基于rTMS的联合治疗在脑卒中手功能康复中的应用

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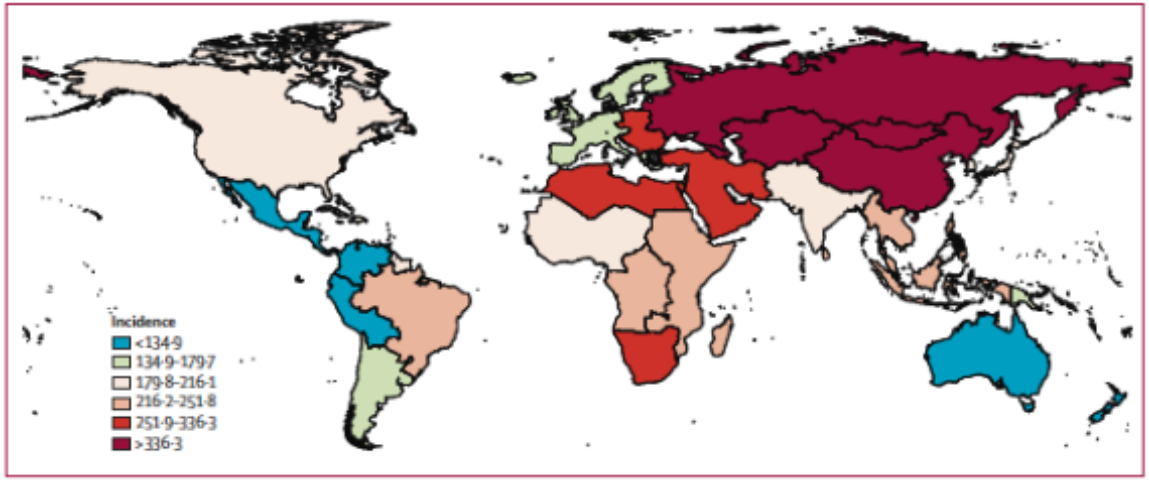
脑卒中

- 从全球来看
  - 60岁以上人群死亡的第二大原因
  - 15 - 59岁人群死亡的第五大原因
- 在中国
  - 首次中风一年期总体存活率大约为86.4%



2010年年龄标准化的卒中患病率每10万人年

（摘自Valery Feigin 等，lancet，2014）

脑卒中

ICF 成分	ICF 类目
身体功能	意识状态
	定位功能
	肌肉力量
	语言功能
	注意功能
	记忆功能
身体结构	脑的结构
	上肢结构
活动和参与	步行
	言语
	如厕
	吃饭
	洗漱
	穿衣
	信息言语交流
环境因素	直系亲属
	健康专业人员
	健康服务、系统及政策

- 发病即有下肢瘫痪者，35%不能恢复功能性步行
- 20 - 25%不能完全独立步行
- 6个月时，65%患者上肢不能完成功能性活动
- 其他：认知，言语等

＊25%患者活动参与能力能恢复到同比非卒中人群水平

脑卒中—上肢&手康复现状

- 卒中早期，□80%的患者存在上肢运□功能障碍（Smania N,2011）
- 即使□□常□的康复，文献□道□有 5–20%的卒中患者能完全恢复上肢及手功能（Nakayama H,1994；Wade DT，1982;）
- 日常生活活□能力以及社会参与、生活□量均因此受累（Lai SM,2002；Johansson A，2007；Nichols-Larsen DS,2005）

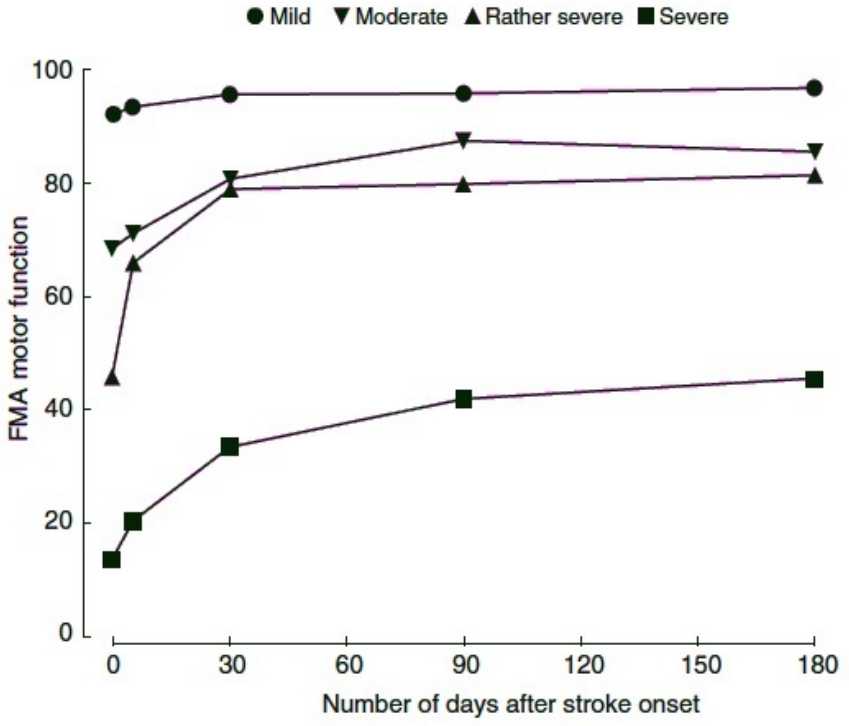


Fig. 2.1 Changes in post-stroke upper limb hemiparesis score. After the stroke onset, the FMA score of upper limb hemiparesis reaches a plateau state on Day 90 regardless of the severity

