

·论著·

## 针刺穴位联合康复训练治疗急性脑梗死上肢运动功能障碍并功能磁共振研究

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**摘要** 目的:观察针刺穴位联合康复训练治疗急性脑梗死上肢运动功能障碍的疗效,并借助功能磁共振探讨对神经功能重塑的影响。方法:选取急性脑梗死上肢运动功能障碍患者60例,随机分为对照组及治疗组,各30例。对照组行常规药物治疗和运动康复训练,治疗组在对照组的基础上给予针刺穴位治疗;均治疗3个月。于治疗前、后,对2组患者行美国国立卫生院脑卒中量表(NIHSS)评分、Fugl-Meyer上肢运动量表(FMA-UE)评分、患肢的食指轻叩试验检查、握力测量及运动任务态的功能磁共振扫描。结果:治疗后,2组的NIHSS评分、FMA-UE评分、患肢食指轻叩试验及握力测量均较治疗前改善(均P<0.01),且治疗组改善程度较对照组明显(均P<0.01)。治疗前,2组患者左手握拳运动可稳定激活对侧初级运动区(M1)及辅助运动区(SMA);治疗后,2组患者左手握拳运动时,对侧M1区及双侧SAM区较治疗前激活增强(P<0.01),且治疗组较对照组激活增强明显(P<0.01)。结论:针刺穴位联合康复训练治疗急性脑梗死上肢运动功能障碍疗效肯定,促进对侧M1及双侧SAM脑区的激活、调节神经功能重塑可能是其机制之一。

**关键词** 急性脑梗死;肢体运动;康复训练;针刺穴位;功能磁共振

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**An Functional MRI Study of Effects of Acupuncture Combined with Rehabilitation Training on Recovery of Upper Limb Motor Function in Ischemic Stroke Patients** LI Chun-yong<sup>1a,2</sup>, CHEN Huan<sup>3</sup>, LUO Gao-quan<sup>1a</sup>, WU Xiao-na<sup>1a</sup>, LIU Liu<sup>1a</sup>, JIANG Che<sup>1a</sup>, HAN Li-xin<sup>1b</sup>. 1a. Department of Neurosurgical Vascular and Gamma-ray Disease, b. MRI Room, the General Hospital of Guangzhou Military Command of PLA, Guangzhou 510010, China; 2. Department of Encephalopathy, Guangzhou Conghua District Hospital of Traditional Chinese Medicine, Guangzhou 510010, China; 3. Department of Comprehensive Rehabilitation, the Community Health Service Center of Jiekou Street, Guangzhou 510010, China

**Abstract Objective:** To investigate the effects of acupuncture combined with rehabilitation training on the recovery of upper limb motor function in patients with acute ischemic stroke and to study brain function remodeling using functional magnetic resonance imaging (fMRI). **Methods:** Sixty acute ischemic stroke patients with motor dysfunction of the upper limbs were randomly divided into the treatment group and control group, with 30 patients in each. Patients in both groups were treated with routine drugs and exercise rehabilitation training for 3 months, and patients in the treatment group were additionally given acupuncture treatment. All patients were assessed before and after treatment by the NIHSS score, Fugl-Meyer assessment for upper extremity (FMA-UE), index finger tapping test, grip strength measurement, and exercise task-based fMRI scanning. **Results:** After treatment, the index finger tapping test, hand grip strength, NIHSS score, and FMA-UE score in both groups were improved compared with those before treatment (all P<0.01), and the degree of improvement in the treatment group was significantly higher than that in the control group (all P<0.01). Before treatment, both groups showed activation of the contralateral primary motor region (M1) and supplementary motor area (SMA) during gripping exercises; after treatment, both groups showed enhanced activation in the contralateral M1 and bilateral SMA (P<0.01) compared to before treatment, and the treatment group showed a greater enhancement than the control group (P<0.01). **Conclusion:** In acute ischemic stroke patients with upper limb motor dysfunction, acupuncture combined with rehabilitation is an effective treatment that can promote activation of the bilateral SMA and contralateral M1 and remodeling of brain function.

