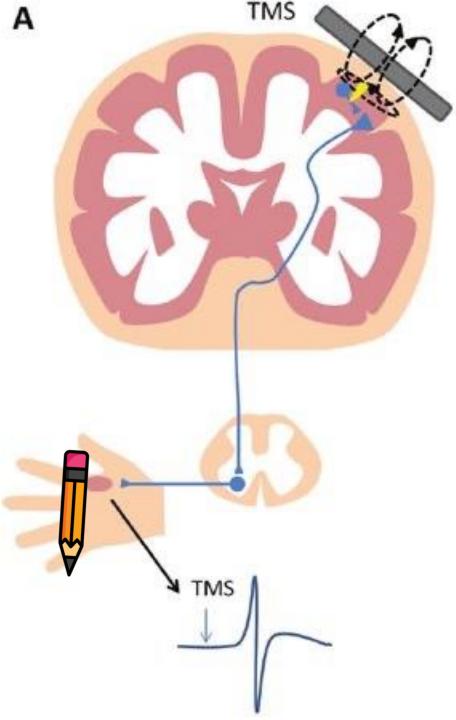
# 經顱磁刺激後, 合併上肢訓練是否可以 提升訓練成效!?

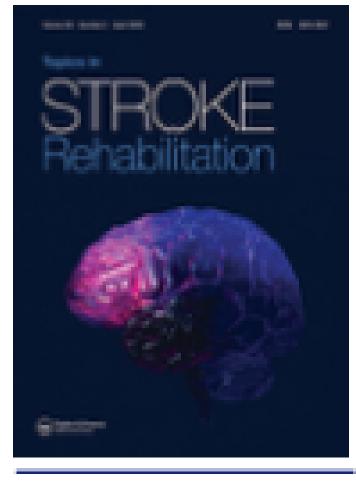
#### 職能治療師 蔡翰霆 2024.11.20



Does noninvasive brain stimulation combined with other therapies improve upper extremity motor impairment, functional performance, and participation in activities of daily living after stroke? A systematic review and meta-analysis of randomized controlled trial

Ishtiaq Ahmed, Rustem Mustafaoglu, Nesrine Benkhalifa & Yakhoub Hassan Yakhoub

非侵入性腦刺激合併上肢訓練, 是否可以提升訓練成效!?