Duncan PW et al.,1992，Jorgensen et al，1999

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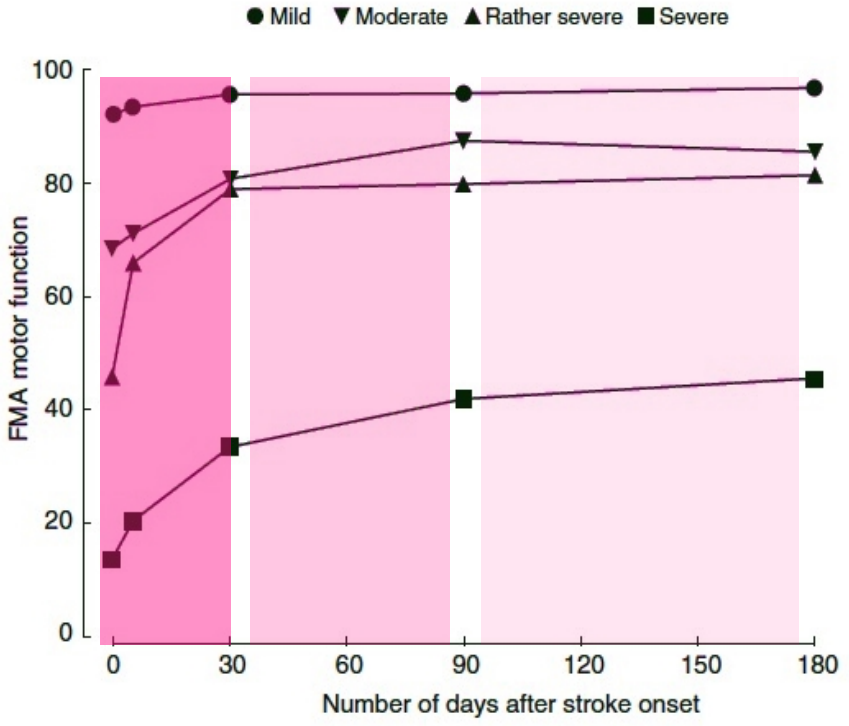

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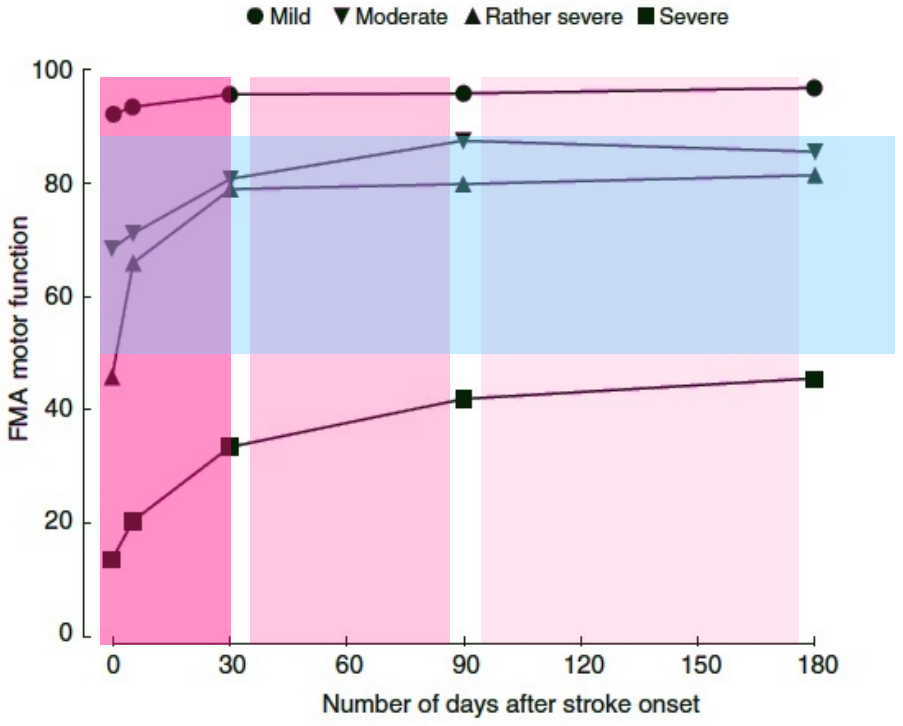

