

# BBCA Analysis of Functional and Structural Networks

A. K. Smith<sup>1</sup>, D. J. Madden<sup>1</sup>, P. Gaur<sup>1</sup>, and N-K. Chen<sup>1</sup>

<sup>1</sup>Brain Imaging and Analysis Center, Duke University, Durham, North Carolina, United States

**Introduction.** The medial cortical regions, including the posterior cingulate and medial prefrontal cortex, have been shown to exhibit significantly decreased brain activity during task conditions. It has been proposed that these regions form the nodes of a default mode network (DMN) that is continuously and spontaneously active, even in the absence of an external task [1]. However, this activity must be suppressed during externally-directed cognitive tasks and is expressed as task-related deactivation. Changes in the functioning of the default mode network have been reported for healthy older adults, relative to younger adults, in several studies of the mean level of activation. Overall, these studies suggest that older adults exhibit increased difficulty in suppressing the spontaneous signal fluctuations within the default mode network, possibly reducing attentional allocation to task-relevant processing. The following analysis describes a behavior-based connectivity analysis (BBCA) method, in which whole-brain data are used to identify behaviorally-relevant intrinsic and functionally connected (FC) networks and the fractional anisotropy (FA) that indicates the level of connection between areas.

**Materials and Methods.** *MRI Data Acquisition:* Diffusion Tensor Imaging (DTI) and functional MRI (fMRI) datasets from 38 healthy adults, 19 aged 63 to 78 and 19 aged 20 to 28 were acquired on a 4T GE scanner. The participants performed three types of behavioral tasks: choice reaction time, episodic memory, and semantic memory. The tasks were performed during four fMRI runs in the following order: a choice RT task, an off-task interval, and a memory retrieval task. An encoding phase for the memory tasks was performed just prior to the fMRI analysis, during which DTI was conducted.

*Image Analysis:* BBCA consists of two major steps: low-pass filtering the acquired fMRI data to suppress the task-evoked signal changes, and then processing the filtered data using a FC analysis to identify major behaviorally-relevant functional and structural networks. The output from step one was a set of filtered, normalized images similar to data acquired during resting-state. The data then was segmented into 116 ROIs using the Automated Anatomical Labeling (AAL) [2]. The correlation coefficients ( $r$  values) between time-series data from different anatomical regions were calculated and stored in a 116X116 2D matrix. Each element of this 2D matrix represents the FC between two anatomical regions. For each age group, behaviorally-relevant functional networks were then identified by thresholding these correlations at  $p < 0.005$ . Similar approaches were used to process DTI data, assessing the inter-region connectivity levels based on the averaged FA values in fiber tracts connecting a pair of pre-segmented brain regions.

**Results.** At a threshold of  $p < 0.005$  (uncorrected), none of the younger adults' connectivity matrix elements were significantly correlated with the choice RT, however, 33 elements for the older adults were significantly correlated. All of these correlations were negative, reflecting increased RT as a function of decreasing connectivity. The majority of these networks were found to be located in the inferior frontal cortex. A linear regression analysis of the FC values, using age group, choice RT, and their interaction as predictors, indicated the predictors could account for 40% of the variance in FC. In this regression model, the Age Group-RT interaction was significant; indicating the relation between RT and FC varied significantly across age group, and is illustrated by Figure 1. Older adults exhibited a significant correlation between RT and FC,  $r = -0.83$ ,  $p < 0.0001$ , whereas the younger adults exhibited no significant relation between these variables. Given the role of FC as a mediator of older adults' behavioral performance in the present data, the role of cerebral white matter integrity as a potential mechanism of individual differences in the older adults' FC values was performed using DTI data. The mean FA values for several ROIs, which represent some of the major pathways connecting cortical regions that are critical to cognitive function, were found. Fig-2 illustrates the degree of FA with respect to FC of the genu. Higher FA values exhibited higher mean FC across all 13 regions associated with the inferior frontal gyri.

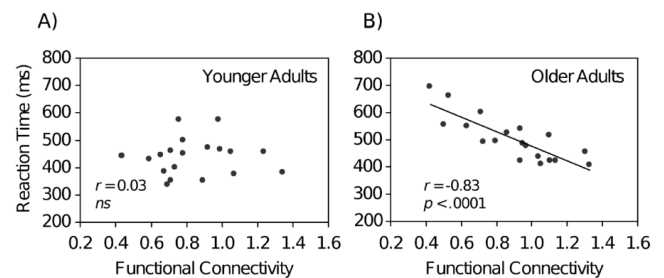
**Discussion.** The degree to which the relation between years of age and RT was influenced by FC was then examined for the older adults. When years of age was the sole predictor of the older adults' RT, only 29% of the variance was accounted for in their RT. However, when FC was entered into the regression model before age, age accounted only for an addition 3.7% of the variance in RT, which means FC attenuated the age-related variance in RT by 86%. This indicates that FC is a mediator of the age-related slowing in the older adults' behavioral performance.

Analysis of cerebral white matter integrity, indexed by FA from DTI, revealed a significant relation between white matter integrity and older adults' mean FC. Those older adults with higher white matter integrity were those with higher values of mean FC across the regions connecting the inferior frontal gyri. The correlation between the older adults' genu FA and FC is consistent with other investigations, using DTI, which have demonstrated a relation between white matter integrity and intrinsic FC.

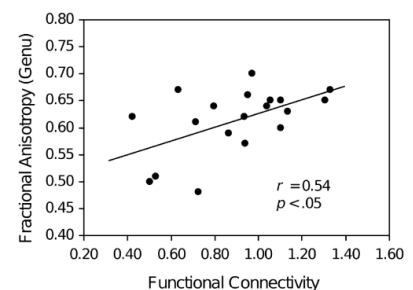
In applying the BBCA method to fMRI and DTI data of healthy, younger and older adults, we obtained three main findings. First, significant age-related change was evident in the behaviorally-relevant connectivity networks. Second, it identified behaviorally-relevant, intrinsic connectivity outside of the default mode network. Third, intrinsic FC was related to structural connectivity as reflected in cerebral white matter integrity.

**References:** [1] Raichle ME, et al, *Proc Natl Acad Sci* 98: 676-682, 2001.

[2] Tzourio-Mazoyer N et al, *Neuroimage* 15: 273-289, 2002.



**Figure 1:** Relation between choice reaction time and functional connectivity (in networks connected with inferior frontal gyri), for younger adults (a) and older adults (b).



**Figure 2:** Relation between FA in the genu and the FC (in networks connected with inferior frontal gyri), for older adults