Creation and validation of a white matter importance map using traumatic brain injury patient data

A. Kuceyeski[1], and A. Raj[1]
[1]Radiology, Weill Cornell Medical College, New York, NY, United States

Introduction: Many brain diseases such as stroke, multiple sclerosis and traumatic brain injury result in brain damage and disability from cell death. The location and size of the effected area greatly influences the amount and type of disability that the patient incurs. Current MRI-based diagnosis of brain injury is qualitative, involving subjective assessment of severity and prediction of impairment by the physician. Even when augmented by 3D processing tools that allow for accurate measurement of lesion or tumor volume, this approach is insufficient in characterizing the effect on brain function. This is because functional impairment is determined by both the *extent and location* of damage, and can be properly assessed only by looking at the connectivity of the affected region to the rest of the brain via its fiber architecture. A computational method assigns quantitative scores to the overall decrease in brain connectivity resulting from damage to a given region. This information, presented in the form of a 3 dimensional quantitative connectivity importance map of the brain, can greatly bolster physicians' knowledge and could lead to improved surgical planning, assessment of disease severity and possibly the development of a rehabilitation program.

Data and Methods: The data consisted of 14 normal controls and 15 mild to moderate traumatic brain injury (TBI) patients, with both structural (T1) and diffusion (b = 1000, 30 directions) images. Connectivity between gray matter regions in the brain was determined in the following way: 1) structural MRI (T1) brain volumes are co-registered with diffusion volumes 2) the T1 volumes are parcellated into 116 gray matter structures, using Statistical Parametric Mapping (SPM) software [1] and a standard 116-region anatomic atlas 3) the parcellated structures seed corresponding regions in the DTI volume and tractography is performed 4) all tracts originating and terminating in any pair of cortical regions are probabilistically "counted" and a connectivity matrix is constructed, as in [2]. Once the intact brain connectivity matrix is calculated, the importance map is created by removing a small portion of white matter, as well as any white matter tracts passing through that region, and recalculating the connectivity matrix. The difference in the new connectivity matrix versus the original is assigned to that voxel as its relative importance. Once the importance map has been calculated per subject, SPM's coregistration software is used to normalize each map to a common (MNI) space.

It has been shown in many studies that FA decreases with the severity of TBI; in [3] the FA of particular tracts was shown to explain much of the variation in perfromance as measured by the Attention Network Test (ANT) and the California Verbal Learning Test (CVLT), two clinical exams that measure functional loss. Therefore, as subsequent validation of the importance map, the fractional anisotropy (FA) of each of the normal and TBI patients are calculated and the z-scores for the FA of the TBI patients found. The dot product of the importance map and the z-score map (i.e. the sum of the product of each voxel's importance and z-score) is a scalar assigned to the patient as the Importance Map (IM) score. This measure, where smaller scores mean more a detrimental effect, combines the level of white matter integrity loss (z scores) and the importance of that same white matter region (IM). This IM score is then correlated with the two sets of clinical measures that we have for the TBI patients, namely, the ANT and CVLT.

Results: Figure 1 shows the average importance map for the 14 normal controls; note regions of higher importance in the occipital and temporal regions, particularly near the precuneus, a region commonly associated with a high level of connectivity. Table 1 lists the correlation of the average z scores of FA and the previously described IM score with each of the measures in the two tests individually, as well as with the projection onto the first principal component of the covariance matrix of the scores (called PCA, this is essentially a linear combination of all of the scores that maximizes variance). With few exceptions, the correlations are higher when including the importance map information. In fact, we see that only the correlations between the IM score and ANT's overall mean, Total Recall portion of the CVLT, and the principal component reach a significance level of 0.05. We see a relatively low correlation of both average z-scores and IM scores with the more specific clinical measures like the ANT alerting and conflict tasks, but a higher correlation when we look at the more general tasks like overall mean of reation time in the ANT. This could be due to the lack of specificity of the importance map to any functional subnetworks in the brain; recall that ours is a measure in *overall* brain connectivity loss. In the future, we will compute the importance map for specific functional subnetworks to further improve the results.

Clinical Measure	Z score	IM score
CVLT – LD Free Recall	0.45	0.51
CVLT – SS Total Recall	0.43	0.52*
CVLT – SS Total Recognition	0.07	0.23
ANT – Overall mean	-0.43	-0.67*†
ANT – Alerting	0.03	0
ANT - Orienting	0.34	0.43
ANT - Conflict	0.06	-0.01
PCA of Covariance Matrix	0.48	0.71*†

Table 1: The correlation of the average z-scores of the FA and the IM scores with the various clinical measures for the 15 TBI patients. *significant at the level $p < 0.05$, † significant at the level $p < 0.01$.

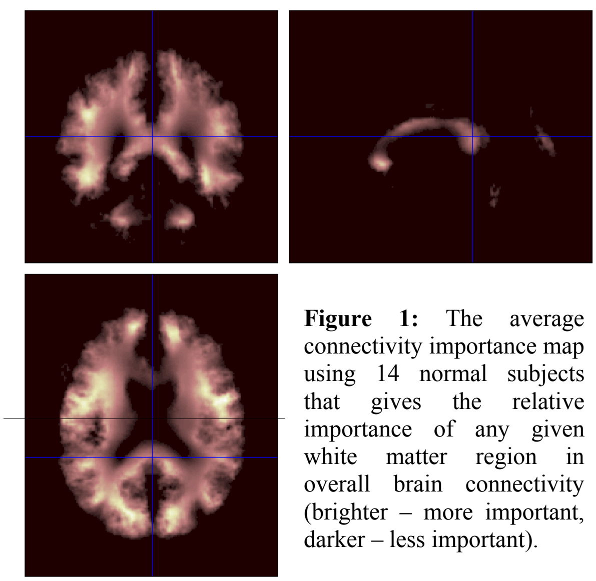

Figure 1: The average connectivity importance map using 14 normal subjects that gives the relative importance of any given white matter region in overall brain connectivity (brighter – more important, darker – less important).

[1] Friston KJ, Ashburner JT, Kiebel SJ, Nichols TE, Penny WD. *Statistical Parametric Mapping: The Analysis of Functional Brain Images*. Academic Press; 2006:656.
[2] Iturria-Medina Y, Sotero R, Canales-Rodríguez E, Alemán-Gómez Y, and Melie-García L. (2008) *Studying the human brain anatomical network via diffusion-weighted MRI and Graph Theory*. NeuroImage. 40(3): 1064–1076.
[3] Niogi SN, Mukherjee P, Ghajar J, et al. Structural dissociation of attentional control and memory in adults with and without mild traumatic brain injury. *Brain : a journal of neurology*. 2008;131(Pt 12):3209-21.