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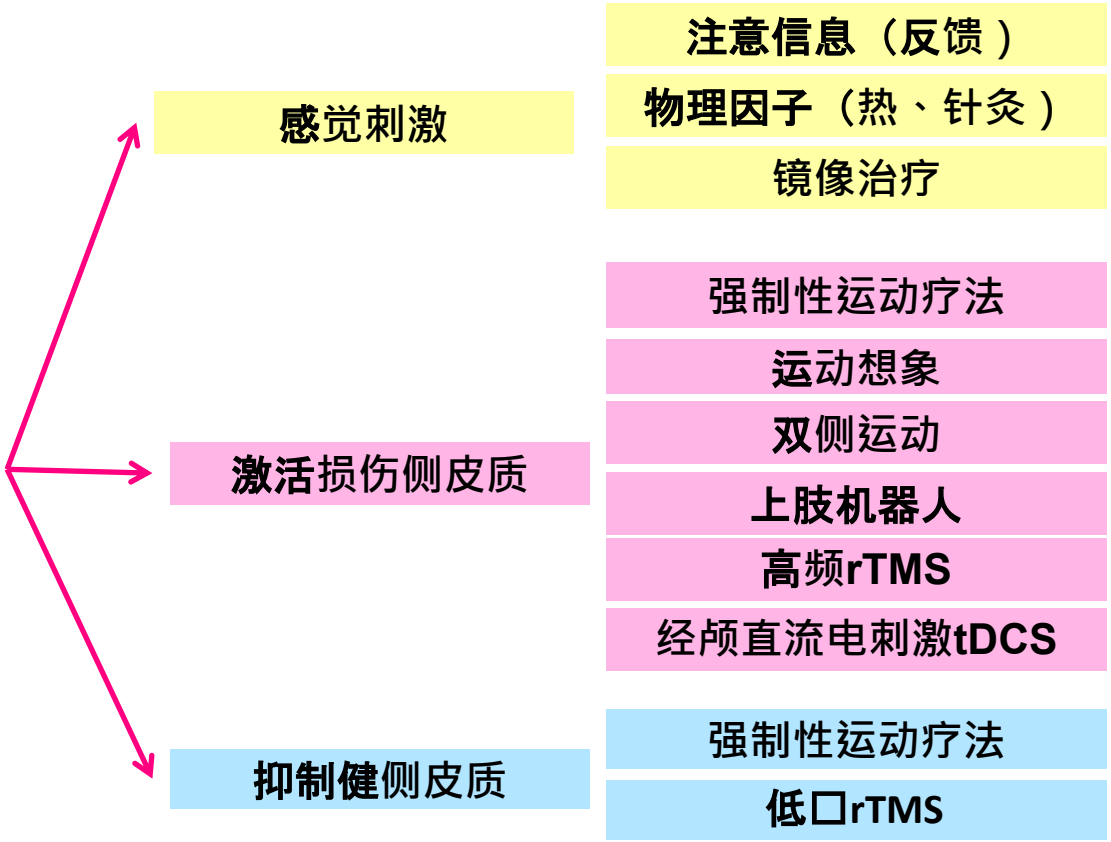
脑卒中—上肢&手康复现状

- 肌电生物反馈
- 电刺激
- 高强度刺激
- 运动想象疗法
- 重复性任务训练
- 机器人辅助训练
- 支具辅助训练
- 综合性训练
- 运动再学习训练
- 神经发育疗法
- 限制诱导训练



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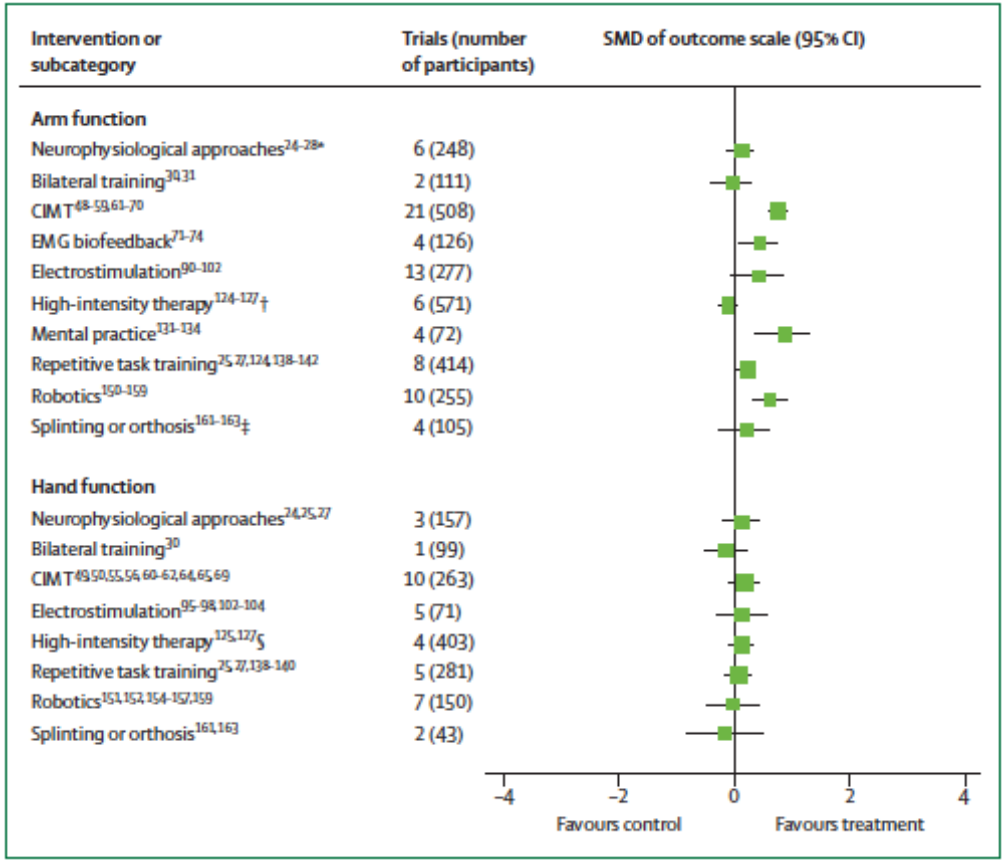

