LONGITUDINAL WHOLE-BRAIN FUNCTIONAL NETWORK CHANGE PATTERNS OVER A TWO-YEAR PERIOD IN THE ABCD DATA

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ABSTRACT

Functional network connectivity (FNC) is a useful measure for evaluating the temporal dependency among brain networks. Longitudinal changes of intrinsic function are of great interest, but to date there has been little focus on multivariate patterns of FNC changes with development. In this paper, we proposed a novel approach that uses FNC matrices to estimate multiple overlapping brain functional change patterns (FCPs). We applied this approach to the large-scale Adolescent Brain and Cognitive Development (ABCD) data. Results reveal several highly structured FCPs showing a significant change over a two-year period including brain functional connectivity between visual (VS) and sensorimotor (SM) domains. This pattern of FNC expression becomes stronger with age. We also found a differential pattern of changes between male and female individuals. Our approach provides a powerful way to evaluate whole brain functional changes in longitudinal data.

Index Terms— Delta FNC, Longitudinal study, ICA, MRI

1. INTRODUCTION

The resting-state human brain can be used to reveal time-varying functional connectivity (FC) dynamics [1-4]. There are various neuroimaging techniques that can be used to quantify FC. Functional magnetic resonance imaging (fMRI) is the most commonly used technique for the computation of the temporally coherent between brain blood oxygenation dependents. The FC between two brain regions from resting state functional magnetic resonance imaging (rfMRI) data can be computed via a measure of pairwise statistical dependency (most commonly Pearlson correlation) between the time courses. Data driven decomposition techniques such as independent component analysis (ICA) can be used to extract co-activated brain networks, whose time courses can be used to calculate the functional network connectivity (FNC) [5].

There is a growing research interest in estimating age-related anatomical and functional changes. Spontaneous blood oxygenation level-dependent (BOLD) signals have been frequently used to identify the regional FC and investigate the changes in a variety of neurological and psychiatric disorders [6]. During the adolescence period, the human brain exhibits remarkable changes both in function [7, 8] and structure [9, 10]. Several studies have reported age-related FC changes during the adolescence period, but the obtained results are somewhat inconsistent [11]. Small data size, the absence of longitudinal data, variation in fMRI data preprocessing, and the choice of different analysis methods contribute to this inconsistency. Vasa et al., have investigated changes in human brain function during adolescent and found two distinct modes (disruptive and conservative) of age-related change in FC. Age-related changes in FC have been studied including findings showing a progressive reduction in FC among different age groups [12]. The impact of aging on functional networks has also been reported in [13]. However there has been little work in evaluating multivariate patterns of change in functional (network) connectivity with development.

In our work, we propose a new technique to visualize within individual changes in whole-brain FNC with increased age. We estimate the FC change patterns (FCPs) by first computing cellwise within individual ΔFNC matrix and then estimating covarying multivariate patterns via ICA on the ΔFNC matrices. A one sample t-test on the resulting component loading parameters reveals several FCPs showing significant longitudinal differences. To the best of our knowledge, our proposed procedure is the first approach to estimate multiple overlapping brain functional change patterns (FCPs) over a two-year period in the developing brain. The remainder of the research paper is organized as follows. In the materials and methods section, we introduced the data preprocessing and the analysis procedures. Next, in the result section, we show brain functional coupling change with age. Finally, we discuss the findings in the conclusion section.

2. MATERIALS AND METHODS

2.1 Summary of ABCD data:

The present work used the dataset from the release 2.01 of the Adolescent Brain Cognitive Development (ABCD) study

(https://abcdstudy.org/). The ABCD contains over 11,800 children aged 9–11 years with multiple MRI scans from two image sessions (baseline and second year follow-up), and collected a diverse range of demographic and health backgrounds. The parent's full written informed consent and the child's assent were obtained for each participant under protocols approved by the Institutional Review Board (IRB). The ABCD dataset is shared by the National Institute of Mental Health Data Archive (NDA) (https://nda.nih.gov/), which makes available open-source datasets collected from wide range of research projects across many scientific domains to enable collaborative science and discovery. In this study we used 3,489 subjects who had been scanned both at baseline and at a two-year follow-up visit.

