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· 论 著 ·

不同形式重复经颅磁刺激治疗卒中后非流利性失语症的疗效观察

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[摘要] **目的** 探究不同形式重复经颅磁刺激(rTMS)治疗卒中后非流利性失语症的疗效。**方法** 纳入2021年1月至2022年10月于海军军医大学(第二军医大学)第一附属医院脑血管病中心住院治疗的卒中后非流利性失语症患者45例,根据随机数字表法分为伪刺激组、单侧rTMS治疗组和双侧rTMS治疗组,每组15例。伪刺激组患者予常规语言训练,单侧rTMS治疗组患者在常规语言训练基础上予单侧rTMS治疗,双侧rTMS治疗组患者在常规语言训练基础上予双侧rTMS治疗。比较治疗前后3组患者西方失语成套测验(WAB)自发语言评分、听理解评分、命名评分、复述评分及失语商。**结果** 治疗前,3组患者的WAB自发语言评分、听理解评分、命名评分、复述评分和失语商差异均无统计学意义($P>0.05$)。治疗后,3组患者的WAB自发语言评分、听理解评分、命名评分、复述评分和失语商均较治疗前提高($P<0.05$)。治疗后,单侧rTMS治疗组、双侧rTMS治疗组的WAB自发语言评分、听理解评分、命名评分、复述评分和失语商均高于伪刺激组($P<0.05$),但单侧rTMS治疗组和双侧rTMS治疗组上述指标差异均无统计学意义($P>0.05$)。**结论** 常规语言训练联合rTMS治疗可有效改善卒中后非流利性失语症患者的语言功能,但双侧rTMS治疗的效果并不优于单侧rTMS治疗。

[关键词] 重复经颅磁刺激;卒中后失语症;非流利性失语症;语言训练

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Different forms of repetitive transcranial magnetic stimulation on post-stroke non-fluent aphasia: efficacy observation

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[Abstract] **Objective** To explore the efficacy of different forms of repetitive transcranial magnetic stimulation (rTMS) on post-stroke non-fluent aphasia. **Methods** A total of 45 patients with post-stroke non-fluent aphasia who were hospitalized in Neurovascular Center of The First Affiliated Hospital of Naval Medical University (Second Military Medical University) from Jan. 2021 to Oct. 2022 were randomly assigned (1 : 1 : 1) to pseudo-stimulus group, unilateral rTMS treatment group, or bilateral rTMS treatment group. Patients in the pseudo-stimulus group received conventional language training, patients in the unilateral rTMS treatment group received unilateral rTMS therapy on the basis of conventional language training, and patients in the bilateral rTMS treatment group received bilateral rTMS therapy on the basis of

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conventional language training. The spontaneous speech score, listening comprehension score, naming score, retelling score and the aphasia quotient (AQ) in the Western aphasia battery (WAB) of the 3 groups were compared before and after treatment.

Results Before treatment, there were no significant differences in WAB scores (spontaneous speech, listening comprehension, naming, or retelling) or AQ among the 3 groups (all $P>0.05$). After treatment, the WAB scores (spontaneous speech, listening comprehension, naming, or retelling) and AQ of the 3 groups were significantly increased (all $P<0.05$); the WAB scores (spontaneous speech, listening comprehension, naming, or retelling) and AQ of the 2 treatment groups were significantly higher than those of the pseudo-stimulus group (all $P<0.05$), but there were no significant differences in the above indexes between the unilateral or bilateral rTMS treatment groups (all $P>0.05$). **Conclusion** Conventional language training combined with rTMS therapy can significantly improve the language function of patients with post-stroke non-fluent aphasia, but the effect of bilateral rTMS is not superior to that of unilateral rTMS.