**Key words** acute ischemic stroke; limb movement functions; rehabilitation training; acupuncture treatment; functional MRI

脑梗死发病率、致死率和致残率高,约60%的脑梗死患者存在不同程度的上肢运动功能障碍<sup>[1]</sup>,是康复治疗的难点。研究显

示神经功能可塑性与脑损伤后的神经功能修复密切相关<sup>[2]</sup>。氟西汀、文拉法辛及多奈哌齐等药物均被证实有可能干预神经功能

重塑,促进损伤神经修复<sup>[3-6]</sup>,但其疗效尚需进一步证实。中医针刺穴位治疗通过刺激相关穴位而反复刺激神经,增加大脑皮质相关功能区兴奋性,促进神经功能重塑<sup>[7,8]</sup>。康复训练通过反复、强化的固定练习,促进神经功能重塑,有利于肢体功能康复。因此,针刺穴位联合康复训练通过激活皮质特定运动功能区,调节神经功能重塑,有望改善脑梗死患者上肢运动功能障碍。本研究采用随机对照临床试验的方法,结合血氧水平依赖功能磁共振成像技术(blood oxygen level dependent-functional magnetic resonance imaging, BOLD-fMRI)<sup>[9]</sup>,观察针刺穴位联合康复训练治疗急性脑梗死上肢运动障碍的疗效及皮质功能区的重组情况,现报告如下。

## 1 资料与方法

### 1.1 一般资料

选择2017年1月至2019年1月在我科住院治疗的急性脑梗死后左上肢运动功能障碍患者60例。纳入标准:年龄40~80岁;符合全国第4届脑血管病学术会议通过的急性脑梗死诊断标准<sup>[10]</sup>;左上肢有轻至中度运动功能障碍,Brunnstrom分期<sup>[11]</sup>为Ⅲ~Ⅴ期;签署知情同意书。排除标准:处于脑梗死非急性期(病程>2周);既往有脑卒中史,存在左上肢运动功能障碍;患肢有外伤性疾病或周围神经损伤;合并心、肝、肺、肾或血液系统严重疾病;神志不清,生命体征不稳定,不能配合康复治疗者。

采用随机数字表法将60例患者随机分为对照组及治疗组,每组30例。对照组男性18例(60%),年龄(65.8±1.8)岁,病程(18.0±7.0)h;治疗组男性16例(52%),年龄(64.6±1.7)岁,病程(16.0±6.0)h;2组一般资料差异均无统计学意义( $P>0.05$ ),具有可比性。

### 1.2 方法

1.2.1 治疗 2组均给予急性脑梗死常规药物治疗(包括调控血压、血糖、血脂,抗栓,改善循环,清除自由基等)及左上肢常规康复治疗。常规康复治疗包括肌力增强训练、关节活动度训练及手指活动训练等,每次40分钟,每周5次,持续治疗3个月。治疗组在对照组的基础上加用针刺穴位治疗,穴取对侧头皮针运动区及患侧合谷、阳溪、曲池、内关、手三里、八邪、肩髃、肩贞等;急性期按泻法用针,恢复期按补法用针,每次30分钟,每周5次,连续治疗3个月。

1.2.2 观察指标 于治疗前及治疗3个月后对2组患者行美国国立卫生院脑卒中量表(National Institutes of

Health Stroke Scale, NIHSS)评分<sup>[12]</sup>、Fugl-Meyer上肢运动量表(Fugl-Meyer upper extremity motor assessment, FMA-UE)<sup>[13]</sup>评分、患肢食指轻叩试验检查<sup>[5,14]</sup>、手握力检查<sup>[5,14]</sup>及BOLD-fMRI检查。

fMRI检查采用组块设计。试验任务为左手动手作业220秒,分11个时相,20秒/时相,按静止和动手相交替。在动手阶段,被试以1Hz的节律行左手握拳动作;静止阶段被试保持全身放松、手腕手指均不动。患者通过视觉信息严格控制时间和运动频率。图像采集应用Siemens Sonata 3.0T超导型磁共振仪,梯度场40 mT/m,切换率200 mT/m/ms,使用标准头部线圈射频,头部运动被严格控制。首先对被试者头颅进行轴位T<sub>1</sub>WI扫描,然后采集被试在运动任务状态及休息状态的BOLD信号。采用梯度回波结合单次激发回波平面成像技术,参数为:TR 2000 ms, TE 49 ms, FOV 210 mm, 矩阵64×64, 层厚4 mm, 层间距1 mm, 扫描层面28层<sup>[4,5]</sup>。

