Cleveland Clinic

Understanding Inter-hemispheric Inhibition in Stroke to Develop Severity-Specific Brain Stimulation

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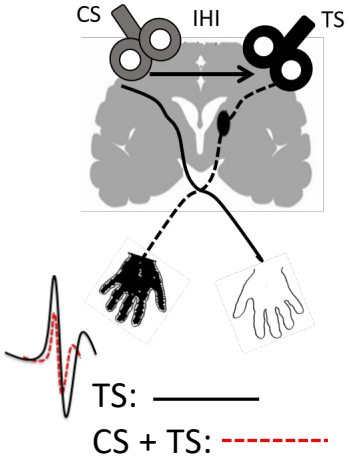
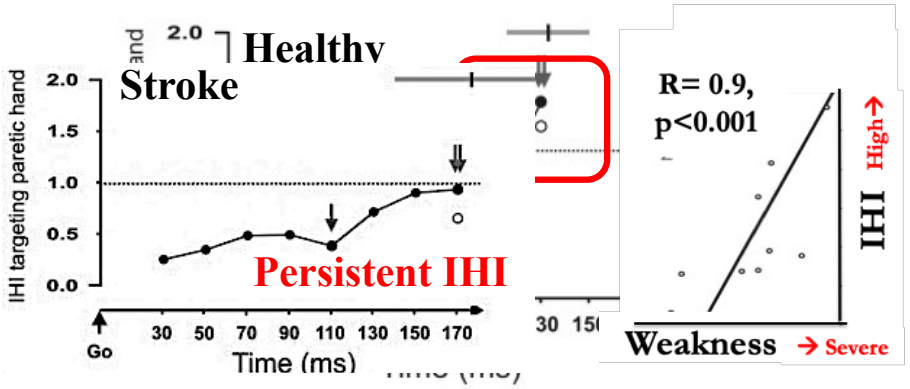
Role of the Intact, Contralesional Motor Cortex

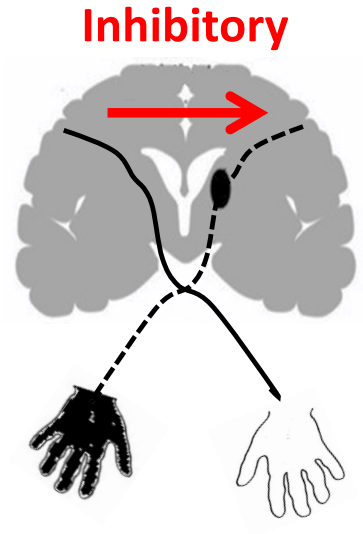
- In motor function of paretic upper limb
  - Widely debated
  - Inhibitory v.s. Supportive (compensatory)

Role of the Intact, Contralesional Motor Cortex

- Classical evidence
  - Contralesional motor cortices impose excessive inter-hemispheric inhibition (IHI) on the weak ipsilesional motor regions