[**Key words**] repetitive transcranial magnetic stimulation; post-stroke aphasia; non-fluent aphasia; language training

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失语症是指由于各种原因引起的器质性脑疾病导致支配大脑语言表达和听力理解的相关脑区受损,使患者无法进行正常的语言表达、无法理解对方语言的一种语言障碍综合征^[1]。失语症是脑卒中最常见的后遗症之一^[2]。据统计,脑卒中患者失语症的发生率为20%~40%^[3]。非流利性失语症是卒中后失语症最常见的类型,其导致的语言表达失败主要为语言输出、句子处理、语音编辑等障碍,临床表现主要有语音错误明显,说话费力、犹豫、经常停顿等^[3-5]。即使是轻微的失语症,也会对患者的功能结局、情绪、生活质量、社会参与度和重返工作岗位的能力产生负面影响^[6]。

语言训练是卒中后失语症患者首选的治疗方法^[7]。但合并中度至重度非流利性失语症的脑卒中幸存者自然恢复通常较差,传统语言训练治疗可能无法改善^[8],且随着时间的推移语言训练的有效性也会降低^[9]。研究发现,非侵入性脑刺激技术可以诱导神经兴奋性发生持久变化,从而导致功能重组,最终达到改善语音和语言功能的目的^[10-11]。重复经颅磁刺激(repetitive transcranial magnetic stimulation, rTMS)是治疗卒中后失语症的一种非侵入性脑刺激技术^[12],其原理是通过头皮上的刺激线圈传递短暂而强烈的电流诱导时变电磁场,磁场穿透头皮后又会在刺激部位产生微弱且短暂的电流,从而诱导神经元放电^[13]。低频(≤ 1 Hz) rTMS抑制大脑皮质,高频(≥ 5 Hz) rTMS兴奋大脑皮质,低频和高频 rTMS 都有利于改善亚急性和慢性失语症患者的语言预后^[6]。有研究表明,

rTMS作为一种神经调节技术,能够增强传统语言训练治疗的效果^[7]。本研究拟观察不同形式 rTMS 治疗卒中后非流利性失语症患者的疗效,为卒中后失语症患者提供临床治疗依据。

1 资料和方法

1.1 研究对象 选择2021年1月至2022年10月在海军军医大学(第二军医大学)第一附属医院脑血管病中心住院治疗的急性脑卒中后非流利性失语症患者46例,按随机数字表法分为伪刺激组、单侧 rTMS 治疗组、双侧 rTMS 治疗组。纳入标准:(1)年龄为18~80岁;(2)明确诊断为脑卒中后非流利性失语症,诊断依据为西方失语成套测验(Western aphasia battery, WAB);(3)首次发病,为左侧大脑半球单侧病灶,病程 <2 周,且美国国立卫生研究院卒中量表(National Institutes of Health stroke scale, NIHSS)评分 <8 分;(4)母语为汉语;(5)受教育程度为小学及以上;(6)右利手;(7)自愿参加本研究并签署知情同意书。排除标准:(1)有严重的认知功能障碍;(2)有视听觉障碍;(3)有精神病史;(4)有癫痫病史;(5)植入心脏起搏器或患有其他严重心脏病。脱落标准:(1)希望停止参与试验;(2)无法完成疗程;(3)无法参与基线评估。本研究方案符合《赫尔辛基宣言》原则,获得海军军医大学(第二军医大学)第一附属医院伦理委员会审批(CHEC2018-003)。

1.2 治疗方法 伪刺激组仅予常规语言训练;单

侧 rTMS 治疗组在常规语言训练基础上,予右侧大脑半球 Broca 镜像区 rTMS 治疗;双侧 rTMS 治疗组在常规语言训练基础上,予双侧大脑半球 Broca 区及 Broca 镜像区 rTMS 治疗。

(1) 常规语言训练:应用以 Schuell 刺激疗法为基础的语言功能训练,结合旋律语调治疗^[14]、强制诱导等常规语言训练^[6],对患者进行强且集中的语言刺激、听觉刺激、触觉刺激,激发并强化患者正确的语言反应,从而促进患者语言功能的恢复和改善。具体训练内容根据患者的失语症类型及严重程度确定,实施一对一言语训练。每次治疗 20 min,每天治疗 2 次,共治疗 20 次。