Langhorne P, et al.,2009,Lancet Neurol

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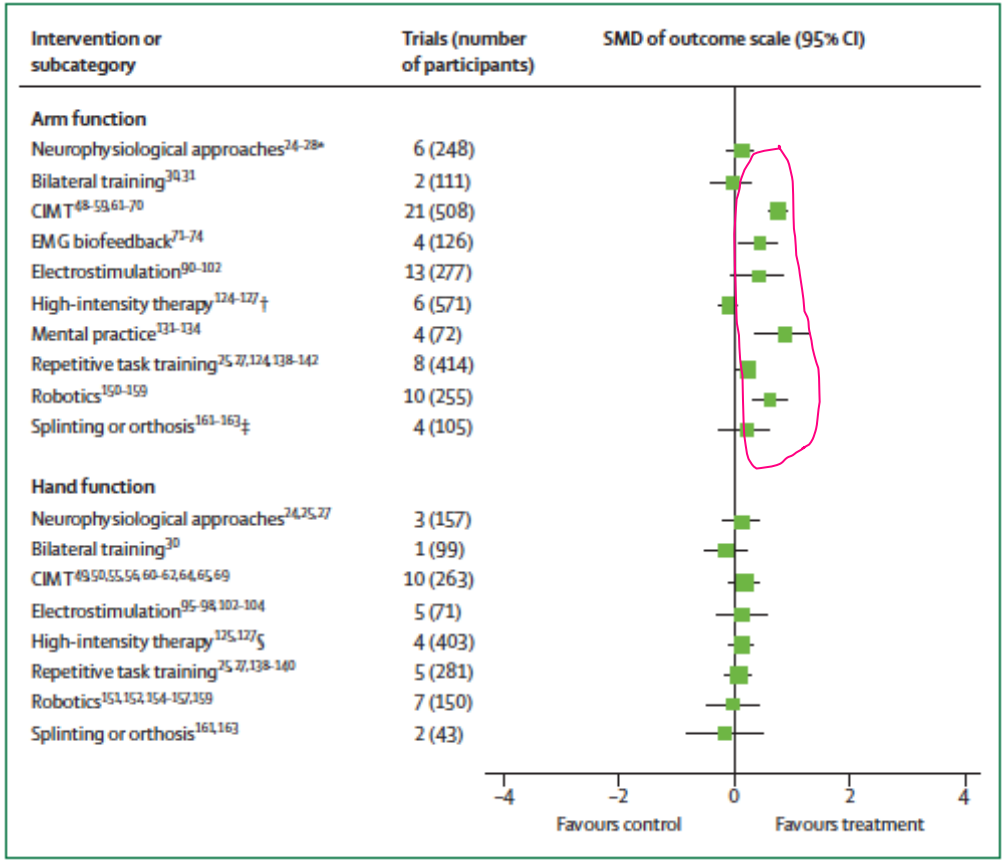

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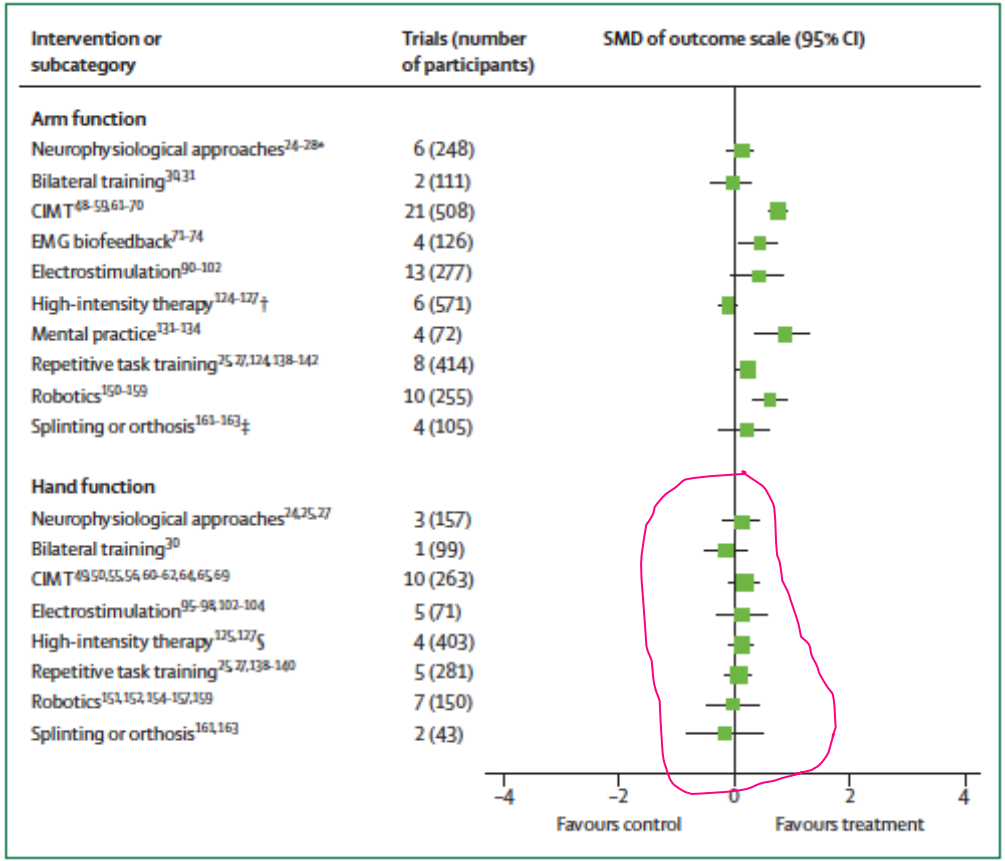


Langhorne P, et al.,2009,Lancet Neurol

脑卒中－上肢&手康复现状

临床指南－*motor disorders and ADL*

- 尽早开始康复治疗以促进功能恢复和降低功能障碍(Grade A)
- 在疾病的早期，推荐增加康复训练的频次和数量，能更有效的促进康复(Grade A)
- 神经促进技术（Bobath，PNF, Brunnstrom等）可以进行，但是无高质量证据证明比传统康复更有效(Grade C1)

Shinohara Y, Ogawa S, et al. Japanese guidelines for the management of stroke. Tokyo: Kyowa Kikaku; 2009. p. 308–12

