

Journal Club : Stroke Recovery–Related Changes in Cortical Reactivity Based on Modulation of Intracortical Inhibition

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OUTLINE

Background, concept, protocol

Results

Discussion, limitations, possible
directions for the future

Background

- Mechanisms sustaining motor improvement in the few weeks after a stroke are still not fully understood
- Excitotoxic strong release of **glutamate** VS inhibitory **GABA** through cell hyperpolarization
- In mice : phase where inhibition is beneficial last 3 days, In human : we don't know
- A shift in the **inhibition/excitation** balance occurs and the excitation becomes beneficial for plasticity
- Could be one pivotal mechanism at the origin of neural plasticity after injury BUT needs to be checked in humans

Concept

- Induce potentials in the lesioned motor regions using TMS, and assess the amplitude of the evoked potentials to directly assess the neuronal properties of the lesioned motor regions
- Ipsilesional motor cortical excitability is higher in chronic stroke than in controls and is related to poorer motor function AND reduced intracortical GABA-B inhibition (Bai et al)
- Longitudinally evaluated a stroke cohort using a TiMeS framework and SICl (=short interval intracortical inhibition) protocol

Methods

- Patients :

First group : first week post stroke, motor deficit of upper limb, over 18 years old, no contraindications for TMS.

Second group : fifteen age matching healthy patient for control.

- Protocol :

3 sessions of assessment. One at 1 week, one at 3 week and one at 3 months post stroke ; EEG-TMS and motor evaluations at each session.

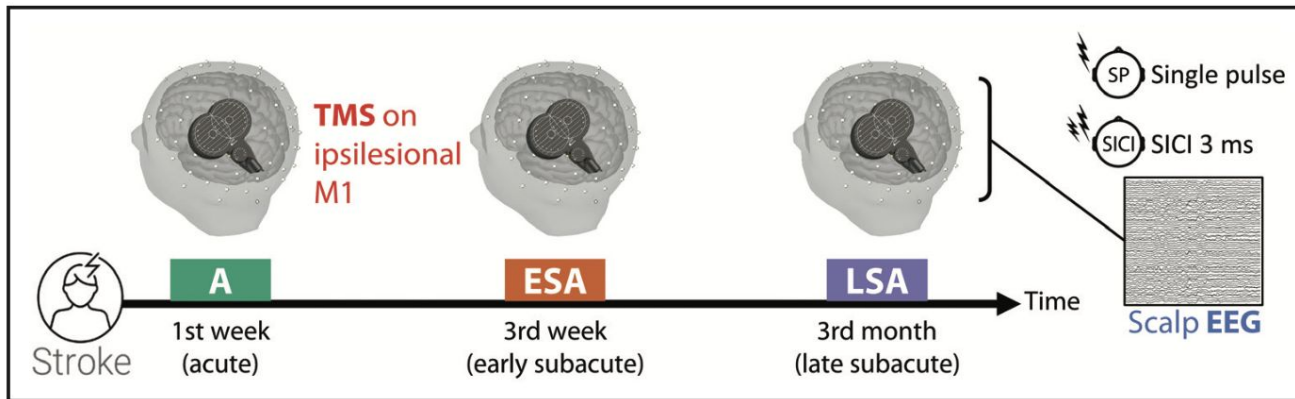


Figure 1 : Protocol Design [1]

Methods

- Behavioral assessment :
 - 1/ Fugl-Meyer (FM) of the upper extremity
 - 2/ The maximum fist, key, and pinch force assessed in 3 trials and performed using a hand dynamometer at the hand and the wrist, for the two hands
 - 3/ The Box and Blocks
 - 4/ The Nine Hole Peg (9HP)



Figure 2 : JAMAR hydraulic hand dynamometer

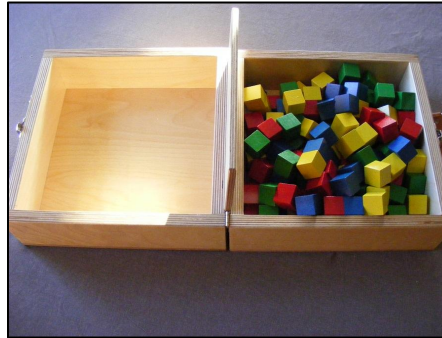


Figure 3 : Box and Block Test



Figure 4 : Nine Hole Peg Test

Methods

- Data acquisition and analysis :

Suprathreshold single-pulse (SP) and SICI stimulations (infra threshold conditioning pulse followed by a suprathreshold SP, with an interstimulus interval of 3 ms).

