Predicting recovery from stroke using baseline imaging biomarkers of structural connectome disruption

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Target audience Clinicians and researchers alike will benefit from the information gained in this study.

Purpose The Network Modification (NeMo) Tool[1] quantifies disruptions in the brain's structural connectome by mapping areas of damage or abnormality onto a large collection of healthy connectomes. This tool has a main advantage in that it uses MRI sequences that are routinely obtained in the acute clinical setting and does not require expertise in advanced diffusion image processing and tractography. This allows for a clinically feasible method of quantitatively predicting from an MRI in the acute phase of stroke the areas that may be most affected by connectivity disruption with the aim of providing insight as to type and severity of impairment. Knowledge of connectivity disruption is important because losses in white matter integrity have been associated with functional deficits and motor recovery after stroke.[2] Therefore, it may be helpful for clinicians to be able to predict which regions have more structural disconnection, as it could enhance their prognostic abilities and enable more focused rehabilitative strategies.[3] In this work, we hypothesized that models based on the NeMo Tool's measure of baseline structural connectome disruption would better predict recovery 6 months post-stroke as measured using the Activity Measure for Post-Acute Care (AMPAC) than models based on lesion volume.

Methods *Subjects and Data* This study consisted of 18 subjects (age: 70.7±13.6 years) with ischemic stroke (NIHSS: 6.1±4.1) that were admitted to the rehabilitation facility at New York Presbyterian Hospital. MRIs were acquired upon admission to the hospital. T1 and diffusion-weighted images (DWI) were collected on 3.0 or 1.5 Tesla GE Signa EXCITE scanners (GE Healthcare, Waukesha, WI, USA). T1 scans were acquired axially (repetition time/echo time/inversion time = 600/12/0 ms) with a 288 x 192 matrix over 30 5.0-mm thick slices. DWIs were acquired axially via an echo-planar imaging sequence, with b = 1000 s/mm^2 and b = 0 s/mm^2 from 30 5-mm thick slices and 128 x 128 matrix size, repetition time/echo time/inversion time = 8000 or 10000/100/0 ms. Three AMPAC measures of daily activity, basic functions and cognition were collected 6 months post-stroke.

The NeMo Tool Brain areas of ischemia that show up as hyperintense on the DWI were identified by hand. Coregistration of the individual's T1 scans into the NeMo tool's common space was performed using linear and non-linear registration in SPM8; the resulting transformation applied with nearest-neighbor interpolation to the lesion mask. The coregistered lesion mask was then superimposed on the NeMo Tool's connectivity maps, and regional structural connectivity losses were estimated via the Change in Connectivity (ChaCo) score (i.e., the percent of streamlines connecting to a given region that pass through the lesion mask). The 116-region AAL atlas of cortical and subcortical areas was used.

Statistical Analysis Standard linear regression was performed using lesion volume (log transformed), age and gender as independent variables to predict AMPAC scores. Partial Least Squares Regression (PLSR) was implemented using the ChaCo scores, age and gender to predict AMPAC scores. PLSR is a method of dimensionality reduction that finds the directions on which to project the data such that the correlation with the outcome variable is maximized. We can observe the relative contribution of the different regions to the model's prediction by visualizing PLSR coefficients. Model quality was assessed using R^2 and Akaike Information Criterion (AIC).

Results The NeMo/PLSR models based on ChaCo scores had higher goodness-of-fit and lower AIC (R^2: 0.57-0.62, AIC: -10.5 to -3.3) than models based on lesion volume (R^2: 0.27-0.32, AIC: 2.0-3.3), see Fig 1A for NeMo/PLSR model results. The three AMPAC models had gender as a large and significant predictor; males tended to have better scores than females. The daily activity subtest had significant positive coefficients (more disconnection = higher scores) in left subcortical areas, but these were very small in value (see Fig 1B). The basic mobility subtest had non-significant negative coefficients in medial/cingulate regions while the applied cognition subtest had significant but small negative coefficients in right attention network regions. Large, non-significant coefficients in the left superior parietal region were found for all tests. This region was also found to be important in visual-spatial reasoning and orientation (unpublished results).

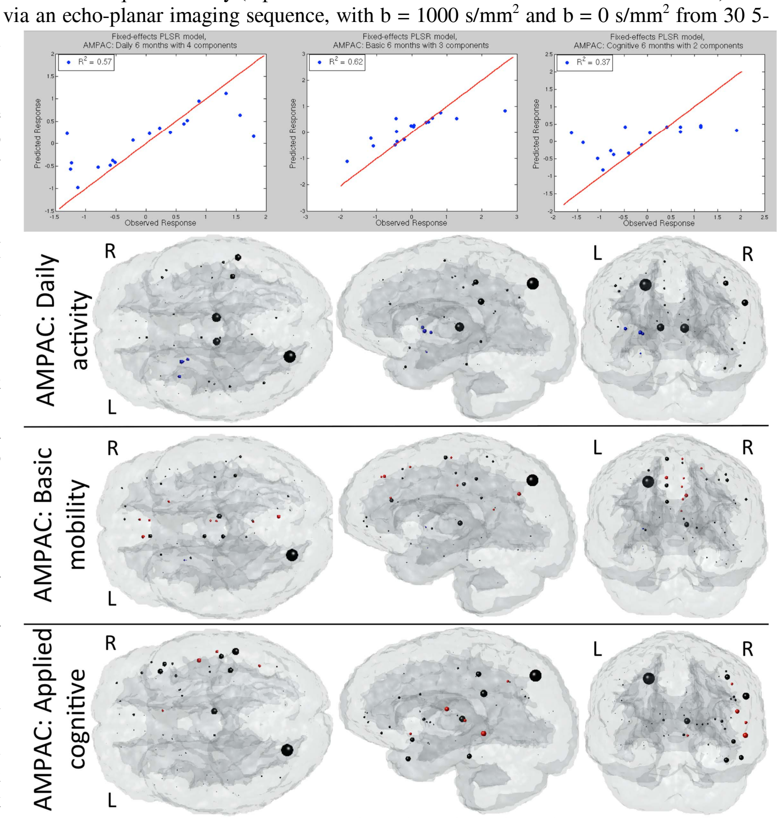

Figure 1: Panel A shows the predicted versus actual AMPAC measures for the PLSR/ChaCo models. Panel B shows the PLSR coefficients for each region (black: not significant, red: significant/negative, blue: significant/positive.)

Discussion PLSR/ChaCo models based on network disruption information proved superior to models based on lesion volume in predicting recovery from stroke in that they had higher prediction accuracy and lower AIC. Higher disconnection in the right attention network regions was associated with lower cognitive scores, which is somewhat unsuprising. A left superior parietal region that showed up in the coefficient plots for each of the ACRM measures was found to be important in other tests of higher cognitive function, i.e. tests of visual-spatial/executive and orientation. These results are somewhat preliminary and will be carried out in larger populations in order to increase the power and robustness of the results.

Conclusions After thorough validation and additional data, this method could be a valuable quantitative tool for clinicians in developing prognoses and rehabilitation plans for post-stroke recovery.

References 1. Kuceyeski A, Maruta J, Relkin N, Raj A. The Network Modification (NeMo) Tool: elucidating the effect of white matter integrity changes on cortical and subcortical structural connectivity. *Brain Connect*. 2013;3(5):451–463.

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