脑卒中－上肢&手康复现状

临床指南－*upper limb function*

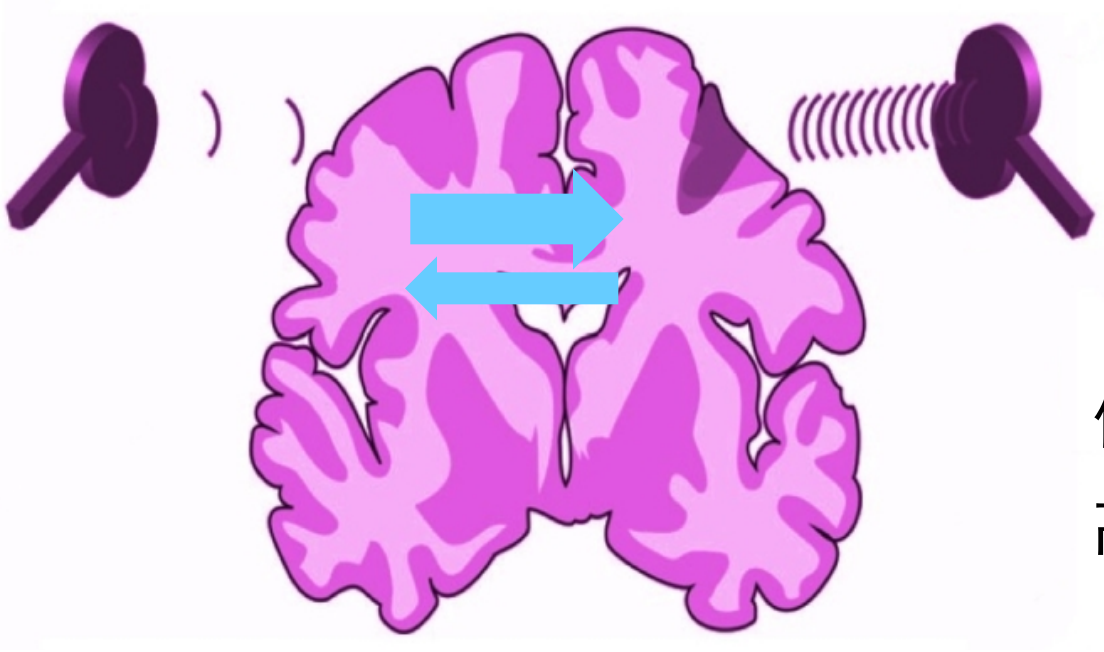
- 受累上肢推荐主动重复特定任务训练（包括上肢够物活动，双侧上肢重复性活动，目标为导向的活动，运动想象等）(Grade A)
- 对于轻瘫者，推荐限制健侧，强制日常生活中使用患侧的治疗(Grade B)
- 对于中度瘫痪患者，电刺激对强化伸腕肌肉的力量训练尤其推荐(Grade B)

Shinohara Y, Ogawa S, et al. Japanese guidelines for the management of stroke. Tokyo: Kyowa Kikaku; 2009. p. 308–12

重复性经颅磁刺激(rTMS)

LF-rTMS（低频）

HF-rTMS（高频）



直接刺激大脑皮层而促进大脑重组功能

低频<=1Hz，　抑制作用

高频>＝5Hz，兴奋作用

rTMS—脑卒中手功能康复的疗效

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对手指运动功能以及手功能有正性影响

REVIEW & ANALYSIS

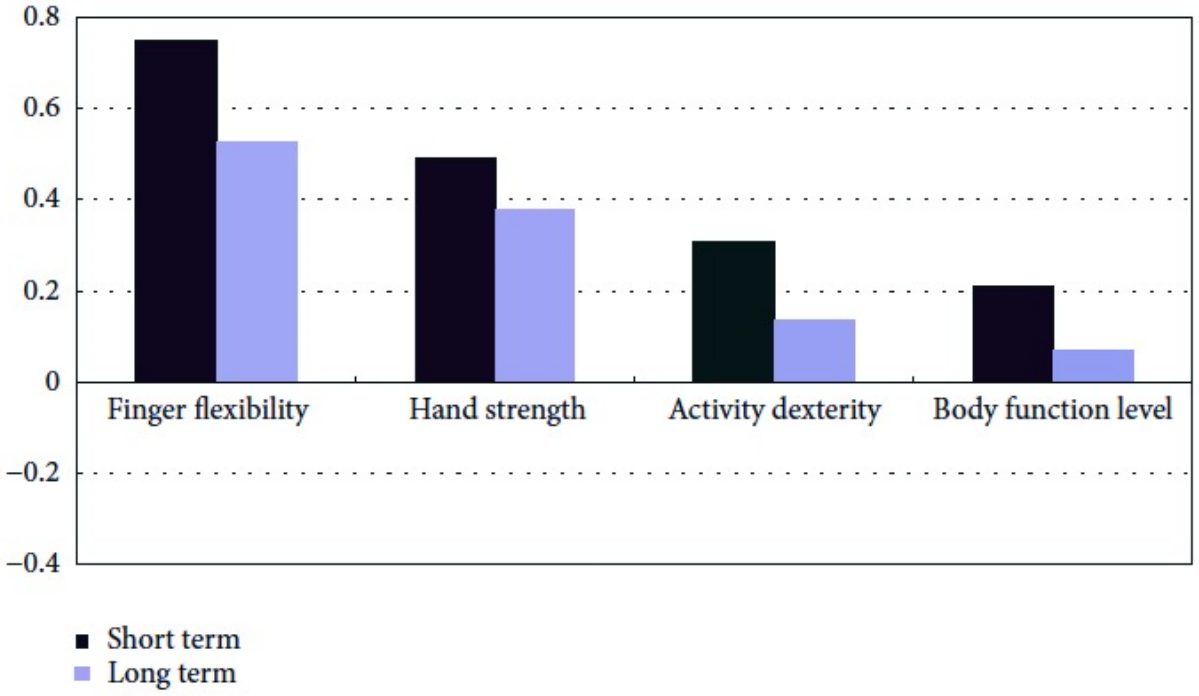
Effects of Repetitive Transcranial Magnetic Stimulation on Hand Function Recovery and Excitability of the Motor Cortex After Stroke

A Meta-Analysis

Results: Of 1668 articles identified, 8 articles ($N = 273$) were included in this study. The summary effect size indicated positive effects of rTMS on finger motor ability (standardized mean difference, 0.58) and hand function (standardized mean difference, −0.82). However, this study showed that the changes of neurophysiologic measurements were not significant in the included studies. Even so, the trend of these changes was positive. Few adverse events were observed.