EEG data preprocessed using TESA toolbox.

- Statistics :

Early TEPs compared with cluster-based permutations. Bayes factors were used to quantify statistical evidence. LMFP (local mean field power) was evaluated using Bayesian 1-way ANOVA and ANCOVA. Regression quality score (RQS) between stroke stages analysed with 2-way ANOVA.



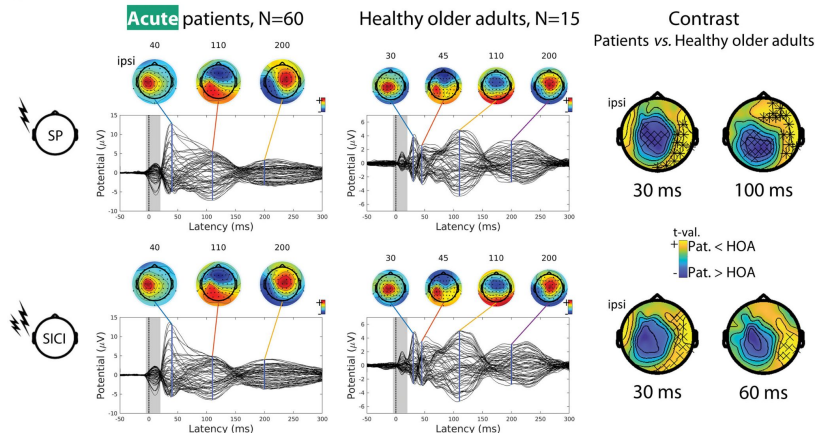
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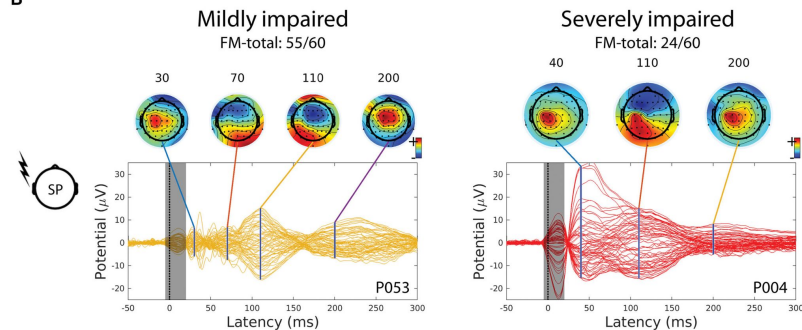
Results

Discussion, limitations, possible
directions for the future

A



B

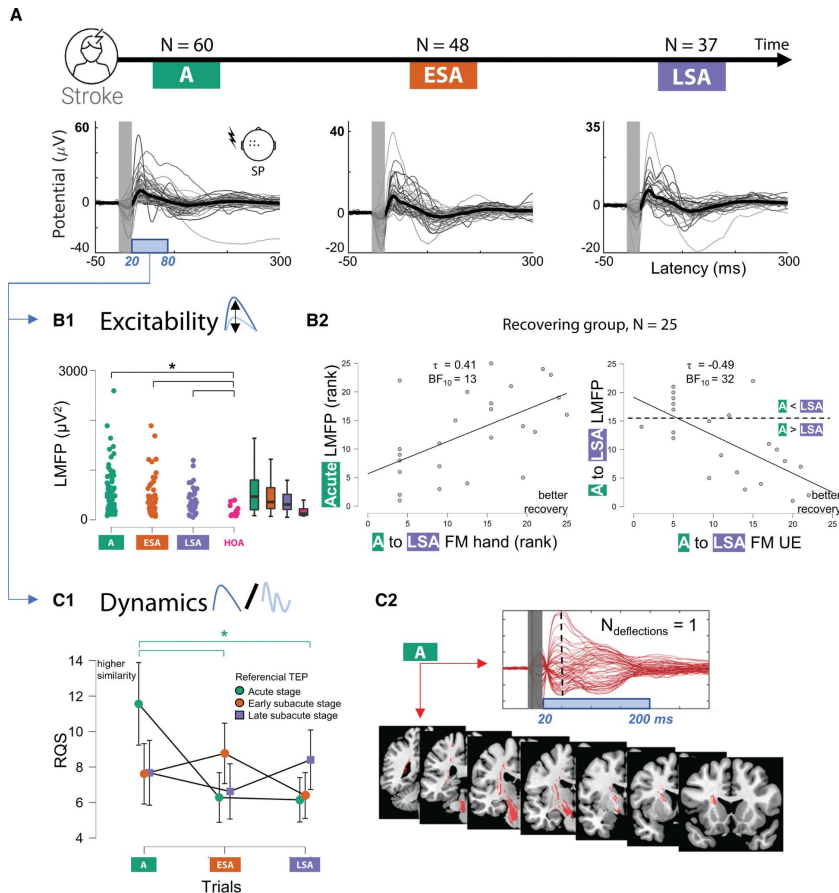


Test group : 60 patients around 68 years old.