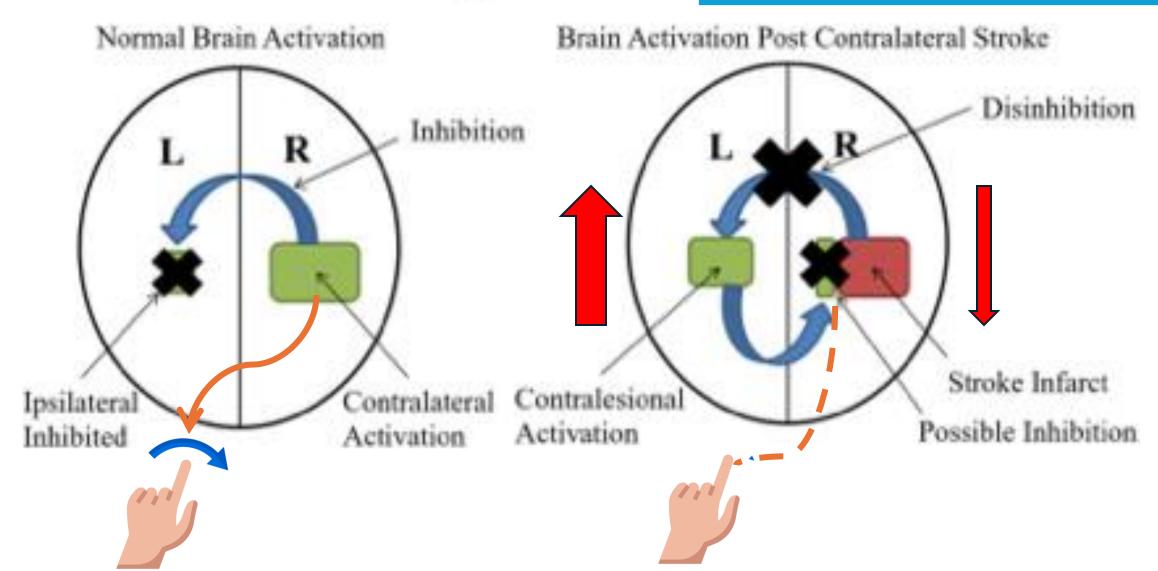




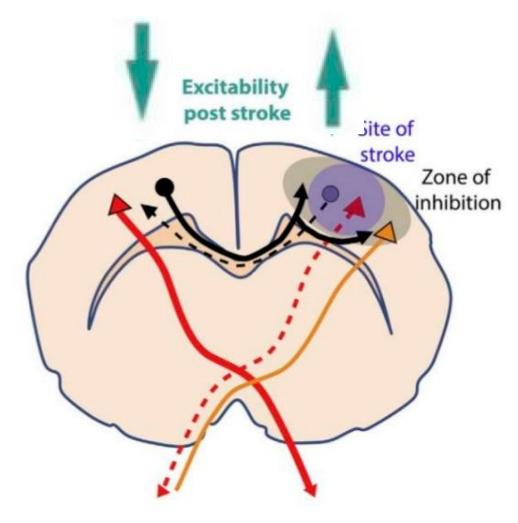
TOPICS IN STROKE REHABILITATION 2023, VOL. 30, NO. 3, 213–234

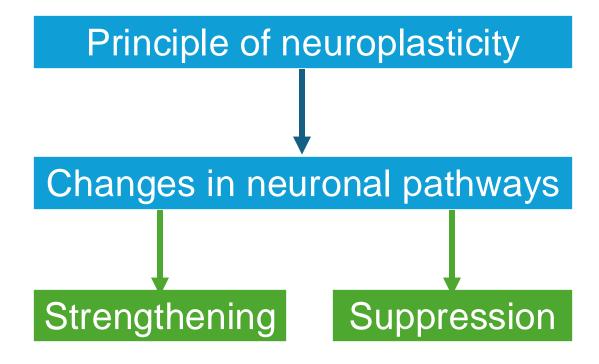
## Hemisphere coordination

# Non-lesioned hemisphere increases its activity



#### **Neural Modulation with NIBS**





#### Aim of this study

To investigate the effect of NIBS with other therapies on upper limb motor impairment, functional performance, and participation in activities of daily living (ADLs)

To determine the most appropriate stimulation time and number of sessions for these applications

## Search strategy

The standard guideline of Cochrane Collaboration

The PRISMA Statement for randomized controlled trial

**English articles** 

2010.01.01 - 2020.12.30

#### Literature Search

Web of Science (WOS)

Medline (PubMed)

Cochrane Central Register of Controlled Trials (Cochrane CENTRAL)

Google Scholar

# Search strategy

#### Eligibility criteria

"rTMS" or "tDCS" combined with other therapies

control group in which sham "rTMS" or "tDCS" combined with other therapies

Quality assessment

Cochrane Risk of Bias assessment tool

#### Outcome measures

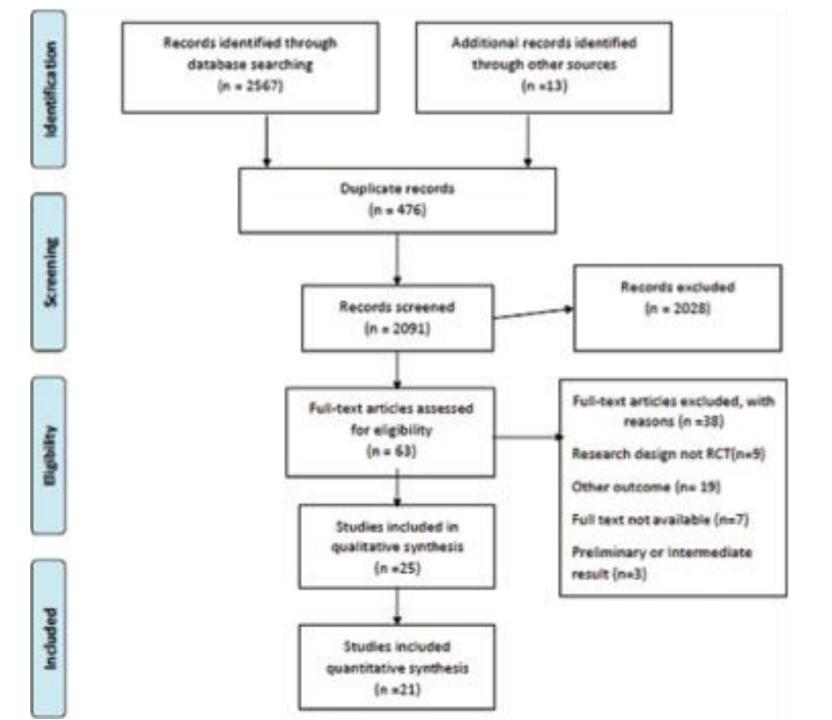
#### ICF framework

Motor impairment	Functional performance
Fugl- Meyer Assessment- Upper Extremity	Wolf Motor Function Test

