Changes in neural activity patterns during recovery of fine finger control after stroke

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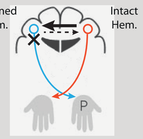
Introduction

What are the roles of the two hemispheres in stroke recovery?

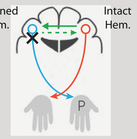
A. *Interhemispheric competition model*



The good hemisphere is overactive and inhibits the lesioned hemisphere. This suppression needs to be overcome in recovery.

Predictions:
- Lesioned hemisphere is initially suppressed below normal control baselines.
- Good hemisphere is overactive.
- Suppression of the lesioned hemisphere normalizes during recovery .

B. *Interhemispheric compensation model*



Both hemisphere exchange information for normal movement production. After unihemispheric stroke, representations in the good hemisphere can compensate for deficits in the bad hemisphere.

Predictions:
- Ipsilateral activated areas contain movement representations.
- This representation gets stronger with recovery.

C. *Contra-lateral recovery model*

While the two hemispheres may communicate, recovery occurs only when the lesioned hemisphere regains control.

Predictions:
- Lesioned hemisphere activities and digit representation correlate with hand function recovery
- Non-lesioned hemisphere activities and digit representations do not correlate with functional recovery.

The evidence so far...

A: Severely affected patients show more ipsilateral activity during paretic hand movements (Ward & Frackowiak, 2006)
A: Interhemispheric inhibition (good->lesioned) is higher in severe patients (Murase et al., 2004).
B: Normal force enslaving pattern on both hands disrupted immediately after stroke (see Ejaz et al.)
B: Uni-manual finger movements result in mirror-symmetric activity patterns across both hemispheres (Diedrichsen et al., 2013)
B: For patients with unilateral stroke, disrupting cortical activity in premotor area of a single hemisphere leads to behavioral deficits in both hands (Johansen-Berg et al. 2002)
C: Force enslaving in both hands start resembling 'healthy' patterns of enslaving during recovery (see Ejaz et al.)
C: Animal and patient studies indicate that plasticity in peri-infart and premotor areas drive recovery (Nudo, et al., 1996; Cramer et al., 1997; Liu & Rouiller, 1999).

Aim of the study is to track finger representations during stroke recovery using multivariate

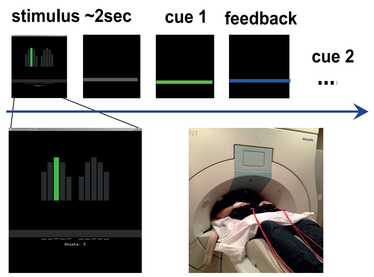
Methods

Tracking spontaneous motor recovery after stroke

In a multi-center study, we tracked spontaneous motor recovery after stroke using clinical scales, psychophysics, functional and structural brain imaging, and noninvasive brain stimulation. Patients with first time ischemic stroke were enrolled from Johns Hopkins University, Columbia University, and University of Zurich.

Task:

Patients were asked to depress each individual finger on a response keyboard. Real-time isometric force produced from each finger was recorded.
- 8 runs, 24 trials/run
- within each run: 8 fingers, 3 trials/finger randomized, 4



Experimental paradigm

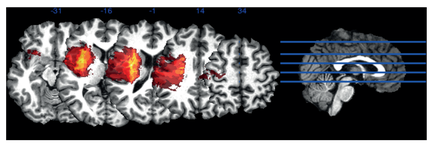
Participants:

37 Patients: Age 56+/-13 years; Gender: 13 female, 24 male; Lesion side: 13 left, 24 right.

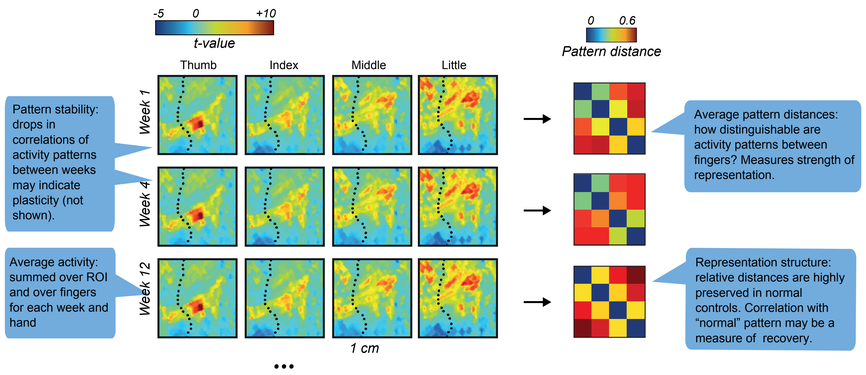
11 age- and education-matched healthy controls: Age 64+/-9 years; Gender: 4 female, 7 male.