Le Q,et al., 2014

rTMS—脑卒中手功能康复的疗效

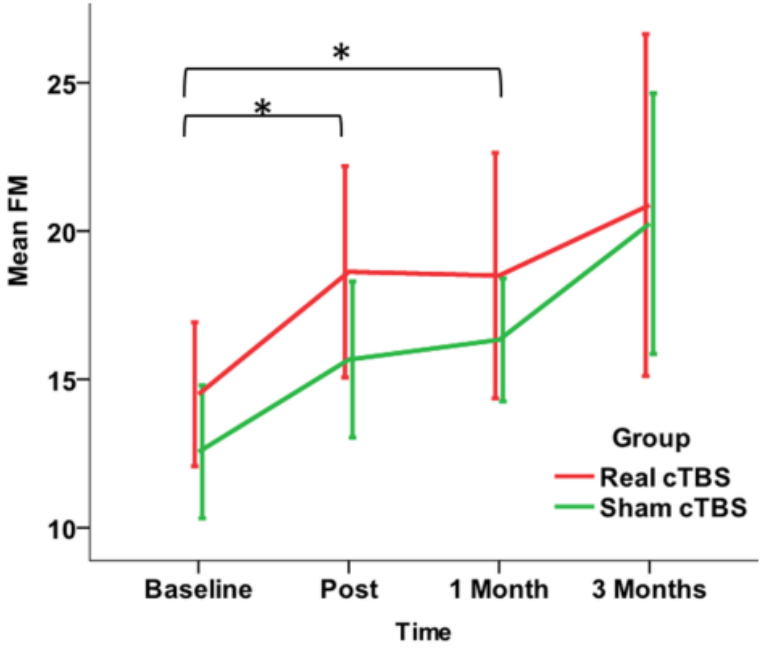


- LF-rTMS作为一种附加治疗手段，可以显著改善上肢功能，特别是卒中后的手功能
- 叠加治疗的效果更值得研究

Lan Zhang,et al., 2017

rTMS联合治疗—脑卒中手功能康复的疗效

cTBS+机器人辅助治疗



更适合BMS 4-5期患者

Lazzaro, V. D.et al,2016

rTMS联合治疗—脑卒中手功能康复的疗效

rTMS+任务为导向训练

Clinical Study

Combining rTMS and Task-Oriented Training in the Rehabilitation of the Arm after Stroke: A Pilot Randomized Controlled Trial

Introduction. Repetitive transcranial magnetic stimulation (rTMS) is a promising technique for promoting rehabilitation of arm function after stroke. The feasibility and impact of rTMS as an adjunct to traditional task-oriented training to improve arm function have not yet been demonstrated. *Objective*. Evaluate the feasibility of a randomized controlled trial aimed at determining the efficacy of rTMS as an adjunct to task-oriented therapy in facilitating restoration of arm function after stroke. *Methods*. Stratified block-randomized controlled trial set in the general community. Eleven stroke persons with mild to severe arm deficits were recruited and randomized to receive 8 sessions of *real*-rTMS or *sham*-rTMS followed by ninety minutes of arm tasks designed to improve function. *Results*. Medium to large, statistically significant effect sizes (0.49 to 1.63) were observed in both groups on several measures of arm function at the postintervention evaluation. Three out of four subjects in the *real*-TMS condition showed increased levels of corticomotor excitability after the first stimulation session. *Conclusions*. Preliminary evidence suggests that an rTMS protocol potent enough to induce transient increases in cortical excitability of the lesioned hemisphere is feasible but did not show promising results as an adjunct to task-specific training. This trial is registration with Clinical Trials.gov NCT00850408.

联合治疗未显示比单纯对任务导向训练更显著的效果 Higgins, J.,2013

rTMS联合治疗—脑卒中手功能康复的疗效

rTMS+肌电触发功能性神经肌肉电刺激EMG-FNMS

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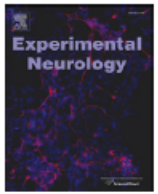


Functional neuromuscular stimulation to improve severe hand dysfunction after stroke: Does inhibitory rTMS enhance therapeutic efficiency?

Steven Theilig [a], Jitka Podubecka [a], Kathrin Bösl [a], Ralf Wiederer [a], Dennis A. Nowak [a,b,*]

[a] Neurologische Fachklinik Kipfenberg, Kipfenberg, Germany
[b] Neurologische Universitätsklinik, Philipps-Universität Marburg Marburg, Marburg, Germany

- 手功能（手指+手腕）和肌张力都显著改善，但两者无统计学意义
- 严重手功能障碍者运动功能改善与健侧兴奋性正相关，依赖于健侧的高激活

Theilig S.et al., 2011

rTMS联合治疗—脑卒中手功能康复的疗效

rTMS+限制诱导训练CIMT

Primed low-frequency repetitive transcranial magnetic stimulation and constraint-induced movement therapy in pediatric hemiparesis: a randomized trial

BERNADETTE T GILLICK[1], LINDA E KRACH[1], TIM FEYMA[2], TONYA L RICH[3], KELLI MOBERG[3], WILLIAM THOMAS[4], JESSICA M CASSIDY[1], JEREMIAH MENK[5], and JAMES R CAREY[1]

[1]Department of Physical Medicine and Rehabilitation, University of Minnesota, Minneapolis, MN

[2]Pediatric Neurology, Gillette Children's Specialty Healthcare, Saint Paul, MN

[3]Occupational Therapy, Gillette Children's Specialty Healthcare, Saint Paul, MN

[4]Division of Biostatistics, School of Public Health, University of Minnesota, Minneapolis, MN

[5]Biostatistical Design and Analysis Center, Clinical and Translational Science Institute, University of Minnesota, Minneapolis, MN, USA.

