**Functional connectome reorganization after pontine stroke is associated with better motor outcomes**

Emily Olafson1, Keith Jamison1, Hesheng Liu2, Joel Bruss3, Aaron Boes3, Amy Kuceyeski1

**Institutions**:

1Weill Cornell Medical College, New York, NY,

2Harvard Medical School, Cambridge, MA,

3University of Iowa, Iowa City, IA

**Introduction**: Motor recovery following ischemic stroke is contingent on the ability of surviving brain networks to compensate for damaged tissue [(Corbetta et al. 2005)](https://paperpile.com/c/jXIju4/dHdr). In rodent models, sensory and motor cortical representations have been shown to remap onto intact tissue around the lesion site [(Winship and Murphy 2009; Brown et al. 2009)](https://paperpile.com/c/jXIju4/Z2p7+evNS), but remapping to more distal sites (e.g. in the contralesional hemisphere) has also been observed [(Brown et al. 2009)](https://paperpile.com/c/jXIju4/evNS). Resting state functional connectivity (FC) analysis has been employed to study compensatory network adaptations in humans but mechanisms underlying recovery are not well understood. Here, we examine longitudinal FC in 23 first-episode ischemic stroke patients and utilize a graph matching approach to identify patterns of regional functional connectivity reorganization between imaging sessions. We hypothesize that brain regions with more structural damage due to the lesion will more frequently functionally reorganize; that more impaired subjects will have more global functional reorganization; and that the amount of functional reorganization will correlate with the change in motor impairment between subsequent sessions.

**Methods**: Twenty-three individuals (34-68 years old; 9 males; 9 right-handed) with first-episode brainstem stroke were enrolled in the study. Participants’ motor recovery was assessed via the Fugl-Meyer, collected during five sessions across a period of 6 months (7, 14, 30, 90, 180 days post-stroke). Resting-state functional MRI was also obtained for each of the five sessions; FCs were extracted via a regularized precision approach [(Liégeois et al. 2020)](https://paperpile.com/c/jXIju4/pVYF) over a 268 region atlas [(Finn et al. 2015)](https://paperpile.com/c/jXIju4/ZTMm). In graph matching, a one-to-one correspondence between nodes (i.e. gray matter regions) in FCs from successive imaging sessions is determined based on maximizing the similarity of the two FCs (Figure 1a). A region that is assigned to a different region in the subsequent FCis considered to have been functionally remapped. Regional remapping frequencies were calculated as a proportion of the stroke subjects in which that region remapped. In addition, the extent of regional structural (white matter) connectivity disruption due to the lesion was assessed for each stroke subject with the Network Modification (NeMo) Tool [(Kuceyeski et al. 2013)](https://paperpile.com/c/jXIju4/tXLJ). The NeMo Tool uses virtual tractography to calculate for each gray matter region the proportion of its streamlines that intersect with the lesion, aka the Change in Connectivity (ChaCo) score.

**Results**: Functional remapping frequency and ChaCo (structural disconnection) scores were highest in the brainstem and cerebellum (Figure 2a, b). For each pair of longitudinal, subsequent time points, there was a significant, positive correlation between regional ChaCo scores and functional remapping frequency, indicating those regions with more baseline structural connectivity disruption also had more remapping over time (Figure 2b).. Individuals’ Fugl-Meyer scores at baseline (7 days post-stroke) were significantly correlated with their total number of remapped nodes between 7 and 14 days post-stroke (Figure 2c), indicating individuals with more baseline impairment also had more early-stage functional remapping. Furthermore, the change in Fugl-Meyer scores across time correlated positively with the total number of remapped nodes between 14 and 30 days post stroke and between 30 and 90 days post stroke (Figure 2d) indicating that more remapping in that time period is associated with better motor recovery.

**Conclusions**: Post-stroke functional reorganization as measured with graph matching may be a subject-specific biomarker of functional plasticity and may represent an important component of motor recovery.

**References**

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