HOA control group: 15 patients

Abnormal Brain Reactivity:

- patients who suffered acute strokes exhibited atypical, larger, and simpler TMS-evoked potentials (<100ms) in the ipsilesional motor cortex compared to healthy controls.



A=Acute

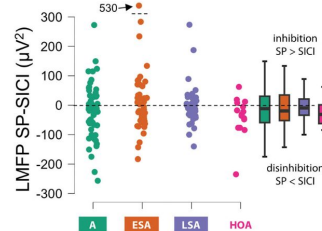
ESA= Early Subacute (3 weeks)

LSA= Late Subacute (6 month)

Hyperexcitability in Acute Phase:

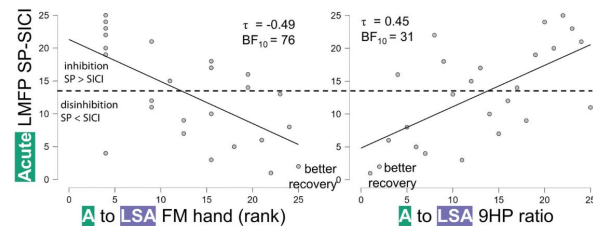
- Increased cortical excitability (local mean field power, LMFP) was observed in the acute stage and in both of the early and late subacute stages.
- A decrease of LMFP over time, was correlated with better motor recovery.

B1 SP vs. SICI Excitability

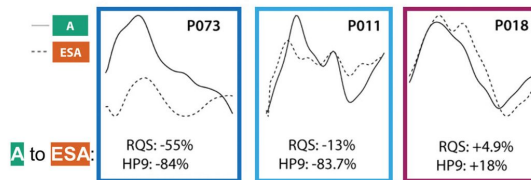
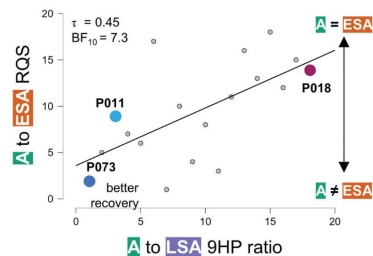


B2

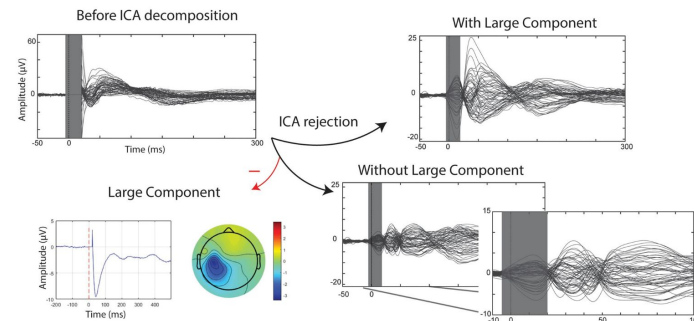
Recovering group, N = 25



c SICI Dynamics



A



Removal of large evoked components revealed additional inhibitory mechanisms during SP vs SICI :

- Acute disinhibition, characterized by reduced GABAergic inhibition, was associated with enhanced neuronal plasticity and improved motor outcomes.