安全，有效的治疗手段

Gillick B T, 2014

rTMS联合治疗—脑卒中手功能康复的疗效

rTMS+作业治疗强化训练　　NEURO-15 program

RESEARCH　　Open Access

A multi-center study on low-frequency rTMS combined with intensive occupational therapy for upper limb hemiparesis in post-stroke patients

Wataru Kakuda[1], Masahiro Abo[1*], Masato Shimizu[2], Jinichi Sasanuma[3], Takatsugu Okamoto[4], Aki Yokoi[1], Kensuke Taguchi[1], Sugao Mitani[2], Hiroaki Harashima[5], Naoki Urushidani[4] and Mitsuyoshi Urashima[6], for The NEURO Investigators

204名受试者，5个机构, BRS 3-5. 病程大于12个月，单次卒中

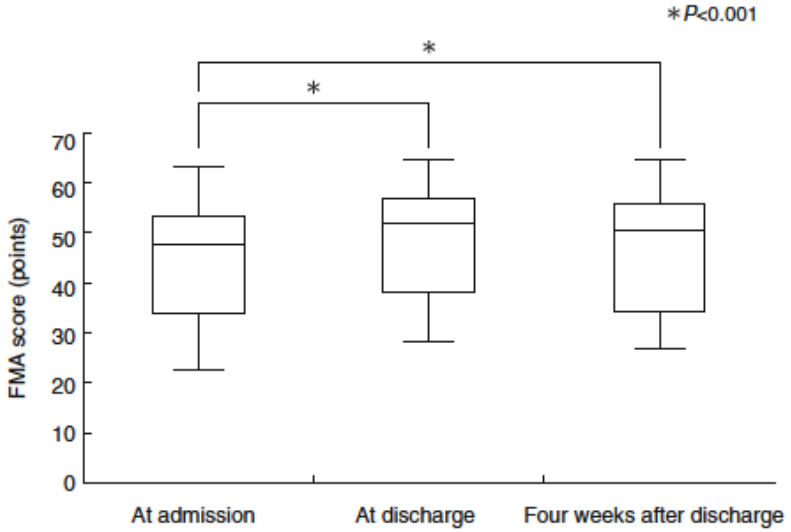
2014.10.31, 2008 名患者，13个机构

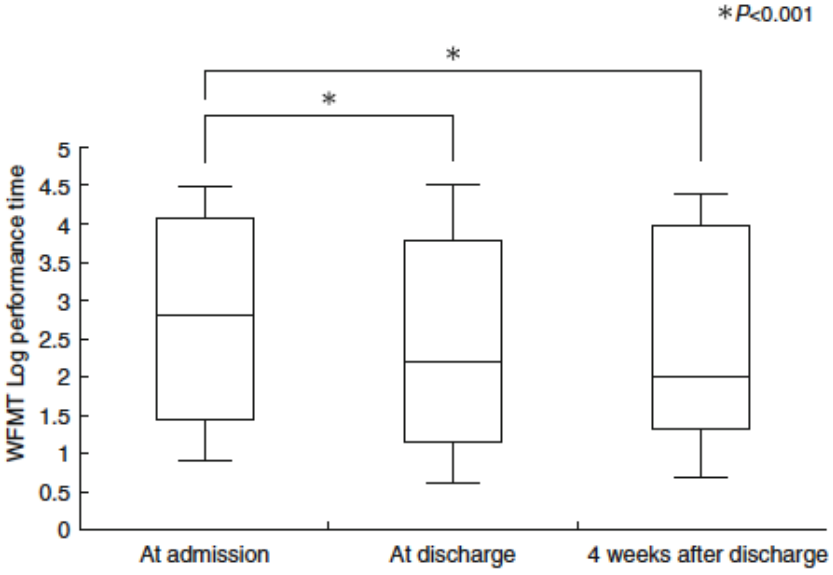
Kakuda et al.2012,

rTMS联合治疗—脑卒中手功能康复的疗效

rTMS+作业治疗强化训练

NEURO-15 program



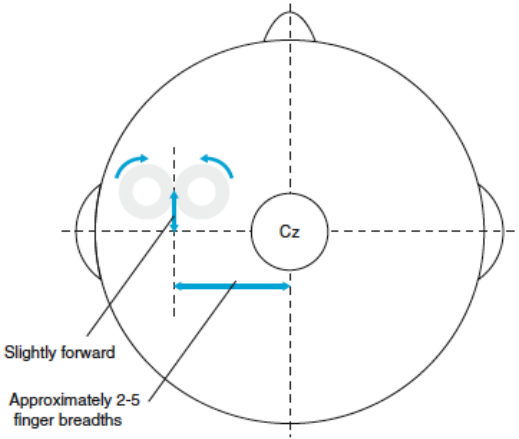


Kakuda et al.2012,

rTMS联合治疗—脑卒中手功能康复的疗效

rTMS+作业治疗强化训练（intensive OT）

- 部位：健侧初级运动皮层手部区域
- 参数：1Hz，90 % MT, 20min，1200P，2次/d，15天
- 联合：2次/d， OT强化训练(60min 一对一训练 + 60min自我锻炼)