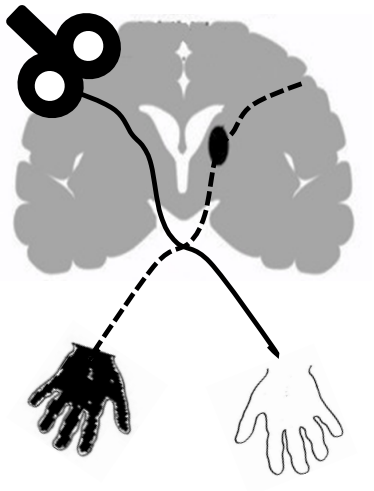


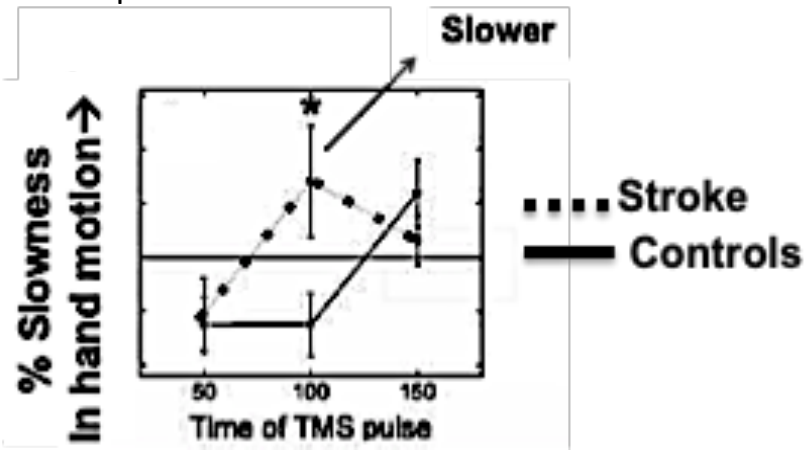
Murase, Cohen et al. *Ann Neurol* 2004

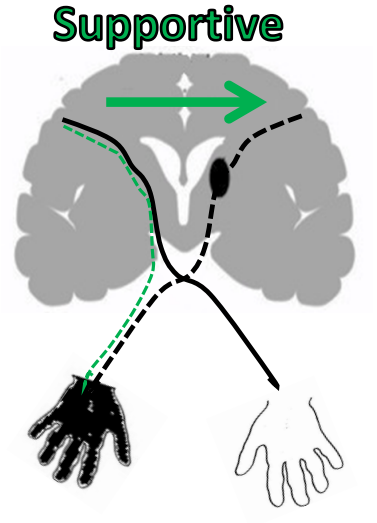
Role of the Intact, Contralesional Motor Cortex

- More recent evidence
  - Contralesional motor cortices can make **supportive** contributions towards paretic limb movement

Single-pulse TMS interferes contralesional premotor cortex







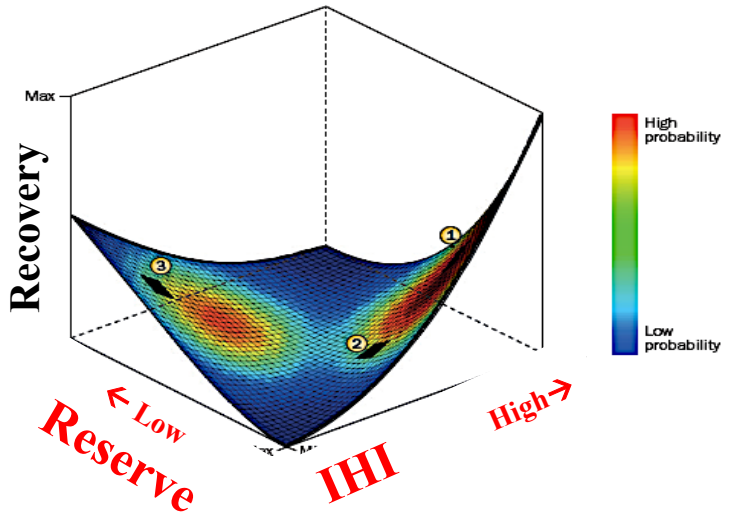
Johansen-Berg et al. *PNAS* 2002

Bestmann et al. *J Neurosci* 2010

Mohapatra et al. *Neurosci Lett* 2017

Role of the Intact, Contralesional Motor Cortex

- A new theory: Bimodal-Balance Recovery Model
  - Based on the amount of ipsilesional reserve available to contribute to recovery
    - High reserve → Inhibitory
    - Low reserve → Supportive



Di Pino et al. *Nature Rev Neurol* 2014 (*Adapted*)

Questions

- Whether the role of intact, contralesional motor cortices indeed varies in a bimodal manner with severity of injury /deficit?
  - Identify a criterion

- How patients with different levels of severity respond to inhibitory or facilitatory brain stimulation over contralesional cortices?

Experiment I

- Purposes:
  - To characterize the relationship between
    - Contralesional influence (measured as IHI)

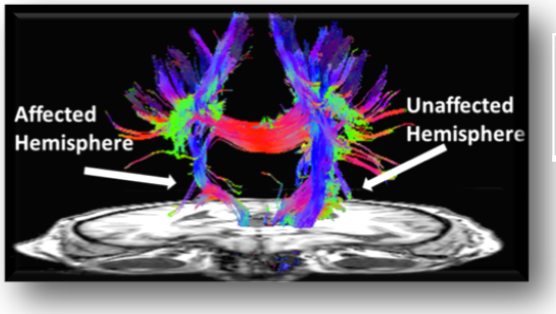
    V.S.
    - Severity of motor impairment and corticospinal damage
  - To identify a criterion of severity separating patients

Experiment I

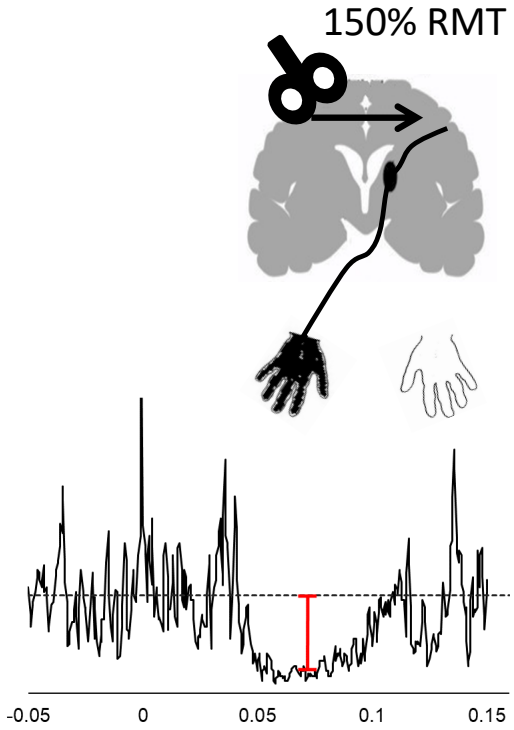
- Subjects:
  - 24 patients
    - Age: 61.7 ± 8.9 years,
    - Chronic stroke (> 6 months)
  - Upper Extremity Fugl Meyer (UEFM) between 15-65