#### Participation

**Barthel Index** 

## Flow diagram



## Cochrane risk of bias

	NIBS
tDCS:12	rTMS:13
Othe	er therapy
Robot:4 VR:3	Conventional therapy:18
tDC	S protocol
Anodal tDCS:8	Cathodal tDCS:4
rTM	S protocol
High frequency:5	Low frequency 8

Mod-to-	hi	gh	q	ua	lit	У
<ul> <li>Low risk of bias</li> <li>Unclear risk of bias</li> <li>High risk of bias</li> </ul>	Random sequence generation (selection b	Allocation concealment (selection bias)	Binding of participants and personnel (ped	Binding of outcome assessment (Betection	Intertion to heat analysis	Description of losses and exclusions
Ackerley 2015	۲	۲	۲	۲	۲	۲
Allman 2016	۲	۲	۲	۲	•	۲
Bolognini 2011	•	•	۲	۲	۲	۲
Bornheim 2019	۲	۲	۲	۲	۲	۲
Cha 2015	۲		۲	۲	۲	۲
Chang 2010	۲	•	۲	۲	۲	۲
Chen 2019	۲	۲	۲	۲	۲	۲
Di Lazzaro 2016	۲	۲		۲	۲	۲
Dongya Wu 2013	۲	•	۲	۲	۲	۲
Figlewski 2017	•	۲	۲	۲		
Fusco 2014		•	•	(D)	1	(2)
Galvao 2014	•		۲	۲	۲	۲
Harvey 2018	۲	۲	۲	۲	۲	۲
Hosomi 2016		۲	۲	۲	۲	۲
J. Edwards 2019	۲	۲	۲	2		۲
K. Rose 2014	۲	•	۲	۲		
10m 2020	•	۲	1	۲	•	
Meng and Song 2017		•	•	۲	•	۲
Nela V. Ilic 2016		۲	۲	۲	۲	۲
Rabadi and Aston 2017	•	•				
Seniów 2012	۲	۲		Ø	•	1
Straudi 2016			2			
Tedesco Triccas 2015	۲	•	۲	۲	2	
Mana 2014	۲	۲		۲		
Yao 2020		•		۲		•
Zheng 2015	۲	•	•	۲		•

#### **NIBS on UE-FMA**

#### a) NIBS on UE-FMA (N=722)

	NES+d	ber there	gies	Shire NES	+other Dee	apies		Mean Difference		Mean Differen	min.
italy or Subgroup	Mean	50	Tetal	Mean	50	Total	Weight	N, Reed, 95%-CI	Year	NLFaed, 99	50
1.1 Type=TDCS	16.01	1,125	12.27		191	1993	1997	2.532.60.0515	10.00	0	
ao et el 2020	10.1	10.9	20	8.4	53	20	1.9%	3701-278,1018	2025		-
dwards et al. 2019	7	4	-37	22	4.9	40	19,7%	-0.7012.60,1.28	2018		_
traud et al. 2016	5.17	43	12	5.5	4.97	11	5.4%				
lman at al. 2016	11.46	9.8	11	8.11	10.45	53	1.2%	23515.76,10.48	2016		
iccae et al. 2016	8.73	18.18	33	7.73	9.78	11	1.1%	1201734,934	2015	•	
0.00 et al. 2014	4	5	5	4	6	6	1.2%	8.80   6.50, 6.53	2014	•	_
ina et al. 2014	9.9	5.7	10	7.5	7.5	10	2.5%	1.80[-3.84,7.44]	2054		
ongyu Wu et al. 2013 deviai (15% Ct)	10.65	8.63	45	1.65	4.57	45	14.4%	8.00 (6.67, 11.37) 2.70 (1.42, 3.87)	2013	8	6
derogenally Chill+ 42.75,						1.00	10,010	The loss shot			
tfor overall effect Z = 4.1											
2 Type=r1MS											
n et al. 2020	10.3	2.4	- 36	18	87	-20	38%	0.5014.01,5.01	2121		
en et al. 2019	1.32	12.5	11	-2.87	13.6	11	0.7%	4.29 (6.63, 15.21)	2019	•	
vey et al. 2018	5.6	8.5	132	6.2	0.4	87	12.7%	-5.60   3.00, 1.88	2018		
g and Song et al. 2017	16.7	4.8	10	10.4	5.87	10	2.5%	8.30 (1.80, 11.00)	2017		
omi at al. 2018-	4.22	2.17	18	8.28	3.8	21	21.4%	-2061397,-0.15	2016		
lose et al. 2014	4.6	4.5	8	38	4.74	10	4.5%	0.7033.46,4.88	2014		
had of all 2014	5.4	6.2	10	8.6	5.8	10	2.8%	-3 20 10 50, 2 10	2014	•	_
niów et al. 2012	6.3	8.4	20	6.8	5.4	20	2.6%	-0801612,492	3812	•	
Motal (95% CB			246			169	52.0%	4.62[-1.84, 0.61]			
brogeneity: Ch/#= 12.82,	d=7@=	0.00); P=	45%								
t for overall effect Z = 0.9											
tal (95% CB)			397			325	100.0%	0.97 (0.09, 1.86)			•
terogeneity: Ch/*= 69.03,	#= 15 P -	0.00001	1. 1= 78	6 · · ·				AU 20 (DU 20 (DU 20 )		-+ +	
of for overall effect Z = 2.1			1	Sec. and						0 D P	-
at for subordup difference			1 (F - D)	1007 F- 97	10.					Shan 1005-John Therapies, 708	[]-;#