上午	rTMS	一对一OT 60min	自我训练OT 60min
下午	rTMS	一对一OT 60min	自我训练OT 60min

Masahiro Abo et al.,2014

rTMS联合治疗—脑卒中手功能康复的疗效

rTMS+作业治疗强化训练（intensive OT）NEURO-15 program

要点

- ☑ 训练计划当包含足够的每日常规活动
- ☑ 训练应包含粗大活动、灵活性、以及双手整合运动
- ☑ 清晰说明训练过程中上肢部分的注意事项
- ☑ 功能性训练应当循序渐进的方式向作业活动过渡
- ☑ 要有有足够的活动让患者自我锻炼
- ☑ 原则上，不限制健侧
- ☑ 运动反馈不仅限于言语指导，也包括手把手的方式
- ☑ 患者对活动对理解应训练时详细描述内容进行强化，确保患者理解
- ☑ 从上肢粗大活动向手灵活性以及双手整合训练的逐渐过渡
- ☑ 强调患者的主动以及治疗师在训练过程中的协助／反馈

Masahiro Abo et al.,2014

rTMS与脑卒中手康复

早期开展rTMS研究证据不足

rTMS与脑卒中手康复

早期开展rTMS研究证据不足

癫痫，卒中早期的癫痫发作是住院死亡率的独立的预后因素之一，因此需要谨慎评估rTMS的适用性

rTMS与脑卒中手康复

早期开展rTMS研究证据不足

急性期自发恢复扮演重要角色，因此纳入的条件更严谨或者研究采用大样本随机RCT或者交叉COT设计

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当被作为一个RCT分组进行治疗的时候，是否符合伦理

rTMS与脑卒中手康复

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当被作为一个RCT分组进行治疗的时候，是否符合伦理

COTs延长干预期，不适用于急性医院的缩短平均住院时间的质控

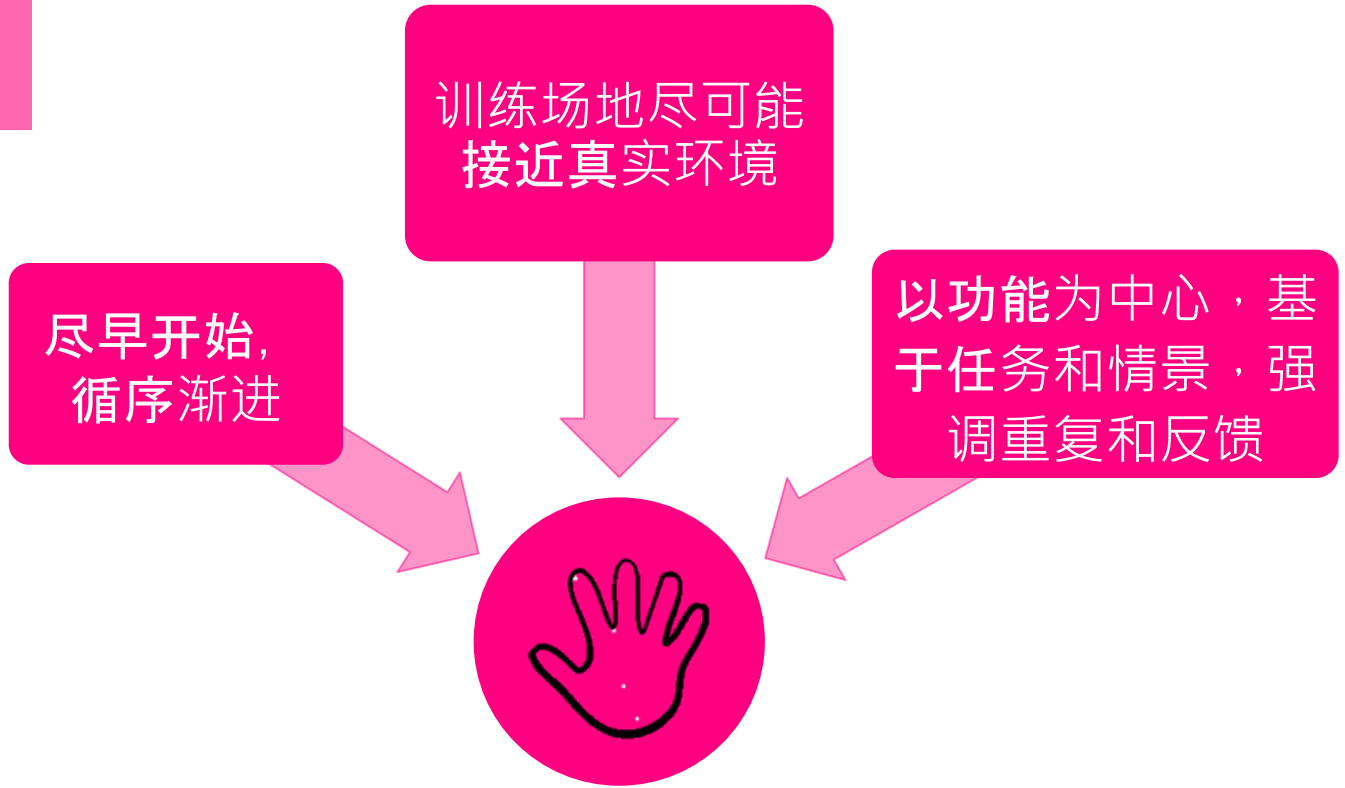
rTMS与脑卒中手康复

未来方向

- 最多可行性组合治疗
- 用于的时间点（急性 vs 亚急性 vs 慢性）
- 最佳刺激策略（健侧 vs 患侧）
- 最佳刺激参数（频率，强度，时间）
- 最佳适应症（皮层下 vs 皮层）

rTMS与脑卒中手康复

未来方向



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Thank you!♪