并不显著。但相关研究采用的样本量较小,且所用的训练任务较简单、抽象(如在电脑屏幕上探测形状不同的图案^[23]),可能都限

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制了干预的有效性和显著性。Kerckhoff 等^[25]改进视觉注意的训练方式,要求干预组患者以平滑的眼球运动追踪屏幕上沿直线移动的视觉目标,对照组患者则单纯按一定空间顺序扫视屏幕上静止的视觉目标,并进行命名或计数任务,研究共纳入了 24 例患者并进行随机分组,在干预前、干预 4 周时及干预结束后 2 周,两组患者分别接受了多种注意和其他生活功能评估。分析发现,接受“平滑追踪”训练的患者,在偏侧忽视测验上的得分,在干预刚结束后及其后的两周内都有显著上升;而对照组仅在干预刚结束时有所改善。此外,通过对患者日常生活中的忽视表现进行评估发现,“平滑追踪”组患者在干预结束后,生活中的忽视现象有显著改善,而对照组则无明显改善。

还有一些研究关注了运动(或运动相关的)训练/干预对脑卒中患者半侧空间忽视现象的改善作用,包括肢体激活治疗(让患者在忽视侧肢体佩戴仪器,“激活”其更多地使用、运动忽视侧肢体)^[26]、探索性躯干旋转运动训练^[27]、“躯体意识”训练(要求患者在进行平衡和姿势训练时意识到自身的运动状态)^[28]和机器人辅助的上肢运动训练^[29]等。虽然研究设计的统计效力不一,但这些研究结果均提示,相应的运动训练对改善脑卒中患者半侧空间忽视现象有一定效果。但相对于这些采用身体运动训练的方案,Fanthome 等^[30]采用眼球运动反馈(当患者一段时间没有看向忽视侧时给予提示)进行研究后,发现虽然该训练使患者的眼球运动习惯发生了显著改变,但患者的半侧空间忽视症状并未得到显著改善。这一系列的研究似乎支持了部分研究者提出的理论,即初级感觉及运动皮质在空间注意相关的认知加工过程中有一定作用,且脑卒中患者的半侧空间忽视障碍可能部分是由于感觉、运动皮质的功能异常所引起的^[31-32],但目前该理论解释仍待进一步实验依据支持。

此外,还有研究发现,经过一段时间的视觉输入信息调控(如利用棱镜影响输入光刺激的偏角^[33]、遮蔽非忽视侧视觉刺激信息^[34]等,可显著提高患者在接收正常视觉信息输入时在半侧空间忽视测验上的得分。但这一效果是否可显著改善患者的日常生活功能则并不明确。此外,聆听愉快音乐也被发现可改善患者即时的半侧空间忽视症状并提高注意力^[35-36]。但这一效应是否可通过训练得到巩固,并延伸到无音乐刺激时,仍有待进一步研究。

近年来,虚拟现实技术也被广泛应用到脑卒中患者半侧空间忽视症状的认知康复训练中。Katz 等^[37]研究了非浸入式的交互现实环境训练对患者半侧空间忽视症状的影响。结果发现,虽然两组患者在干预结束时,在半侧空间忽视测验上的得分提高并无显著差异,但虚拟现实组在真实环境(通过视频记录患者穿越道路的情况)中的表现好于对照组。Mi 等^[38]利用虚拟现实环境和运动任务,测试患者对忽视侧目标的反应,研究结果发现,相比于传统的空间忽视训练,参与虚拟现实环境训练的患者在 3 周训练结束后,在部分半侧空间忽视测验上的得分更好。

此外,也有研究针对希望重新驾驶汽车的脑卒中患者进行了针对性的空间注意功能训练,特别关注了视觉加工速度、分散注意和选择性注意^[39-40]。主要通过虚拟现实技术模拟真实场景进行训练^[41]。研究结果提示,相关训练在短期内对患者的视觉注意功能和驾驶技能有显著改善,但这种改善与对照组比较,差异并无显著统计学意义。

Bowen 等^[42]对 1998 年至 2005 年进行脑卒中后偏侧忽视认知康复训练的随机对照研究进行了 meta 分析,结果发现认知训练对改善患者在半侧空间忽视测验任务上的表现有显著效果,但这一效应是否可延伸到实际生活中则需进一步研究。

