
New Zealand
Is the uninjured hemisphere a suitable target for noninvasive brain stimulation after stroke?
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NEW ZEALAND
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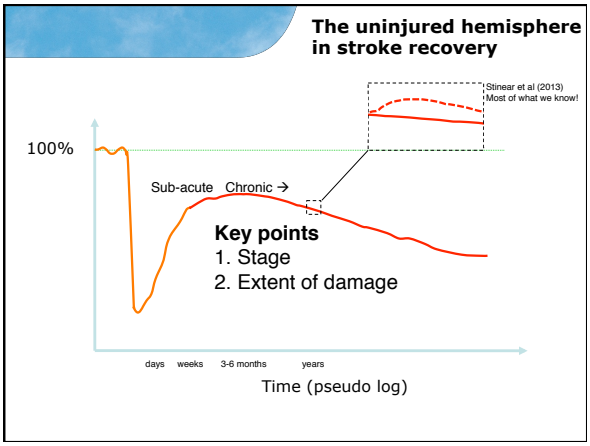
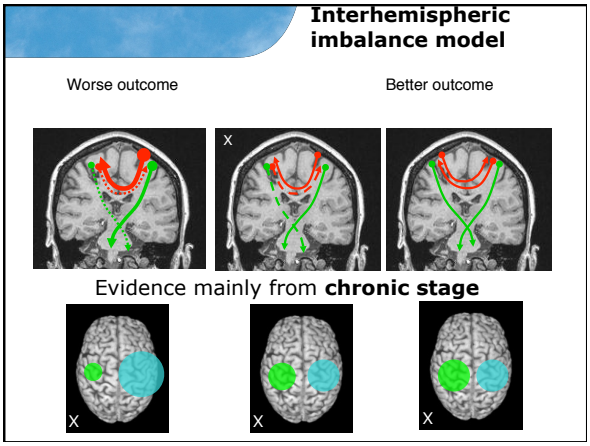
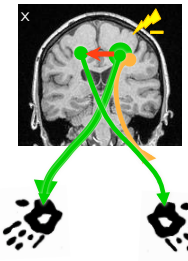
hrc Health Research Council of New Zealand
Te Kaunihera Rangahau Hauora o Aotearoa
STROKE FOUNDATION OF NEW ZEALAND INC
No other financial disclosures or COI.


The uninjured hemisphere in stroke recovery
Stinear et al (2013)
Most of what we know!
100%
Sub-acute
Chronic →
Key points
1. Stage
2. Extent of damage
days
weeks
3-6 months
years
Time (pseudo log)


Interhemispheric imbalance model
Worse outcome
Better outcome
X
Evidence mainly from chronic stage
X
X
X

The Uninjured Hemisphere
The Foe Argument



Suppress excitability of the uninjured motor cortex.

c-tDCS suppresses excitability of **crossed** pathways.
Nitsche & Paulus 2000

HOWEVER…

c-tDCS also suppresses excitability of **uncrossed** ipsilateral pathways
Bradnam et al 2010, 2011, 2013; McCambridge et al 2011, 2014

Weak hand

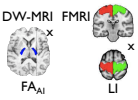
Cerebral Cortex
doi:10.1093/cercor/bht344

Contralesional Hemisphere Control of the Proximal Paretic Upper Limb following Stroke

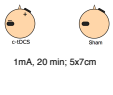
Lynley V. Bradnam[1,2], Cathy M. Stinear[2,3], P. Alan Barber[2,3] and Winston D. Byblow[1,2]

- Chronic stage, subcortical stroke
- NIHSS, mRS, ASH, FM, ARAT

DW-MRI FMRI



FA_{AI} LI

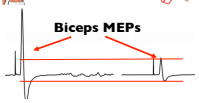


c-tDCS Sham

1mA, 20 min; 5x7cm

Flexion

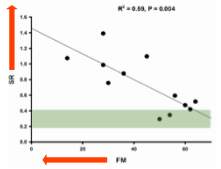
Pronation



Biceps MEPs

SR (Selectivity Ratio)
The ability to neurally suppress undesirable activation Gerachshenko et al 2008; McCambridge et al 2011

N=12 age-matched healthy controls, SR = 0.34 ± 0.03



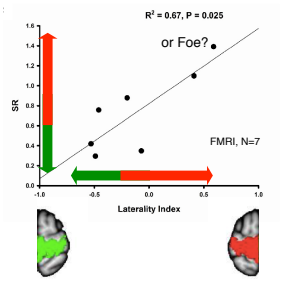
FMRI

Mild Impairment

Mod-Sev Impairment

Friend?