(2) rTMS 治疗:患者取坐位,刺激线圈为“8”字线圈。单侧 rTMS 治疗组患者给予右侧大脑半球 Broca 镜像区低频 rTMS 治疗,频率为 1 Hz,刺激强度为运动阈值的 80%,刺激持续时间为 8 s,间隔时间为 3 s,脉冲总数为 1 000 个。双侧 rTMS 治疗组患者给予右侧大脑半球 Broca 镜像区低频 rTMS+左侧大脑半球 Broca 区高频 rTMS 治疗,刺激强度为运动阈值的 80%,右侧低频频率为 1 Hz,左侧高频频率为 10 Hz。每次治疗 20 min,每天治疗 2 次,共治疗 20 次。在治疗过程中,如患者发生病情变化立即停止治疗。

1.3 临床资料收集与评价指标 收集患者的性别、年龄等人口统计学信息,高血压病、糖尿病、心房颤动等脑卒中危险因素,以及治疗前后 WAB 自发语言、听理解、命名、复述 4 项的评分,并计算失语商:失语商=(自发语言评分+听理解评分+命名评分+复述评分)×2。失语商分值越低表示患者失语程度越严重,失语商<93.8 分即可评为失语症。

1.4 统计学处理 采用 SPSS 23.0 软件进行统计学分析。计量资料以 $\bar{x} \pm s$ 表示,组间比较采用单因素方差分析,组内比较采用配对 *t* 检验;计数资料以例数和百分数表示,采用 χ^2 检验进行组间比较。检验水准 (α) 为 0.05。

2 结果

2.1 基线资料 纳入急性脑卒中后非流利性失语症患者共 46 例,其中 1 例患者因个人原因中途退出,最终伪刺激组、单侧 rTMS 治疗组、双侧 rTMS 治疗组各 15 例。3 组患者的年龄、性别、高血压病史、糖尿病史、心房颤动病史、治疗前 NIHSS 评分及治疗前 WAB 各项评分(自发语言、听理解、命名、复述评分)和失语商差异均无统计学意义 ($P>0.05$)。见表 1。

表 1 3 组卒中后非流利性失语症患者基线资料

Tab 1 Baseline data of patients with post-stroke non-fluent aphasia in 3 groups

Index	Pseudo-stimulus group	Unilateral rTMS treatment group	Bilateral rTMS treatment group	Statistic	<i>P</i> value
Age/year, $\bar{x} \pm s$	68.20 ± 7.50	69.47 ± 6.45	69.87 ± 6.51	<i>F</i> =0.243	0.785
Male, <i>n</i> (%)	10 (66.67)	10 (66.67)	11 (73.33)	χ^2 =0.097	0.908
Stroke risk factor, <i>n</i> (%)					
Hypertension	12 (80.00)	9 (60.00)	13 (86.67)	χ^2 =1.569	0.220
Diabetes mellitus	5 (33.33)	4 (26.67)	8 (53.33)	χ^2 =0.359	0.701
Atrial fibrillation	1 (6.67)	5 (33.33)	3 (20.00)	χ^2 =1.680	0.199
Baseline NIHSS score, $\bar{x} \pm s$	3.87 ± 1.30	3.33 ± 1.59	3.60 ± 1.64	<i>F</i> =0.463	0.632
Baseline WAB assessment, $\bar{x} \pm s$					
Spontaneous speech score	6.87 ± 1.92	8.80 ± 2.88	8.67 ± 2.58	<i>F</i> =2.809	0.072
Listening comprehension score	5.89 ± 1.06	7.04 ± 1.39	6.74 ± 1.46	<i>F</i> =3.083	0.056
Retelling score	6.47 ± 1.30	7.53 ± 1.73	7.07 ± 1.71	<i>F</i> =1.693	0.196
Naming score	6.55 ± 0.97	6.84 ± 1.00	6.51 ± 1.02	<i>F</i> =0.500	0.610
Aphasia quotient	51.55 ± 8.81	60.41 ± 9.50	57.96 ± 11.20	<i>F</i> =3.211	0.051

rTMS: Repetitive transcranial magnetic stimulation; NIHSS: National Institutes of Health stroke scale; WAB: Western aphasia battery.