tDCS

#### Protocol of NIBS on UE-FMA

Darks on Park strength	Margary .	ther thera	Tokal	Mirgan	sto		Weight	Mean Difference N, Fixed, 95%-CI	-		Mean Difference N. Fixed, 95% CI	
Rudy or Saligroup		341	10404	ane un	30	104.08	mage	N.FRIEL YES CI	10.00		NY, FROMA, POINT CA	
11Protocol-Excitatory N				1.00	1000			And the second	diam'r.			
hen ef al. 2018	1.22	12.5	11	-2:97	136		0.7%	4.20[4.43,15.21]				
dwards at al 2019		4	37	3.7	43	41		-5.7012.88,1.28				
ilmanatal 2016	11.48	8.0	11	811	10.45	1.3		2351579,10.40				-
Rosonsi et al. 2018	4.22	2.17	19	6.28	2.8	21	21.4%	-2.0612.07,-0.14				
troudi et al. 2016	517	4.7	12	5.5	4.97	11	5.4%	-0.23E4.14,3.48				1.0
bocas et al. 2016	8.73	10.18	. 11	7.73	6.76	. 11	1.1%	1.00 [-7.34, 9.34]				-
tana et al. 2014	8.3	5.7	10	7.5	7.3	10	2.5%		2014			- *
ubitutul (95% CI)			110			117	51.95	-0.941-2.16, 0.291				
ietoroganiałty CNP+ 410,0			18.									
at for overall effect 2 = 1.4	\$(P+014	9										
1.2 Protocol-Inhibitory MR	8											
ao et al 2020	10.1	10.9	20	5.4	10	20	1.0%	3705278,10.18	2020			
on et al. 2020	10.3	7.4	38	8.8	8.2	20	3.0%	0.5064.01, 5.010				-
larvey et al. 2010	5.6	8.5	132	8.2	8.4	87	12.7%	-0.603-3.08, 1.845	2010			
lang and Sting et al. 2017	16.7	4.0	10	10.4	5.87	10	3.5%	8 30 (1 60, 11 08)				
uson et al. 2014		5	5	4			1.0%	0.00 (-6.50, 8.50)		•		
atrial at al 2014	5.4	87	10	8.6	5.9	10	2.6%	-3.20 (-8.50, 2.10)				
House et al 2014	4.8	45		3.9	4.74	10	4.5%	0.701346,4.88		-		÷
ongou We et al. 2013	10.65	6.53	#5	1.65	4 87	45	14.4%	9.00 (6.67, 11.33)				
lenidw et al. 2012	6.2	8.4	20	6.9	9.4	20	2.6%	-5.603-6.12, 4.92				
administrati (1917-LCD)			7917			208	45,1%	3.84(1.76, 4.31)	****			
aterogenetic Chr <sup>4</sup> = 45.68,	+++++++++	a anatai	P = 125									
est for overall effect Z = 4.8			1.1.14.14									
Contraction of the state												
ntal (95% CB			397			325	185.0%	0.57 [0.09, 1.96]				
laterogeneity Chife 88.53,	E-15.0	2.000	P 200			110		and second cases				_
ot for overall effect 2 = 2.1										-4 -12	erapies NIBS-other therapies	