Lesion maps:

The lesions were defined semi automatically by delineating the hyperintense area in the acute DWI images. The binary maps of the lesions were then mapped to a template in MNI space using linear and diffeomorphic transformations. The lesion maps here represent the spatial distribution of the strokes. The strokes, as expected, were dominated by middle cerebral artery (MCA) territory involvement, with many involving the internal capsule.

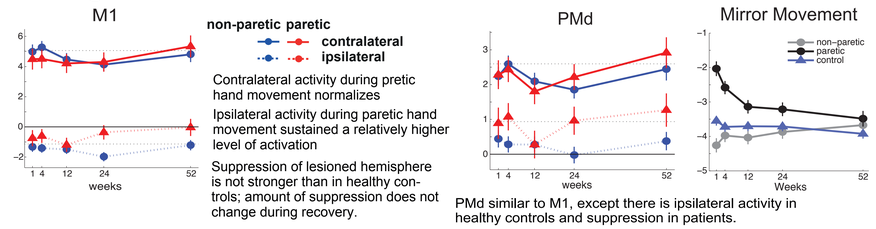


Measures



Results

Average activation



Contralateral activity during pretic hand movement normalizes

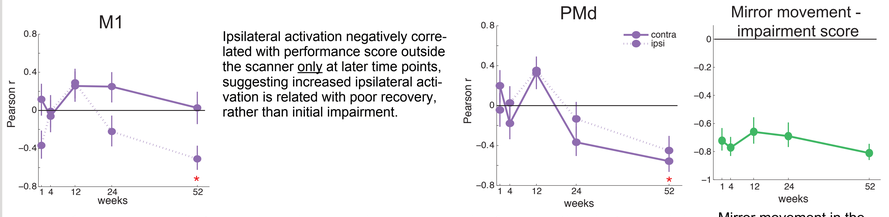
Ipsilateral activity during paretic hand movement sustained a relatively higher level of activation

Suppression of lesioned hemisphere is not stronger than in healthy controls; amount of suppression does not change during recovery.

PMd similar to M1, except there is ipsilateral activity in healthy controls and suppression in patients.

*Increased ipsilateral activation when the bad hand moves was **not** due to mirror movement in the scanner.*

Correlation with bedside performance score in paretic hand

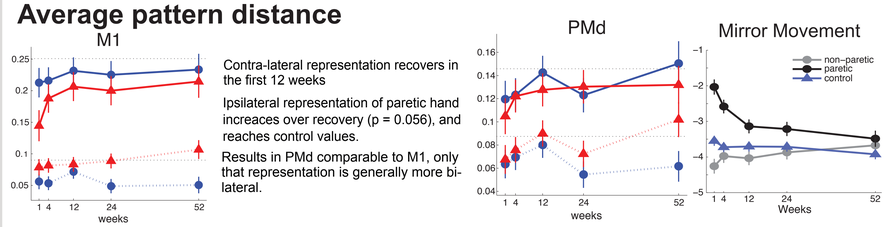


Ipsilateral activation negatively correlated with performance score outside the scanner only at later time points, suggesting increased ipsilateral activation is related with poor recovery, rather than initial impairment.

Mirror movement in the non-paretic hand strongly correlated with impairment in the paretic hand.

*Lack of suppression in the lesioned hemisphere, and lack of correlation between initial ipsilateral activation and performance when good hand moves are **inconsistent** with inter-hemispheric competition model.*

Average pattern distance

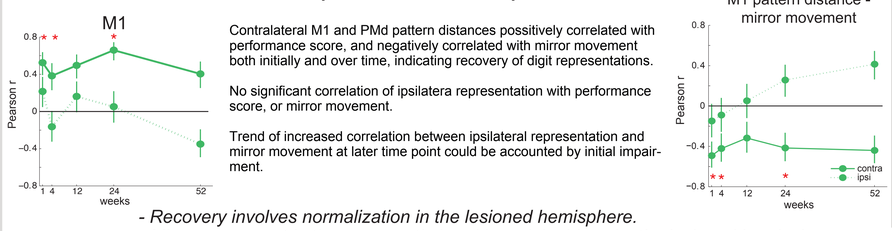


Contra-lateral representation recovers in the first 12 weeks

Ipsilateral representation of paretic hand increaces over recovery (p = 0.056), and reaches control values.