### 1.3 统计学处理

临床数据采用SPSS 21.0软件处理数据。符合正态分布以及方差齐性的计量资料以( $\bar{x}\pm s$ )表示,组间比较采用独立样本均数t检验;计数资料以率表示,组间比较采用 $\chi^2$ 检验; $P<0.05$ 为差异有统计学意义。fMRI图像统计学分析采用统计参数图软件处理数据。数据先进行预处理,包括头动校正、空间标准化和空间平滑处理,然后进行个体分析、组内分析及组间分析。组内分析采用单样本t检验,获得实验任务各个组内的群体激活图,阈值设为 $P<0.01$ (FDR校正), $Ke\geq 10$ 。组间比较采用双样本t检验,比较2组间的激活图像差异,得出对照相关的激活增强图像[(动手-静止)<sub>治疗组</sub>-(动手-静止)<sub>对照组</sub>]>0,域值为 $P<0.01$ (FDR校正), $Ke\geq 10$ 。定量计算激活体积大小(体素值)和激活强度高低( $P<0.01$ 时t检验的T值)<sup>[4]</sup>。

## 2 结果

### 2.1 2组治疗前、后神经功能指标比较

治疗前,2组的NIHSS评分、FMA-UE评分、患肢食指轻叩试验叩击次数、手握力差异无统计学意义( $P>0.05$ )。治疗后,2组的FMA-UE评分、患肢食指轻叩试验叩击次数、手握力较同组治疗前提高,且治疗组高于对照组(均 $P<0.01$ );NIHSS评分较同组治疗前降低;且治疗组低于对照组(均 $P<0.01$ ),见表1、2。

### 2.2 2组治疗前、后fMRI比较

治疗前,2组患者在fMRI检测中,左手握拳运动可稳定激活对侧初级运动区(Primary Motor Area, M1)及

表1 2组治疗前后NIHSS评分、患肢FMA-UE评分比较(分,  $\bar{x}\pm s$ )

组别	例数	NIHSS评分		FMA-UE评分	
		治疗前	治疗后	治疗前	治疗后
对照组	30	13.26±2.35	6.21±1.82 <sup>①</sup>	26.38±12.32	35.26±11.23 <sup>①</sup>
治疗组	30	12.85±2.27	3.34±1.26 <sup>①②</sup>	25.26±11.28	39.35±12.16 <sup>①②</sup>

注:与治疗前比较,<sup>①</sup>P<0.05;与对照组比较,<sup>②</sup>P<0.05

表2 2组治疗前、后患肢手握力、食指轻叩试验比较( $\bar{x}\pm s$ )

组别	例数	手握力/kg		食指轻叩试验/(次/10 s)	
		治疗前	治疗后	治疗前	治疗后
对照组	30	13.26±2.35	18.21±2.82 <sup>①</sup>	20.28±3.32	29.26±2.43 <sup>①</sup>
治疗组	30	12.85±2.27	26.34±3.26 <sup>①②</sup>	19.26±3.05	30.35±3.16 <sup>①②</sup>

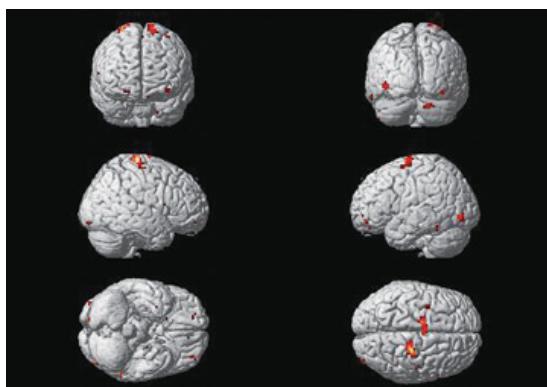
注:与治疗前比较,<sup>①</sup>P<0.05;与对照组比较,<sup>②</sup>P<0.05