#### NIBS on UE-FMA: Acute vs. Chronic

 b) Sensitivity analysis of NIBS on UE-FMA in acute/subacute (n=495) or chronic (n=205) stroke NETS-other therapies Share MIRS+other therapies Mean Difference Moun Difference SD Magn IV. Fixed, 95% CI Study or Subgroup Mean Total 50 Total Weight IV. Fixed, 95% Cl. Year 2.4.1 Acute/Sub acute strake Kim et al. 2020 10.3 7.4 38 2.0 8.7 20 0.5014.01, 5.01) 2020 Yao et al. 2020 10.1 10.9 28 5.4 10 28 1.5% 3701-278 10.100 2020 8.2 Harvey et al. 2019 5.6 0.5 132 2.4 87 12.9% -0.601300,1.00 2010 Mang and Song et al. 2017 16.7 4.10 10 10.4 5.97 10 8.30 (1.40, 11.00) 2017 10% 4.22 2.57 8.26 18 Hospital et al. 2018. 3.8 21 21.7% +3.083-3.97, +0.1% 2016 Fusco et al. 2014 4 6 . 4 2014 0.0014.68.8.60 6.53 45 1.85 4.57 Dongsy Wu et al. 3013 10.95 9.00 (6.67, 51.33) 45 14.0% 2013 Seniller at at 2012 6.3 0.4 20 8.9 9.4 20 -0.6058.12, 4.920 2012 Subtotal (95% CB 286 2009 1,23 (0.61, 2.85) 62.IPL Heterogeneity: CtvP = E1 15, dt = 7 (P < 0.00001) (P = 85% Test for overall effect Z = 3.02 (P = 8.003) 2.4.2 Owned stroke Cheviatal, 2019 1.32 12.5 -2.67 13.6 42955521 2019 t t 0.7% 7.7 4.9 Edwards at at 2019 37 7 40. -0705269 1298 2019 Abthan at al. 2016 9.8 11 8.11 10.45 11.45 13 2.355576,10.488 2016 1.2% 817 4.5 12 4.6 4.97 Etraveli et al. 2018. 11 0.3314.14, 3.400 2016 67 0.5 tů. 2.6 7.3 Viana et al 2014 18 2.5% 1.901384,7.440 2014 6.2 5.6 Oalvas et al. 2014 5.4 t 6 5.9 10 -3.20148-50, 2.100 2.0% 2014 K. Rose et al. 2014 2.5 4.74 4.4 44 10 0701346.488 2014 4.6% Subbolal (95% CI) 100 105 37.7% 4.211 1.77, 1.151 Heterogeneity: Ch/# = 3.15, dl = 6.0F = 0.700; # = 0% Test for overall effect Z = 2.41 (P = 0.60) Total (05% CB) 8.9716.08, 1.861 314 106.0% Helerogeneity: Ch/# = 69.03, df = 14.07 = 0.000013, P = 80%. Test for overall effect Z = 2.15 (P = 0.03) Sham NBS+other therapies NBS+other therapies Test for subgroup differences: ChiP + 4.78, df = 1 (P = 0.02), P = 78.7%.

acute subacute

## NIBS on WFMT

#### No significant difference

	NIDS+of	ber there	pies -	Sharn MITS-	other the	apies .		Mean Difference		Mean Differen
Shady or Subgroup	Mean	SD.	Total	Mean	SD		Weight	N/, Random, 95% Cl	Year	IV, Flandom, 95%
2.5.1 Type-TDCS		10.0	1.1.1.1		4.553		1.5.2.5		23.3	
Edwards et al. 2018	11.2	. 9	37	0.0	13.3	48	8.7%	2.60[2.44, 7.64]	2019	
rightwickli et al. 2017	0.8	0.5	22	0.4	0.5	32	27.2%	0.201-0.10, 0.50	2017	+
Alteriale at al. 2018	9.2	12.1	11	8.3	15.5	13	2.4%	0.901-10.15, 11.95	2018	
viana et al. 2014		12.7	50	3.1	6.8	10	3.0%	4.901-3.97, 12.771	2014	
abtotal (95% CB			90			85	41.9%	0.21[-0.08, 0.51]		<b>C +</b>
teterogeneity Tau <sup>a</sup> -	0.00; ChP =	196,世	17940	500、产生合物						
est for overall effect 3	t=1.42 (P)	- 年159								
2 Type=r1MS										
larvey et al. 2018	3.9	90.1	132	7.6	26.5	67	3.8%	-3.701/12.24, 4.84	2018	
verig et al 2015	19.4	4.8	- 55	83.9	. 8	- 53	15.4%	8.30 (3.37, 9.33)	2016	
Robe et al. 2014	0.87	2.6		0.01	3.3	10	15.0%	0.06(-3.06, 3.18)	2014	
aniów et al. 2012	0.1	3		1.8	2.2	20	24.0%	1.7013.00, -0.400		
BROTAL (95% CB			216			158	58.1%	0.71[-3.53, 4.95]		
eterogeneity: Tau#= 1	14.80; CNP	o 23.22,	df= 2 (P	+ (0.0005); P =	87%					
et for overall effect 2	t + 0.33 (P +	0.740								
dal (95% CD			294			255	100.0%	0.91[-8.00, 2.70]		
eterogeneity Tau <sup>a</sup> = 1	105.CN##	28.44, 6	1=7.100	0.0004X P+ 2	4%				-	1. 1.
of for overall effect 2										10 -6 0
of for substraup diffe			dist if	+ 0.471.P+ 0	× .					um Netro-other therapies . Netro-