Results in PMd comparable to M1, only that representation is generally more bilateral.

Correlation with bedside performance score in paretic hand



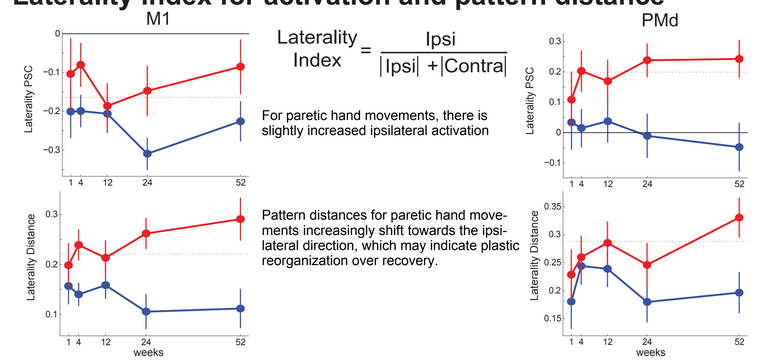
Contralateral M1 and PMd pattern distances possitively correlated with performance score, and negatively correlated with mirror movement both initially and over time, indicating recovery of digit representations.

No significant correlation of ipsilatera representation with performance score, or mirror movement.

Trend of increased correlation between ipsilateral representation and mirror movement at later time point could be accounted by initial impairment.

- *Recovery involves normalization in the lesioned hemisphere.*
- *Mirror movement in the non-paretic hand is mainly driven by the lesioned hemisphere.*
- *Weak evidence for interhemispheric compensation model.*

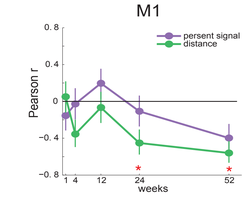
Laterality index for activation and pattern distance



For paretic hand movements, there is slightly increased ipsilateral activation

Pattern distances for paretic hand movements increasingly shift towards the ipsilateral direction, which may indicate plastic reorganization over recovery.

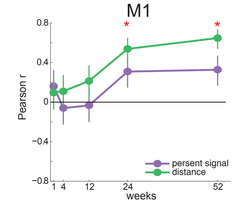
Correlation with bedside performance score



Ipsilateral representation correlates to both impairment and mirror movement at later time point of recovery.

Increased correlation with mirror movement may be accounted for by initial impairment.

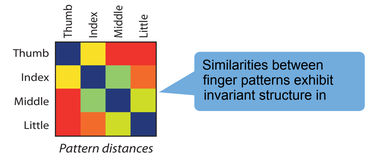
Correlation with mirror movement



*Results support **interhemispheric compensation** model over recovery process.*

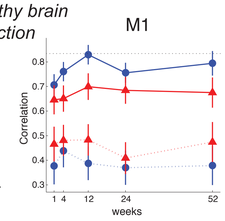
Recovery of representational structure

Finger patterns are arranged in a very specific fashion in the healthy brain
Return to this structure may be essential for recovery of hand function



Increases significantly in the first weeks for both paretic and non-paretic hand

Structure in good hemisphere for paretic hand movements is closer to normal than structure in lesioned hemisphere for non-paretic hand movements



Pattern structure recovers towards the healthy organisation
As the structure of finger enslaving (Ejaz et al.), there is a clear deficit on the non-paretic side, which recovers in parallel with the paretic hand.

Discussion

Pattern analysis shows that ipsilateral activity after stroke contains increased finger representation for paretic finger movements. These increased activity and representation may not be accounted for by mirror movement, suggesting a compensation role in recovery.

The strength and structure of finger representations in the contralateral, lesioned hemisphere recover in the first 12 weeks after a stroke. Strong correlation between these representations and Individuation ability can not be explained by performance confund.

A similar initial deficit and subsequent recovery can be seen in the non-lesioned hemisphere for non-paretic hand movements (similar to results in finger enslaving).

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