Ward et al 2007
Lotze et al 2006
Johannsen-Berg et al 2002
Rehme et al 2011



Cerebral Cortex
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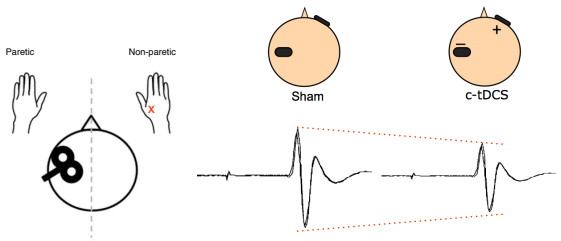

c-tDCS suppressed non-paretic FDI MEPs
(5m post: -28%;30m post: -35%; p<0.005; N=12)

Cerebral Cortex
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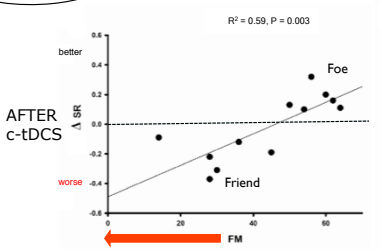
Did control of paretic arm improve or worsen?

It depends on the individual's impairment



FM = Fugl-Meyer

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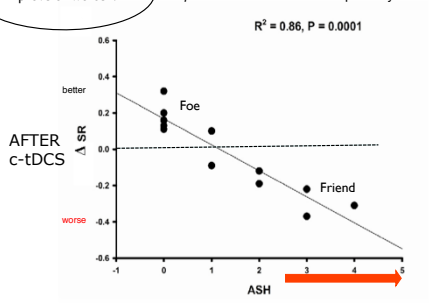
Did control of paretic arm improve or worsen?

It depends on the individual's spasticity



ASH = Ashworth Spasticity Score

Cerebral Cortex
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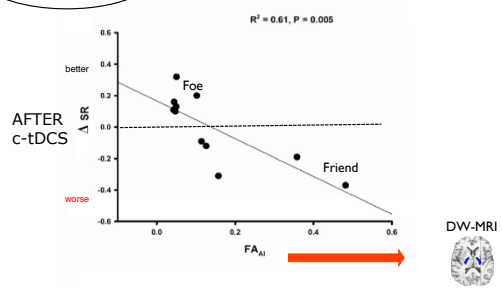
Did control of paretic arm improve or worsen?

It depends on extent of damage to ipsilesional CST



DW-MRI

Cerebral Cortex
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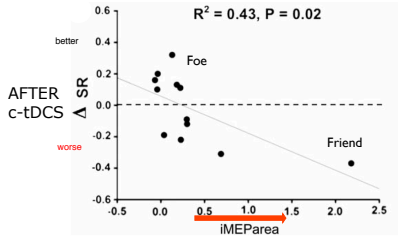
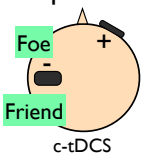
Did control of paretic arm improve or worsen?

It depends on the extent of input from the uninjured hemisphere

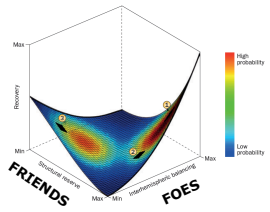


Mild Impairment



More Severe Impairment

Bimodal balance-recovery



REVIEWS

Modulation of brain plasticity in stroke: a novel model for neurorehabilitation

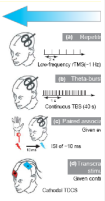
Di Pino et al Nature Reviews Neurology 2014

FRIEND : "Lateralization of neural activity alone is not always able to predict the response to rehabilitation."