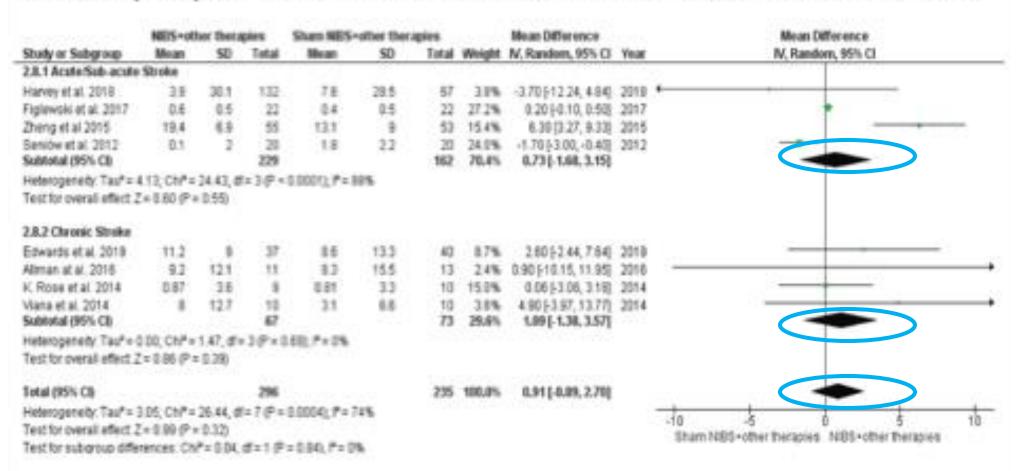
# Protocol of NIBS on WFMT No significant difference

c) Sensitivity analysis of excitatory (n=165) or inhibitory (n=366) protocol of NIBS on UE-WMFT

, commente a	het there		Share NETS				Mean Difference		Mean Difference	
Multy or Subgroup	Mean .	50	<b>Tutal</b>	Maate	3D	<b>Tutal</b>	Weight	N, Handom, 95% CI	Veat	fv/, Handsen, 95% CE
2.7.1 Pretocol+ Excel	dury MUS				1.0					
Edwards et al. 2019	11.2		- 37	8.6	13.2	40	8.7%	2601244,784	2019	
Figlewski et.al. 2017	0.8	0.5	- 22	0.4	0.5	22	27.2%	0.201-0.10, 0.50	2017	
Umah at al 2016	8.2	121	11	8.3	15.5	13		0.00310.15.11.05	2016	
Viana et al. 2014 Subhutut (1975-CB		127	10	11	6.8	10	3.0%	4.003-3.07, 13.771 0.211-0.06, 0.511	2914	
interopenanty Taut+	DEL CHP4	1.86,00	130-10	500, P= 0%						
est tir aveial effect.										
7.2 Protocol- Intribut	hory MICS									
Kanvey at al. 2018	3.9	30.1	133	7.8	29.5	67	1.0%	-3.70 [ 12.24, 4.84]	2018	
Drong et al 2015	18.4	4.8	.95	12.1		53	15.4%	6.30 (3.27, 8.33)	3015	
C Phose et al. 2014	8.87	3.6		0.01	23	10	15.0%	0.0613.08,3.181	2014	
latilities at al. 2012	0.1	- 2	20	1.8	2.2	30	24.0%	-1.701-3.00, -0.40	2012	mont de la constante de la const
Address (1955) CB			216			158	58.1%	8,711-3.53, 4,95]		
Aderogeneity Tau <sup>a</sup> n	14.60; ChP	# 23.21.	8=30	+ 0.0001); P =	87%					
eal for overal effect.	2×035+	11.74)								
lotal (99% CS			294			235	108.0%	0.911-0.89, 2.70]		
Helenopenalty TauP+	3 EL OVP+	28.44,8	1.700	8.00040; P = 2	4%					
Test for overall affect.										Shaw NESS-other therapies, NESS-other therapies
Test for subsroup diff.	Internation Chi	P = 0.05.	8-18	= 0.921 P= 0	s					menter batten under anter aber anter anter anter anter aber alle anter