辅助运动区(Supplementary Motor Area, SMA);治疗后,2组患者左手握拳运动时,对侧M1区及双侧SAM区较治疗前激活增强( $P<0.01$ ),且治疗组较对照组激活增强明显( $P<0.01$ ),见表3、图1。

表3 治疗组与对照组在治疗后脑区激活增强程度差异指标

脑区	感兴趣区的中心坐标(x,y,z)	激活体积(体素)	激活强度(T值)
右侧M1	26.18, -27.71, 72.64	82	6.28
左侧M1	/	/	/
右侧SMA	30.74, -22.00, 72.64	64	6.28
左侧SMA	-20.49, 10.58, 63.53	52	3.14

注:激活体积为体素值;激活强度为 $P<0.01$ 时t检验的T值



注:红色代表在治疗后,治疗组较对照组激活增强程度差异值,主要位于对侧的M1区及双侧的SAM区[ $P<0.01$ (FDR校正), $K_e\geq 10$ ]

图1 治疗组与对照组脑区激活增强程度差异群组分析图

### 3 讨论

上肢运动功能障碍是最常见的脑梗死后遗症之一。神经可塑性是指在脑损伤后,残留部分神经细胞通过轴突侧枝发芽、突触更新、突触调制、神经系统功能代偿等实现神经功能重组<sup>[15,16]</sup>,促进神经功能修复。BOLD-fMRI是基于大脑功能受血氧水平影响的原理的可视化脑功能研究手段,脑功能区活动的加权像信

号高于非活动区<sup>[9]</sup>,可用于研究脑损伤后皮质运动功能区及运动传导通路的重组情况。中医针刺穴位疗法是运用捻转与提插等针刺手法刺激人体穴位治疗疾病。对脑梗死患者的康复治疗研究显示,针刺相关穴位,可通过神经体液调节,促进支配运动功能神经元的兴奋,激活受损脑区,重新建立受损的神经环路,恢复中枢与周围神经的联系,促进运动功能恢复<sup>[17,18]</sup>。

本研究结果显示,针刺穴位联合康复训练治疗急性脑梗死上肢运动功能障碍3个月后,患者的NIHSS评分、FMA-UE评分及患肢的食指轻叩试验叩击次数、手握力均较对照组明显改善。BOLD-fMRI结果也显示治疗组患者在执行动手任务时,对侧M1及双侧SMA脑区的激活增强较对照组明显,提示针刺穴位联合康复训练能促进患者对侧M1及双侧SMA脑区的激活,促进神经功能重组及神经功能修复,有利于上肢运动功能的恢复。SAM脑区位于大脑皮质功能区的布鲁德曼(Brodmann)6区,与布鲁德曼(Brodmann)8区共同构成前运动区,主要参与运动执行的准备、辅助工作;M1脑区位于大脑皮质功能区的布鲁德曼(Brodmann)4区,为初级运动皮质,主要执行控制行为运动。本研究提示,急性脑梗死患者上肢运动功能损伤后初期以对侧M1激活为主,此阶段对侧M1在神经功能重组中起主导作用;脑损伤3个月后,对侧M1及双侧SMA脑区均被激活,均参与了恢复期的运动功能重组。因此,脑损伤后运动功能恢复过程中相关大脑皮质功能区的激活变化是一个动态演变的过程,有可能是从同侧激活转移为双侧激活,值得进一步研究。但实验样本量相对较小,具体机制还需要进一步深入探讨。