Experiment I – Methods & Procedure

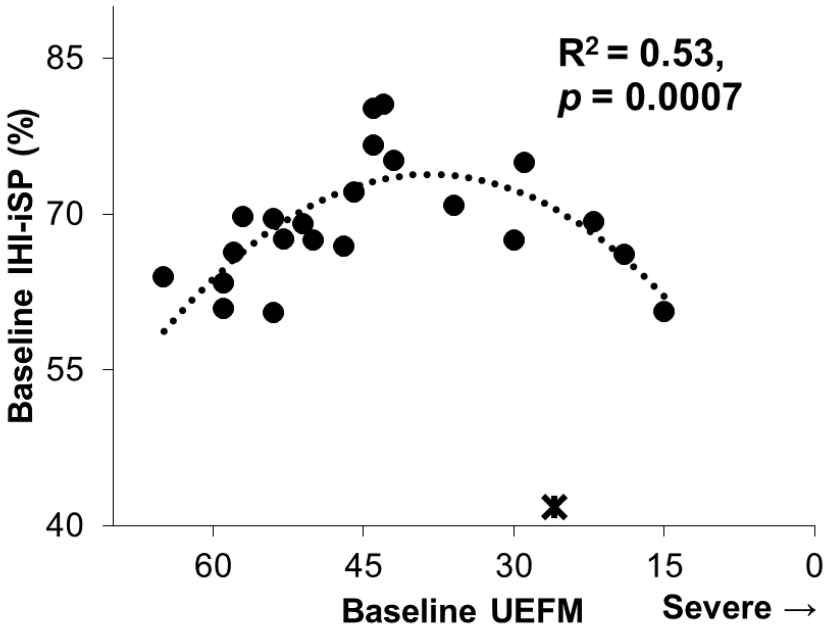
- Inter-Hemispheric Inhibition (IHI):
  - Measured by ipsilateral silent period (iSP)
- Motor impairment: UEFM
- Corticospinal integrity:
  - Fractional Anisotropy asymmetry ($FA_{Asymmetry}$)