2.2 干预效果 治疗后3组患者的WAB自发语言评分、听理解评分、命名评分、复述评分及失语商均高于治疗前 ($P < 0.05$)。治疗后,单侧、双侧

rTMS治疗组上述指标均高于伪刺激组 ($P < 0.05$),但单侧rTMS治疗组和双侧rTMS治疗组上述指标差异均无统计学意义 ($P > 0.05$)。见表2。

表2 3组卒中后非流利性失语症患者干预效果比较

Tab 2 Comparison of intervention outcomes of patients with post-stroke non-fluent aphasia among 3 groups

WAB assessment	Pseudo-stimulus group		Unilateral rTMS treatment group		Bilateral rTMS treatment group	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Spontaneous speech score	6.87±1.92	10.07±2.66*	8.80±2.88	13.93±3.13* [△]	8.67±2.58	15.27±2.55* [△]
Listening comprehension score	5.89±1.06	7.56±0.81*	7.04±1.39	8.43±1.05* [△]	6.74±1.46	8.70±1.04* [△]
Retelling score	6.47±1.30	8.00±1.09*	7.53±1.73	9.11±1.20* [△]	7.07±1.71	9.03±1.08* [△]
Naming score	6.55±0.97	7.70±1.06*	6.84±1.00	8.75±0.84* [△]	6.51±1.02	9.11±0.66* [△]
Aphasia quotient	51.55±8.81	66.66±9.07*	60.41±9.50	80.45±8.40* [△]	57.96±11.20	84.21±8.26* [△]

* $P < 0.05$ vs before treatment of the same group; [△] $P < 0.05$ vs pseudo-stimulus group after treatment. rTMS: Repetitive transcranial magnetic stimulation; WAB: Western aphasia battery.

3 讨论

rTMS治疗卒中后失语症的机制是基于大脑语言功能区恢复过程中脑的可塑性和脑神经功能的网络重组^[15]。语言训练可以提高卒中后非流利失语症患者的语言功能和日常交际能力^[16]。卒中后失语症患者语言功能恢复的关键在于左侧大脑半球语言功能残留区的激活^[17]。正常健康状态下,双侧大脑半球皮质处在一个相互抑制的平衡状态。当左侧大脑优势半球Broca区受损时,这种相互抑制的平衡状态即被打破,右侧大脑皮质的抑制作用便会增强,导致语言功能障碍。影像学研究显示,在进行言语表达时,除左侧大脑半球Broca区被激活,右侧大脑半球Broca镜像区也同时受到很强的激活刺激^[18]。低频rTMS可降低右侧大脑半球皮质的兴奋性,高频rTMS可增强左侧大脑优势半球的兴奋性,所以低频rTMS通常应用于右侧大脑半球^[6],在亚急性和慢性卒中后失语症的相关语言任务中,抑制右侧大脑半球激活,同时刺激左侧大脑半球激活^[19]。有研究指出,rTMS可以通过脑网络和脑神经功能的相互关联,有效调节卒中后失语症患者左右两侧大脑半球的失衡状态,从而改善患者的语言功能^[20]。

本研究结果显示,卒中后非流利性失语症患者治疗后的WAB自发语言评分、听理解评分、命名评分、复述评分及失语商与治疗前相比均得到改善,且单侧rTMS治疗组和双侧rTMS治疗组

的效果均优于伪刺激组,但单侧rTMS治疗组和双侧rTMS治疗组之间差异没有统计学意义。由此表明,双侧rTMS和单侧rTMS联合常规语言训练治疗卒中后非流利性失语症均有效,2种方法均可明显改善卒中后非流利性失语症患者的语言功能。有研究也显示低频和高频rTMS对卒中后非流利性失语症均有效,其中低频rTMS组在治疗后即刻和2个月时WAB评估结果明显改善,患者能够即时获益;而高频rTMS组在治疗2个月后有改善,达到相对远期的获益^[21]。未来仍需进一步探索高频和低频rTMS在何种条件下对卒中后失语症疗效最佳。

综上所述,常规语言训练联合rTMS治疗能更有效地改善卒中后非流利性失语症患者的语言功能,使患者早日回归家庭、回归社会。本研究显示双侧rTMS和单侧rTMS治疗卒中后非流利性失语症的效果都较显著,且疗效相当。但本研究样本量较小,评价指标单一,也并未探讨药物治疗和血管内治疗可能给患者语言功能方面带来的影响,因此对本研究结果仍需谨慎解读。

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