#### NIBS on WFMT: Acute vs. Chronic No significant difference

#### a) Sensitivity analysis of NIBS on UE-WMFT in acute/subacute (n=391) or enrome (n=140) stroke



### **NIBS on Barthel Index**

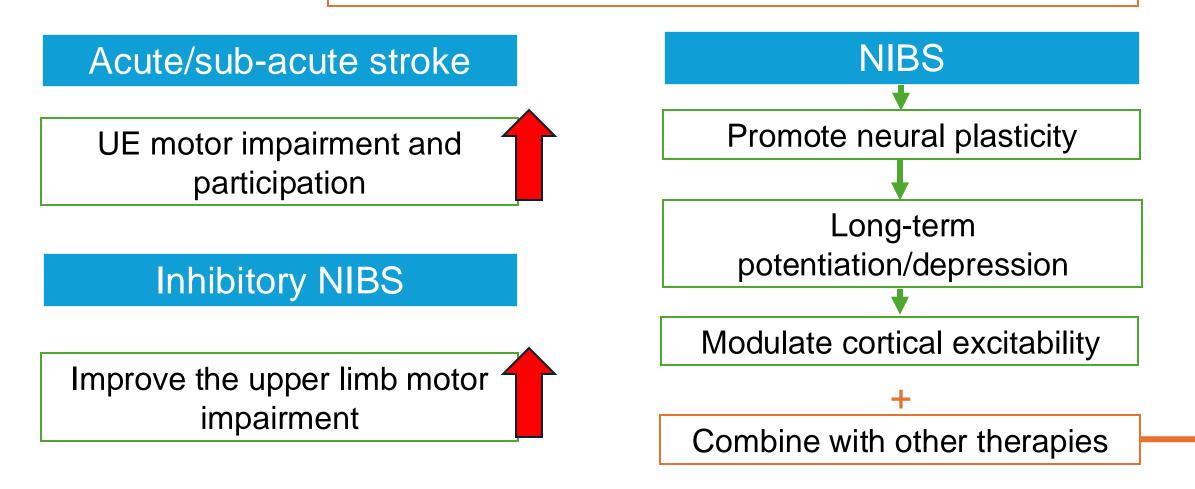
#### Significant difference

	MIS-10	her that a	plies .	Shan NES-	other thes	apies .		Mean Difference		Mean Difference		
Study or Talign rap	Muse.	50	Total	Mean	50	Total	Weight.	N, Random, 95% CI	Teat	Nr, Random, 95% CI		
1.1.1 Tape-TDCS												
Two-et al. 2020	127	18.2	20	8.5	2.2	20	26.7%	4203144,0840	2020			
Fueld et AL 2014	28	.21	5	18	10		0.0%	8.00112.07, 29.07)				
Dorigvi Walet al. 2013	26.3	13	45	8.1	10	45	28.1%	17.20(12.41, 21.98)				
Subhatal (HSS CI)			78			21	63,3%					
Heteropenalty TauP+ SATK;	C67+11.8	l, df = 2 (	F = 0.022	0.7+12%				·				
Test for overall effect Z = 1.8	FP+100											
1.1.2 Type=1105												
Meng and Sorig et al. 2017	18.28	2.1	10	11.36	2.7	10	31.2%	5.03(2.48,7.58)	2017			
Zheng et al 2015	345		10 55	18.2	98	53	5.5%	18.48 10.09, 42.8%	2615			
Factoria (195% CB)			45			63	36.7%	5,13[2,60,7,67]				
Heteropensity Tau*= 0.90, C			0.40, 7	× 0%								
Test for overall effect Z = 3.5	19-+0.000	m)										
Tutal (95) CB			135			134	100.0%	9.11(2.27, 15.95)				
Heterogeneity: Tau <sup>4</sup> + 37.43;	Chillen In Id	1 4		D P. 114					_			
Test to neral effect Z = 18										-20 -10 0 10 20		
Test for subgroup differences				100 C						hare NES+other therapies. NBS+other therapies		

#### b) NIBS on Barthel Index (n=269)

## Improvement in Stroke with NIBS+Other

Induce a more suitable environment for neural plasticity



## **Different NIBS on Motor Outcomes**

tDCS with other therapies improves motor impairment

The acute/subacute phase of is a period of spontaneous recovery

Receive OT/PT or other treatment within 6 months

rTMS with other therapies was ineffective for motor impairment

6/7 studies: Inhibitory signals

3 studies: In acute/subacute

20 min of stimulation/session is more effective

Only 1 study = 20 sessions

#### **Different NIBS on function Outcomes**

#### tDCS and rTMS show no significant

4 studies: excitatory protocol 4 studies: inhibitory protocol Further studies are required to verify the effect of excitatory or inhibitory NIBS on functional performance.

tDCS and rTMS with other therapies improved BI scores

# Study limitation

Differ in terms of stimulation frequency, intensity, duration, and number of sessions per week.

Excitatory NIBS were analyzed together with inhibitory

The duration and intensities of other therapies combined with NIBS were also different from each other.