展望

一、虚拟现实等新技术在空间注意障碍康复中的应用

空间注意是一种复杂的高级认知功能,包含多种认知过程、要素。如,视觉空间注意包括多层次特征信息的筛选及综合,对某一空间范围的选择性注意常涉及多感觉通道信息的整合。虽然既往对脑卒中患者空间注意障碍的康复训练已取得了一定的临床(或实验证实的)效果,但由于设备条件和环境限制,既往采用的训练材料和方式往往比较单一抽象。这种局限可能对患者综合多种信息的能力训练不足,且和现实生活场景有较大差异。近年来,虚拟现实技术快速发展,提供了综合性强、且可量化控制的注意训练方案,解决了任务过于抽象等问题。将这些新技术运用到空间注意功能的训练中去,提升训练材料和环境的丰富性及拟真度,在一定程度上会给脑卒中后空间注意障碍患者的认知康复训练带来新视角、新思维。

二、综合训练多种注意成分以提高患者的空间注意及其他注意功能

脑卒中患者常同时存在多种注意障碍,这可能是由于脑损伤的同时累及了多种与注意相关的脑结构,还可能是“不同”注意成分的认知和神经机制本身存在复杂的交互作用。有研究者提出,半侧空间忽视现象可能部分是由于持续注意障碍所引起^[43],且可明显受到非偏侧化的注意广度/容量影响^[44]。因此,通过利用较详尽准确的注意功能及其相关脑结构/功能的评估(包括认知功能评定、脑结构/功能测定等),分析患者存在的注意障碍类型,并给予综合的康复训练,或许有望使脑卒中患者的空间注意障碍获得更多改善。

三、结合经颅磁刺激等物理因子治疗和认知训练干预脑卒中患者的注意功能障碍

经颅磁刺激/电刺激是一种相对无创的、可有效调控局部脑区神经活动兴奋性的干预手段。近年来,经颅磁刺激等治疗方式已被发现可改善患者脑卒中后的空间注意功能障碍^[45],但相关研究报道较少。结合认知康复训练和经颅磁刺激/电刺激等物理因子治疗,是否可更有效和针对性地改善脑卒中患者注意障碍、提高疗效等,都是极具临床价值和理论意义的研究问题。

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Fampridine for cognition, fatigue and depression in multiple sclerosis

BACKGROUND AND OBJECTIVE Cognitive impairment and fatigue are important symptoms among patients with multiple sclerosis (MS). While disease modifying treatments have been shown to significantly reduce the relapse rates of MS, data are much less clear regarding the effects of these medications on cognitive function. Fampridine is a potassium channel blocker which enhances signal conduction in demyelinated axons. This study was designed to understand the effects of this medication on symptoms of fatigue, as well as cognitive function.

METHODS This randomized, controlled trial included patients diagnosed with MS. The patients were randomized to receive either placebo or PRfampridine 10 mg twice per day, with cognitive functioning assessed twice within the first year and three times within the second year.

RESULTS Of the 32 patients who completed the first year, 20 completed the second year. Treatment with PRfampridine resulted in significant improvement in physical fatigue ($P=0.014$), cognitive fatigue ($P=0.003$), total fatigue ($P=0.0005$), depressive symptoms ($P=0.0049$), tonic alertness ($P=0.024$) phasic alertness ($P=0.042$), psychomotor speed ($P=0.014$), and verbal fluency ($P=0.0002$).

CONCLUSION This study of patients with multiple sclerosis found that treatment with PR-fampridine can improve emotional and cognitive symptoms and total fatigue.

【摘自:Broicher SD, Filli L, Geissler O, et al. Positive effects of fampridine on cognition, fatigue and depression in patients with multiple sclerosis over 2 years. J Neurol, 2018, 265(5):1016-1025.】

Corticospinal excitability and hand motor recovery after stroke

BACKGROUND AND OBJECTIVE Approximately half of stroke victims retain permanent motor deficits, despite rehabilitation. This study compared the changes in cortical excitability to motor recovery of a hand affected by a stroke.

METHODS Subjects were patients with ischemic lesions in the middle cerebral artery territory, with no contraindication for transcranial magnetic stimulation (TMS). Hand motor function was evaluated with the Wolf Motor Function Test (WMFT) and the Action Research Arm Test (ARAT). Corticospinal excitability was evaluated with resting motor threshold (rMT) and motor evoked potentials (MEP).

RESULTS Improvements on the WMFT over the first three weeks directly correlated with baseline hand function as assessed by ARAT ($P=0.005$) and WMFT ($P=0.003$). At the end of seven weeks, increases in ipsilesional MEP at APB were associated with increases in ARAT scores ($P=0.019$). No significant relationship was found between contralesional corticospinal excitability and hand motor recovery.

CONCLUSION This study suggests that a favorable motor recovery of the hand after stroke is associated with increased ipsilateral corticospinal excitability.

【摘自:Veldema J, Bösl K, Nowak DA. Cortico-Spinal Excitability and Hand Motor Recovery in Stroke: A Longitudinal Study. J Neurol, 2018, 265(5): 1071- 1078.】