Predicting stroke severity with structural connectivity network disruption as measured with the Network Modification (NeMo) Tool

Amy Kuceyeski[1], Mark Villanueva[2], Ashish Raj[1], Michael O'Dell[2], and Joan Toglia[3]
[1]*Radiology, Weill Cornell Medical College, New York, NY, United States,* [2]*Rehabilitation Medicine, Weill Cornell Medical College, New York, NY, United States,*
[3]*Occupational Therapy, Mercy College, NY, United States*

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

Purpose: The Network Modification (NeMo) Tool[1] quantifies losses in the brain connectivity network by mapping areas of damage or abnormality onto a large collection of healthy tractograms. This process avoids the difficult issues with performing tractography in subjects with tissue abnormalities that can affect the diffusion signal in non-straightforward ways. In addition, this tool uses MRI sequences that are routinely obtained in the acute clinical setting and does not require expertise in advanced diffusion image processing and tractography techniques. 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 loss of connectivity; this can provide insight as to type and severity of functional loss. Knowledge of how disconnection affects brain regions may be 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 structrual disconnection, as it could enhance their prognostic abilities and enable more focused rehabilitative strategies.[3] In this work, we hypothesized that the NeMo Tool's measure of structural connectivity disruption could better predict baseline severity of stroke as measured by the NIH Stroke Scale (NIHSS) than lesion volume alone.

Methods: *Subjects and Data* This study consisted of 25 subjects (age: 70.8±9.6 years) with ischemic stroke (NIHSS: 7.9±5.6) that were admitted to the rehabilitation facility at New York Presbyterian Hospital. MR images and NIHSS 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.

The NeMo Tool Brain areas of ischemia that show up as hyperintense on the DWI were hand-drawn. Coregistration of the individual's T1 scan into the NeMo tool's common space was performed using non-linear registration in SPM8 and 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 tracks connecting to a given region that pass through the lesion mask). A 116-region atlas of cortical and subcortical areas was implemented.

Statistical Analysis First, we calculate the Spearman correlation between lesion volume and NIHSS to measure their relationship. Partial Least Squares (PLS) regression[4] was then implemented on the ChaCo scores to predict NIHSS. PLS regression is a method of dimensionality reduction that finds the directions on which to project the data such that the correlation with the outcome variable (in this case, NIHSS) is maximized. We can observe the relative contribution of the different regions to the model's prediction by plotting the PLS regression coefficients.

Results: ChaCo scores varied widely across subjects, but areas of pre/postcentral gyri, insula, hippocampus, middle cingulate and subcortical areas were highest in general. Lesion volume was positively correlated with NIHSS (R^2 = 0.28, $p < 0.05$). PLS regression was performed using only two components in an effort to minimize overfitting; the results are given in the top left panel of Figure 1 (R^2= 0.75). The first component had high values for the right supplementary motor area, angular gyri, frontal superior gyri and paracentral gyri. The second component (visualized in Figure 1) clearly differentiates between right and left hemispheres in that the coefficients have opposite signs. The right hemisphere had high values in the superior parietal, precentral and frontal areas while the left hemisphere had higher values in the hippocampus, thalamus and insula.

Discussion Although the ChaCo scores varied across the population, areas that have language, motor and memory functions had higher disruption in general. NIHSS was weakly correlated with lesion volume. An advantage of the ChaCo scores is that it differentiates the effect of stroke amongst gray matter regions, and we see this fact reflected in the PLS regression results. We should note that the model tends to perform worse on the lower ranges of NIHSS (less than 1), so different model approaches may be implemented for lower scores in the future. Interestingly, the second component in PLS regression indicates that the laterality of stroke greatly influences the NIHSS.

Conclusion The NeMo tool was used to investigate the effect of ischemic stroke on the structural connectivity network in 25 individuals. PLS regression was used to predict NIHSS based on this network disruption information. More subjects are needed to validate this model; data is being collected on an on-going basis. In the future, these methods will be further developed in an attempt to predict recovery from stroke, which, if successful, will aid in prognosis development and rehabilitation planning.

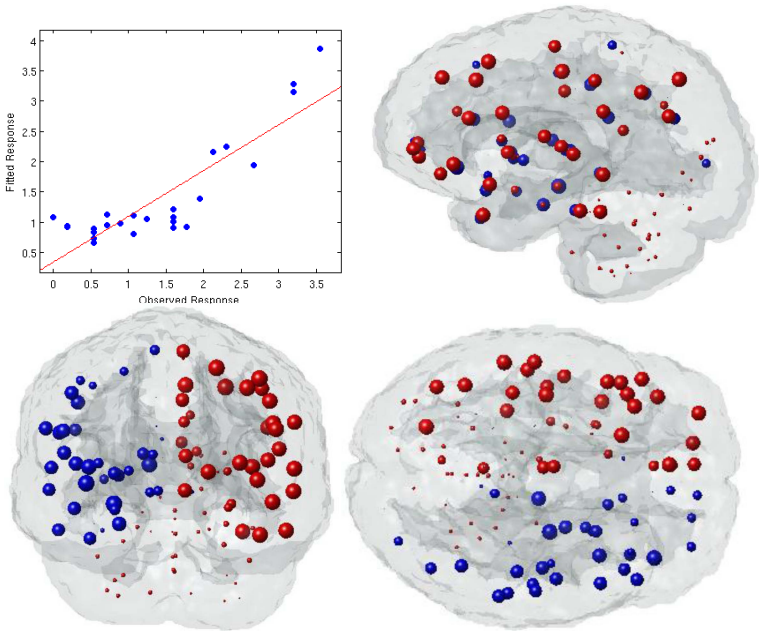

Figure 1: (top left) Observed versus predicted NIHSS using partial least squares regression. (top right and bottom) The coefficients for the second PLS component displayed on the glassbrain. Each sphere corresponds to a different gray matter ROI, the sphere size is proportional to the coefficient value and the color denotes positive (blue) and negative (red).

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 connectivity*. 2013;3(5).
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