### 参考文献

- [1] Eraifej J, Clark W, France B, et al. Effectiveness of upper limb  
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- progression[J]. *Neurobiol Aging*, 2019, 73: 41-49.
- [18] Smith P Y, Hernandez-Rapp J, Jolivette F, et al. miR-132/212 deficiency impairs tau metabolism and promotes pathological aggregation in vivo[J]. *Hum Mol Genet*, 2015, 24: 6721-6735.
- [19] Hernandez-Rapp J, Rainone S, Goupil C, et al. microRNA-132/212 deficiency enhances Abeta production and senile plaque deposition in Alzheimer's disease triple transgenic mice[J]. *Sci Rep*, 2016, 6: 30953.
- [20] Chatterjee N, Sanphui P, Kemeny S, et al. Role and regulation of Cdc25A phosphatase in neuron death induced by NGF deprivation or β-amyloid[J]. *Cell Death Discovery*, 2016, 2: 16083.
- [21] Liu W, Zhao J, Lu G. miR-106b inhibits tau phosphorylation at Tyr18 by targeting Fyn in a model of Alzheimer's disease[J]. *Biochem Biophys Res Commun*. 2016, 478: 852-857.
- [22] Wang X, Xu Y, Zhu H, et al. Downregulated microRNA-222 is correlated with increased p27Kip(1) expression in a double transgenic mouse model of Alzheimer's disease[J]. *Mol Med Rep*. 2015, 12: 7687-7692.
- [23] Delobel P, Lavenir I, Ghetti B, et al. Cell-cycle markers in a transgenic mouse model of human tauopathy: increased levels of cyclin-dependent kinase inhibitors p21Cip1 and p27Kip1[J]. *Am J Pathol*. 2006, 168: 878-887.
- [24] Tian N, Cao Z, Zhang Y. MiR-206 decreases brain-derived neurotrophic factor levels in a transgenic mouse model of Alzheimer's disease[J]. *Neurosci Bull*, 2014, 30: 191-197.
- [25] Rodriguez-Fdez S, Bustelo X R. The Vav GEF Family: An Evolutionary and Functional Perspective[J]. *Cells*, 2019, 8: 465.
- [26] Choi I, Woo J H, Jou I, et al. PINK1 Deficiency Decreases Expression Levels of mir-326, mir-330, and mir-3099 during Brain Development and Neural Stem Cell Differentiation[J]. *Exp Neurobiol*, 2016, 25: 14-23.
- [27] Lane C A, Hardy J, Schott J M. Alzheimer's disease[J]. *Eur J Neurol*, 2018, 25: 59-70.
- [28] Machida T, Tomofuji T, Ekuni D, et al. MicroRNAs in Salivary Exosome as Potential Biomarkers of Aging[J]. *Int J Mol Sci*, 2015, 16: 21294-21309.
- [29] Henriques A D, Machado-Silva W, Leite R, et al. Genome-wide profiling and predicted significance of post-mortem brain microRNA in Alzheimer's disease[J]. *Mech Ageing Dev*, 2020, 191: 111352.
- [30] Li Q S, Cai D. Integrated miRNA-Seq and mRNA-Seq Study to Identify miRNAs Associated With Alzheimer's Disease Using Post-mortem Brain Tissue Samples[J]. *Front Neurosci*, 2021, 15: 620899.
- [31] Swarbrick S, Wragg N, Ghosh S, et al. Systematic Review of miRNA as Biomarkers in Alzheimer's Disease[J]. *Mol Neurobiol*, 2019, 56: 6156-6167.
- [32] Prendecki M, Florcak-Wyspianska J, Kowalska M, et al. APOE genetic variants and apoE, miR-107 and miR-650 levels in Alzheimer's disease[J]. *Folia Neuropathol*, 2019, 57: 106-116.
- [33] Dangla-Valls A, Molinuevo J L, Altirriba J, et al. CSF microRNA Profiling in Alzheimer's Disease: a Screening and Validation Study[J]. *Mol Neurobiol*, 2017, 54: 6647-6654.
- [34] Graner M W. Roles of Extracellular Vesicles in High-Grade Gliomas: Tiny Particles with Outsized Influence[J]. *Annu Rev Genomics Hum Genet*, 2019, 20: 331-357.
- [35] Song Z, Qu Y, Xu Y, et al. Microarray microRNA profiling of urinary exosomes in a 5XFAD mouse model of Alzheimer's disease[J]. *Animal Model Exp Med*, 2021, 4: 233-242.