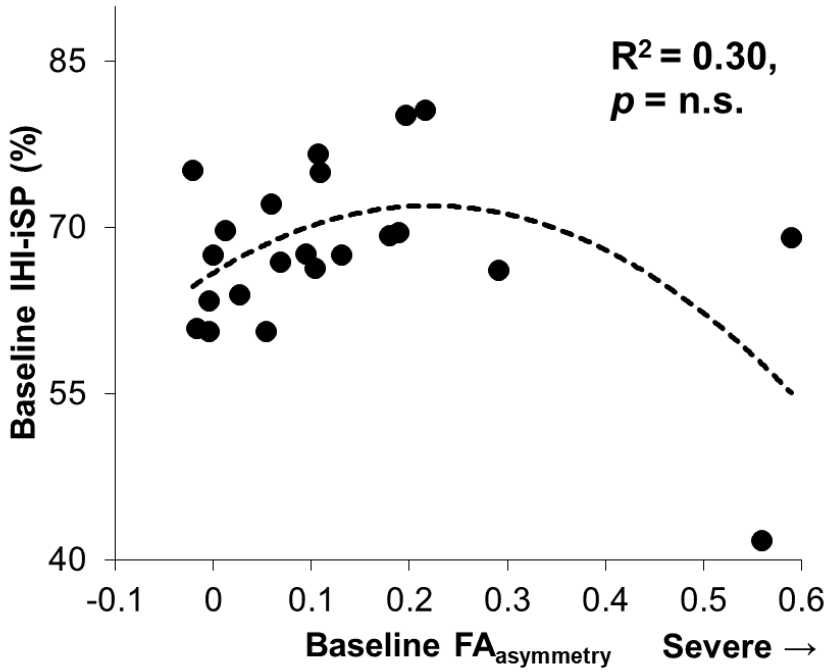


$$FA_{Asymmetry} = \frac{FA_{CONTRALESIONAL} - FA_{IPSILESIONALL}}{FA_{CONTRALESIONAL} + FA_{IPSILESIONALL}}$$



Experiment I – Results & Discussion





Experiment II

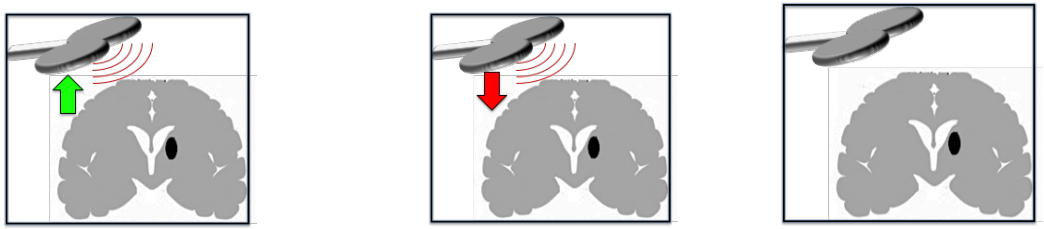
- Purpose:
  - To investigate the responses of patients in different severity groups to inhibitory and facilitatory brain stimulation over contralesional motor cortices
    - Separate subjects into more-affected and less-affected groups (UEFM = 43)

Experiment II

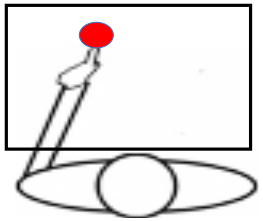
- Subjects
  - 24 patients (age: 60 ± 2 years, chronic > 6 months);
    - More-affected: 12, less-affected: 12.
  - UEFM motor impairment score between 7-64

Experiment II – Methods

- Single-session crossover experiment: immediate effects
  - Repetitive TMS (rTMS) over contralesional motor cortices
  - Facilitatory (5Hz), inhibitory (1Hz), sham,

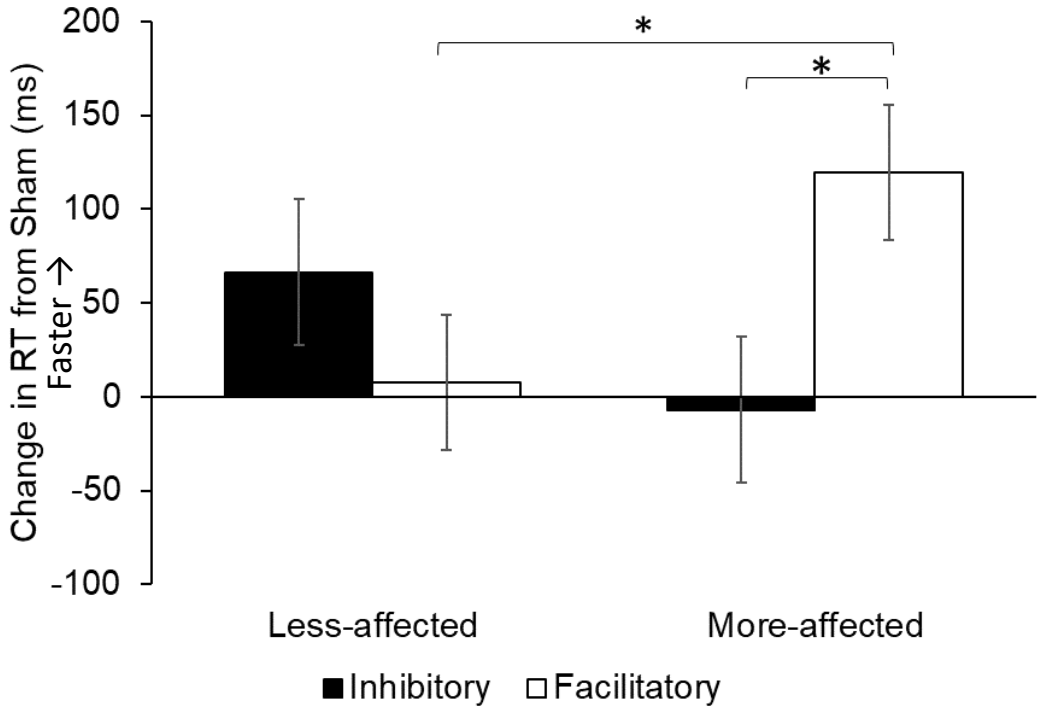


- Outcome measure: reaching time (RT)
  - Change in RT from sham



Sankarasubramanian et al. *Clin Neurophys* 2017

Experiment II – Results & Discussion



Discussion

- When brain stimulation is applied, severity of motor impairment should be considered

- Mechanisms of motor improvement in more-affected patients
  - Interhemispheric pathways
  - Ipsilateral pathways

Acknowledgements

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