There is still a lack of consensus about the ideal intensity, frequency, and duration of NIBS in stroke rehabilitation.

Mod to high-quality studies suggested that NIBS combined with other therapies is effective in improving UE motor impairment and ADL in acute/sub-acute stage of stroke but unable to modify upper extremity motor impairment in chronic stroke.

- 2. Only inhibitory protocol is associated with improved motor impairment.
- 20 min of stimulation/session for ≥20 sessions were found to be effective in improving UE motor impairment.



#### Archives of Physical Medicine and Rehabilitation



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Archives of Physical Medicine and Rehabilitation 2023;104: 1683-97



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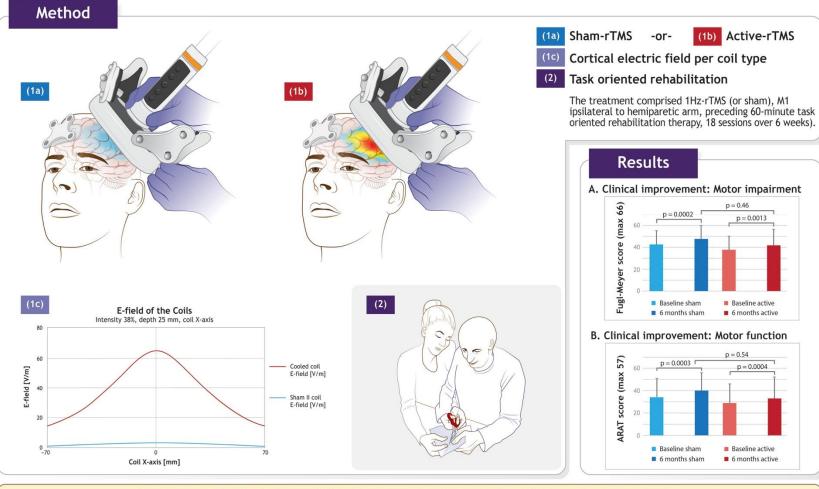
**REVIEW ARTICLE (META-ANALYSIS)** 

Non-invasive Brain Stimulation Techniques for the Improvement of Upper Limb Motor Function and Performance in Activities of Daily Living After Stroke: A Systematic Review and Network Meta-analysis

Ishtiaq Ahmed, DPT, MSc,<sup>a,f</sup> Rustem Mustafaoglu, PhD,<sup>b</sup> Simone Rossi, PhD,<sup>c</sup> Fatih A. Cavdar, MSc,<sup>f,g</sup> Seth Kwame Agyenkwa, MSc,<sup>f</sup> Marco Y.C. Pang, PhD,<sup>d</sup> Sofia Straudi, PhD<sup>e</sup>

1.87 RCTs with 3750 participants were included.

2.NiBS except continuous TBS (cTBS) and cathodal tDCS were significantly more efficacious than sham stimulation for motor function (SMD range 0.421.20) 3.taVNS, anodal tDCS, and both low and high frequency rTMS were significantly more efficacious than sham stimulation for ADLs (SMD range 0.54-0.99)



Conclusions

Intensive motor rehabilitation improved clinical impairment, function, and quality of life six months after treatment.
1Hz-rTMS of primary motor cortex ipsilateral to the hemiparetic hand delivered before therapy did not confer advantage.
Low frequency rTMS treatment based on the interhemispheric competition model was not an effective treatment to improve clinical impairment, function or quality of life in a sample stroke population with mixed lesion location and extent.

(1) 20-minute pre-functional upper limb therapy (individualized from the **Chedoke-McMaster hand** score). (2)10-minute rest (3) NBT delivered at rest targeting M1<sub>CL</sub> (≈15 minutes) (4) 10-minute rest (5)60-minute structured session of goal-directed, task-oriented rehabilitation therapy (individualized from the Chedoke-McMaster hand score).



Dylan J. Edwards. Stroke. Electric Field Navigated 1-Hz rTMS for Poststroke Motor Recovery: The E-FIT Randomized Controlled Trial, Volume: 54, Issue: 9, Pages: 2254-2264, DOI: (10.1161/STROKEAHA.123.043164)

### Conclusion

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NIBS combined with other therapies may improve performance in various ICF domains for post-stroke patients.

However, the optimal dosage or combination of NIBS and other therapies has not yet been established and requires further research for validation.



Patient characteristics may also influence treatment outcomes, which warrants additional investigation in future studies.



In addition to the neuromodulatory benefits provided by NIBS, individualized and high-intensity training programs are essential for achieving better outcomes. 非侵入腦刺激合併上肢訓練, 是否可以提升訓練成效!?



#### Thank you!!!