Functional Imaging Biomarkers Predicting Upper Limb Recovery from Severe Motor Impairment after Stroke

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Introduction

- Predicting recovery outcome after stroke are important to implicate individually-tailored rehabilitation strategy. In case of recovery of upper extremity (UE) motor function, most biomarkers demonstrated low predictive power in patients with severe motor impairment after stroke.
- This study focused on investigation of neuroimaging biomarkers optimally predicting recovery of UE motor function in severe stroke patients. We hypothesized that there may be different primary neuroimaging markers depending on the pattern of later recovery.

Methods

Participants & Experimental Design

- Forty-two subacute ischemic stroke patients with unilateral lesion
- Nineteen years or older at the time of stroke onset
- Fugl-Meyer assessment (FMA) score under 55 at 2 weeks after stroke
- All patients underwent T1-weighted, diffusion tensor imaging (DTI), resting-state functional MRI (rs-fMRI) data acquisition, as well as motor function assessment using the FMA at 2 weeks. FMA was assessed again at 3 ms after stroke.
- Based on proportional recovery rule, patients were divided into Fitter and Non-fitter groups according to their FMA-UE motor recovery at 3 ms whether the improvement achieve 70% of initial FMA score (Fitter) or not (Non-Fitter).

Group	Fitters (n = 23)	Non-fitters (n = 19)
Age (years)		
Mean ± SD	52.3 ± 11.2	63.1 ± 11.4
Sex (n)		
Male / Female	15 / 8	9 / 10
Lesion side (n)		
Right / Left	9 / 14	9 / 10
Lesion location (n)		
Supra- / Infra-tentorial	14 / 9	16 / 3
Initial Impairment, mean ± SD		
FMA-UE	18.0 ± 9.7	8.0 ± 5.7
NIHSS	6.1 ± 3.4	12.7 ± 5.4
Time post stroke (days)		
Mean ± SD	14.8±8.8	17.0±7.5
Risk factors (yes/no)		
Hypertension	14 / 9	8 / 11
Diabetes mellitus	7 / 16	4 / 15
Hyperlipidemia	9 / 14	5 / 14
Ischemic heart disease	3 / 20	0 / 19

Data Processing & Measurements

- Lesion load & Lesion volume
 - The individual lesion was manually drew and the CST template obtained from probabilistic tractography in the healthy DTI data. Lesion load was calculated by overlaying the individual lesion volume onto the CST template.
 - Lesion volume was calculated by counting the number of lesioned voxels from the lesion map and multiplying the voxel volume.
- Fractional anisotropy (FA) analysis from DTI
 - FSL software (eddy current correction, non-linearly registration)
 - Regional specific FA values using the Johns Hopkins University white matter atlas - posterior limb of the internal capsule (PLIC), cerebral peduncle (CP), superior corona radiata (SCR), superior cerebellar peduncle (SCP), genu of the corpus callosum (GCC), body of the corpus callosum (BCC), and splenium of the corpus callosum (SCC)
- Functional connectivity (FC) analysis from rs-fMRI
 - CONN toolbox (head motion, slice timing correction, scrubbing, spatial registration, segmentation, spatial smoothing, removal of nuisance sources, band-pass filtering, linear detrending)
 - Automated anatomical labeling template-based functional connectivity

Results

Group Lesion Map

Functional Imaging Measurements: DTI, rs-fMRI

- FA values of the Non-fitters were significantly lower than the Fitters in the PLIC, CP, SCR, GCC, and SCC.
- There were significant differences in the lesion volume and lesion load between the Fitters and Non-fitters. The lesion load of the CST and lesion volume were greater in the Non-fitters than the Fitters.
- In rs-fMRI, the interhemispheric functional connectivity (IHFC) strength in the Non-fitters was lower than the Fitters.

Investigation of Predictive Imaging Markers

- In the Fitters, the SCP FA value was the significant predictable biomarker ($R^2 = 0.569$, $p < 0.001$). In contrast, the SCC FA value was the significant predictable biomarker in the Non-fitters ($R^2 = 0.293$, $p = 0.016$). Additional analysis of rs-fMRI data, the connectivity strength between the left superior temporal cortex and bilateral occipital cortex showed significant correlation with later motor recovery in Non-fitters. The connectivity between the left Heschl's gyrus (HES) and right superior occipital gyrus (SOG) showed the strongest predictive value ($R^2 = 0.514$, $p < 0.001$).

Conclusions

- The neuroimaging biomarkers for motor recovery were different between both groups. The best predictive marker of each group (SCP FA in the Fitter group; SCC FA and Lt. HES - Rt. SOG FC in the Non-fitter group) showed high prediction power which was higher than PLIC FA.
- This neuroimaging approach is helpful to predict motor recovery in patients with initially severe motor impairment after stroke who are usually considered as highly unpredictable individuals and needed a different strategy for recovery prediction beyond the traditional approaches.

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