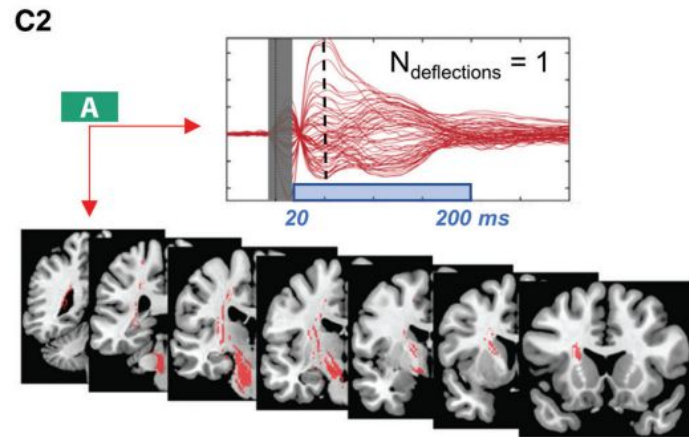
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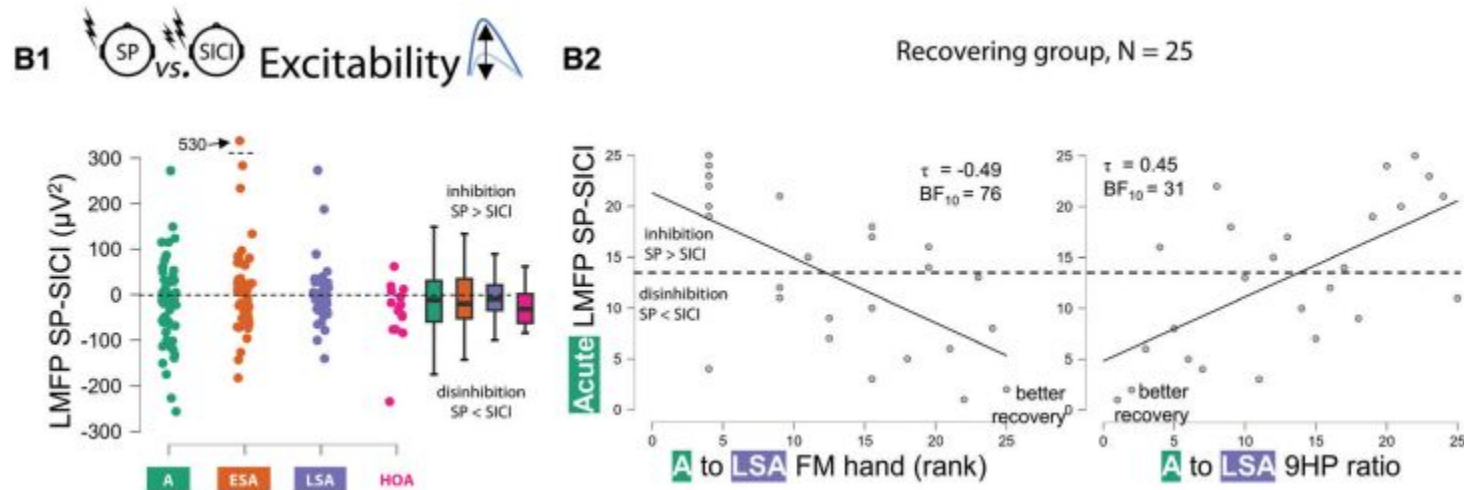
Results

**Discussion, limitations,
possible directions for
the future**

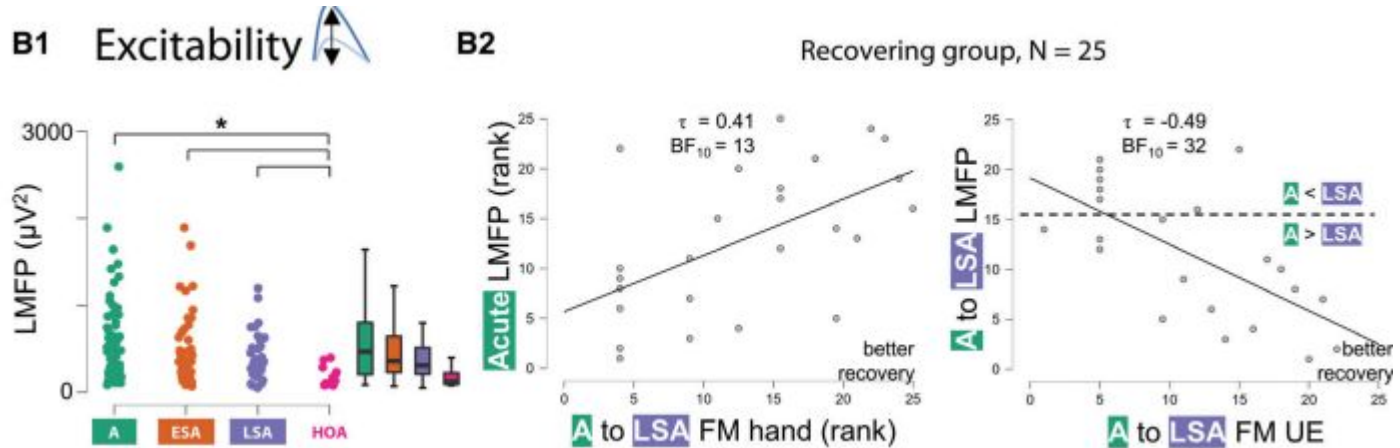
- Abnormal acute reactivity:
 - Signal properties are sensitive to local and global properties, and this highlights poststroke reorganization on both levels
 - Voxel-based Lesion Symptom Mapping (VLSM):
 - Shows that the high acute reactivity is associated with lesions in the internal capsule
- Longitudinal changes underline the reorganization process