FOE : "*Persistence* of interhemispheric imbalance is a predictor of worse outcome" (*italics* mine)

The sub-acute stage

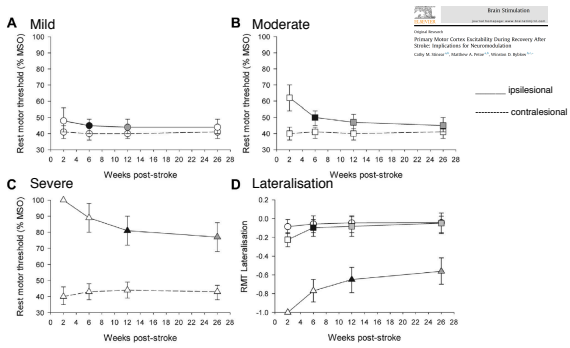
- Contralesional M1 suppression N I Author
  - Reduces impairment 18|Kim 2010
  - Improves dexterity 30|Conforto 2012 36|Khedr 2009
  - Improves strength*, but … 29|Sasaki 2012
  - Improves independence, but… 40|Khedr 2013
  - **No** effect **40**|Seniow 2012 **96**|Hesse 2011
  - Positive FX predominantly at *mild end* of the spectrum.



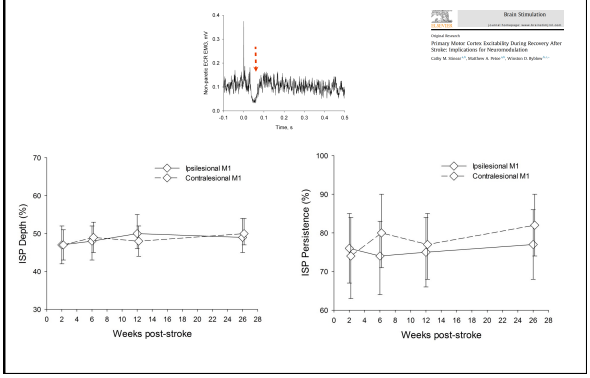
What do we know?

- Ipsilesional M1 excitability
  - Is initially reduced
  - Typically increases in patients who improve
- Contralesional M1 excitability
  - Not different to healthy control subjects
    23|Butefisch 2008 24|Catano 1997
    17|Traversa 1998 15|Manganotti 2002 10|Swayne 2008
  - Stable over time
- Interhemispheric inhibition
  - Reduced from ipsilesional to contralesional M1
    10|Butefisch 2008 21|Shimizu 2002
  - Normal from contralesional to ipsilesional M1
    10|Butefisch 2008
  - Increased from contralesional to ipsilesional M1, but…
    24|Takechi 2014

Motor Threshold Within Hemisphere



iSP Between Hemisphere



Interhemispheric imbalance at sub-acute stage?

- During recovery,
  - Ipsilesional M1 excitability increases / *threshold* ***decreases***
    - Recovery of Na/K pump and voltage-gated ion channel function
    - Remyelination along CST
    - Other?
  - Contralesional M1 excitability / *threshold* ***remains stable***
  - Transcallosal output is balanced and ***remains stable***

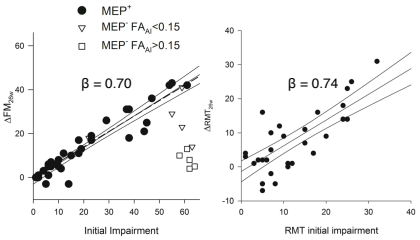
Link between imbalance and *recovery*?

Spontaneous Recovery

UL impairment resolves spontaneously for *most* patients, to 70% of the maximum amount possible.

Which patients?

Prabhakaran et al 2008
Zarahn et al 2011
Winters et al 2014



Patients with functional ipsilesional CST (MEPs) within 5 days of stroke resolve UL impairment proportionally, *regardless of initial impairment.*

Ipsilesional motor threshold resolved in a similar manner.

Data from Byblow et al, Annals of Neurology, 2015
See also Feng et al, same issue.

Spontaneous Recovery

- During recovery,
  - Ipsilesional M1 excitability increases / *threshold* ***decreases***
    - Recovery of Na/K pump and voltage-gated ion channel function
    - Remyelination along CST
    - Other?
  - Contralesional M1 excitability / *threshold* ***remains stable***
  - Transcallosal output is balanced and ***remains stable***
- UL impairment and ipsilesional RMT recover by 70% for patients with a viable CST
- Can the uninjured hemisphere be **targeted** (not suppressed) to promote further functional gains?