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- functional electrical stimulation after stroke for the improvement of activities of daily living and motor function: a systematic review and meta-analysis[J]. *Syst Rev*, 2017, 6: 40.
- [2] Stewart JC, Cramer SC. Genetic Variation and Neuroplasticity: Role in Rehabilitation After Stroke[J]. *J Neurol Phys Ther*, 2017, 41: S17-S23.
- [3] Walker-Batson D, Mehta J, Smith P, et al. Amphetamine and other pharmacological agents in human and animal studies of recovery from stroke[J]. *Prog Neuropsychopharmacol Biol Psychiatry*, 2016, 64: 225-230.
- [4] Chun-yong Li, Xue-zhu Song, Lin-xin Han, et al. The effects of venlafaxine on cortical motor area activity in healthy subjects: a pilot study [J]. *J Clin Psychopharmacol*, 2014, 34: 93-98.
- [5] 黎春镛, 李映凯, 罗高权, 等. 利用静息态功能磁共振研究文拉法辛对健康成人的运动皮质的影响[J]. 中风与神经疾病杂志, 2018, 35: 772-777.
- [6] 黎春镛, 罗高权, 刘榴, 等. 多奈哌齐对急性缺血性脑卒中运动性失语患者言语功能的影响[J]. 神经损伤与功能重建, 2020, 15: 78-80, 107.
- [7] Qian Xu, Jing-Wen Yang, Yan Cao, et al. Acupuncture improves locomotor function by enhancing GABA receptor expression in transient focal cerebral ischemia rats[J]. *Neurosci Lett*, 2015, 588: 88-94.
- [8] Sánchez-Mila Z, Salom-Moreno J, Fernández-De-Las-Peñas C. Effects of dry needling on post-stroke spasticity, motor function and stability limits: a randomised clinical trial[J]. *Acupunct Med*, 2018, 36: 358-366.
- [9] Kim PE, Singh M. Functional magnetic resonance imaging for brain mapping in neurosurgery[J]. *Neurosurg Focus*, 2003, 15: E1.
- [10] 中华神经学会, 中华神经外科学会. 各类脑血管疾病诊断要点[J].

- 中华神经科杂志, 1996, 29: 379-380.
- [11] Chien-Yu Huang, Gong-Hong Lin, Yi-Jing Huang, et al. Improving the utility of the Brunnstrom recovery stages in patients with stroke: Validation and quantification[J]. *Medicine (Baltimore)*, 2016, 95: e4508.
- [12] Vanacker P, Heldner MR, Amiguet M, et al. Prediction of Large Vessel Occlusions in Acute Stroke: National Institute of Health Stroke Scale Is Hard to Beat[J]. *Crit Care Med*, 2016, 44: e336-343.
- [13] Amano, Umeji, Takebayashi, et al. Clinimetric properties of the shortened Fugl-Meyer Assessment for the assessment of arm motor function in hemiparetic patients after stroke[J]. *Top Stroke Rehabil*, 2020, 27: 290-295.
- [14] Chunyong Li, Fuda Liu, Haiyan Peng, et al. The positive effect of venlafaxine on central motor conduction[J]. *Clin Neurol Neurosurg*, 2018, 167: 65-69.
- [15] Wang H, Gau U, Xiao J, et al. Targeting phosphodiesterase 4 as a potential therapeutic strategy for enhancing neuroplasticity following ischemic stroke[J]. *Int J Biol Sci*, 2018, 14: 1745-1754.
- [16] Yefei Sun, Xiaoyu Sun, Huiling Qu, et al. Neuroplasticity and behavioral effects of fluoxetine after experimental stroke[J]. *Restor Neurol Neurosci*, 2017, 35: 457-468.
- [17] Lina M Chavez, Shiang-Suo Huang, Iona MacDonald, et al. Mechanisms of Acupuncture Therapy in Ischemic Stroke Rehabilitation: A Literature Review of Basic Studies[J]. *Int J Mol Sci*, 2017, 18: 2270.
- [18] Lin Lu, Xiao-guang Zhang, Linda L D Zhong, et al. Acupuncture for neurogenesis in experimental ischemic stroke: a systematic review and meta-analysis[J]. *Sci Rep*, 2016, 6: 19521.

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