- Disinhibition is a key mechanism for stroke recovery
 - Acute-stage: GABA-mediated ipsilesional cortical inhibition is reduced
 - Associated with better recovery → Fine-tuned inhibitory activity is critical for skilled hand functions (it promotes plastic changes)



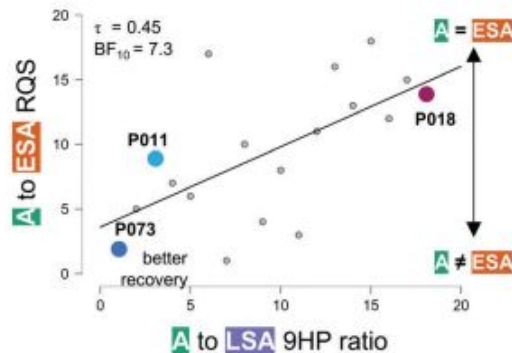
- Changes of intracortical inhibitory activity is associated with recovery
 - Decrease of disinhibition is associated with better recovery
 - Shown indirectly through decreasing excitability



- Changes of intracortical inhibitory activity is associated with recovery
 - Decrease of disinhibition is associated with better recovery
 - Shown directly through SICI-evoked dynamics analysis:

Quick changes in SICI dynamics

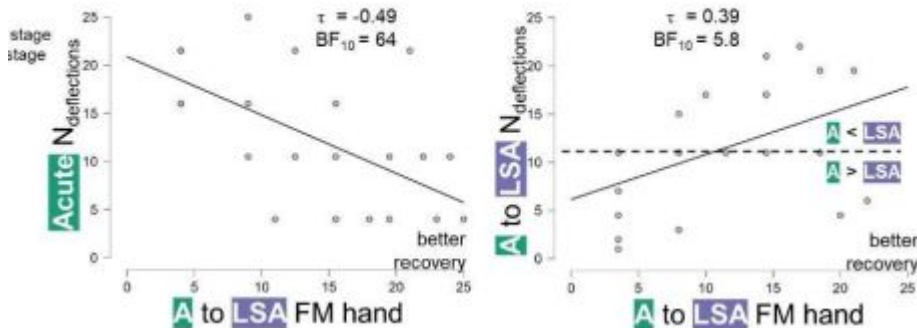
c 



Increasing number of deflections in recovering patients

C.2

Recovering group, N = 25

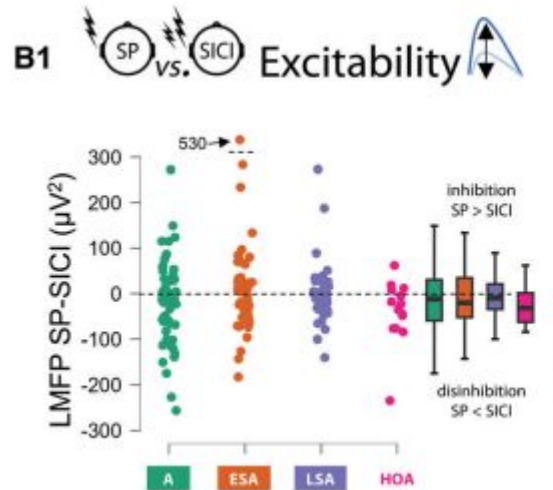


- No sham stimulation
 - However, this study was mostly focused on early components which are known to be much less sensitive to peripheral influence
- Unbalanced cohort of patients
 - 73% of them were males
 - Most were mildly to moderately impaired

Brain responsivity provides an individual readout for motor recovery after stroke

Caroline Tscherpel ^{1 2}, Sebastian Dern ¹, Lukas Hensel ¹, Ulf Ziemann ³, Gereon R Fink ^{1 2},
Christian Grefkes ^{1 2}

- More heterogeneous group of patients
- More research about the natural impact of age on the GABAergic disinhibition in healthy older adults



- New insights into the longitudinal changes of cortical reactivity and local intracortical inhibition in the affected motor cortex after a stroke
- This study underlines the impact of intracortical disinhibition in the acute stage on motor recovery, and the importance of reorganization within the intracortical inhibition system of the lesioned motor cortex for long-term recovery.
- TMS-EEG showed consistent results!



**Thank
you**

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