2.2 Data preprocessing:

We preprocessed the raw fMRI data via a combination of the FMRIB Software Library v6.0 (FSL) toolbox and the Statistical Parametric Mapping 12 (SPM) toolbox, under the MATLAB 2019b environment. First, rigid body motion correction was performed using FSL to correct subject head motion. Then we corrected the distortion in the fMRI images using the field map files acquired with phase encoding in the anterior-posterior (AP) direction and volumes with phase encoding in the posterior-anterior (PA) direction). After distortion correction, fMRI data were subsequently warped into the standard Montreal Neurological Institute (MNI) space with 3 × 3 ×3 spatial resolution and were then smoothed using a Gaussian kernel with a full width at half maximum (FWHM) = 6 mm.

In this study, the Neuromark network templates were used to extract comparable intrinsic connectivity networks (ICNs) via a fully automated spatially constrained ICA approach across subjects from the ABCD dataset. The Neuromark framework used two healthy control datasets, the human connectome project (HCP, 823 subjects after the subject selection) and the genomics superstruct project (GSP, 1005 subjects after the subject selection) to construct the priors. Details of the Neuromark framework and templates can be found at [14]. The selected spatial priors have also been demonstrated to be highly reliable between pipeline and between adult and adolescent datasets [15].

2.3 Models:

In our experiment, we used the subject-wise FNC data from the baseline and two-year scans. We first computed the cell-wise difference between the baseline and two-year FNC data to create change FNC matrices (ΔFNCs). Next, for longitudinal brain functional coupling recognition, to capture covarying patterns of changes, called functional change patterns (FCP) we decompose the ΔFNC matrices with ICA using the infomax algorithm [16]. In this work we estimate 5 components. More specifically the equation for the ICA model can be written as:

$$X = A.S$$

Here, X = Subjects (3489) × ΔFNC cells (1378 cells from the upper triangle of the symmetric matrix); A = subjects (3489) × component number (5) and S = component number (5) × ΔFNC cells (1378)

This effectively models the input data as:

$$\Delta FNC = \sum_{i=1}^{5} a_i FCP$$

Here, $\Delta FNC = F_0 - F_2$, F_0 is the baseline FNC data, F_2 is the two-year FNC data, FCP, the source matrix, represent maximally independent functional change patterns, and a_i are the subject specific loading parameters for each component. The sources represent maximally independent covarying patterns of functional change.

After the ICA estimation, we further evaluated the loading parameters and source matrix. To identify FCPs which show a significant longitudinal change relative to zero, we perform a one sample t-test on the loading parameters and compute the statistical significance with 95% significance level, corrected for multiple comparisons. We also plotted the scatter plot of loadings parameters and generated the spatial map of FNC matrices. A block diagram shown in Figure 1 presents the analysis workflow.

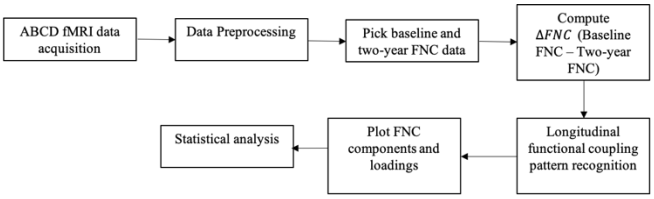

Figure 1: Block diagram of the FCP analysis workflow

3. RESULTS

The Neuromark template identified 53 replicable networks that were divided into 7 domains based on anatomical and functional properties (subcortical, auditory, sensorimotor, visual, cognitive control, default mode and cerebellar) [14]. Figure 2 shows the brain network template where one color in the composite maps represents an intrinsic connectivity network in each subplot.

Experimental results for the FCPs are shown in Figure 3. In the plot, we plot our 5 estimated components and marked the associated T values. From the figure, we see the evidence of considerable modularity in the results, suggesting structured changes with age. The FCPs for components 2 and 4 have the highest positive (component 2) and negative (component 4) T-values. Here the T-value tells us the degree to which each FCP is expressed in the data (either positively or negatively).

A high negative (positive) value of T represents increased (decreased) expression of the given FCP with age.
In the figure, we see that component 4 has the largest negative T value of -14.02 meaning this FCP is strongly (negatively) expressed in the data. In the plot, visual domain (VSN)-sensorimotor domain (SMN) and cerebellar domain (CBN)-sub cortical domain (SCN) exhibit the largest negative values, which implies increasing brain functional coupling over the two-year period. In addition, VSN-CBN and SMN-SCN domains show decreasing change patterns with age.

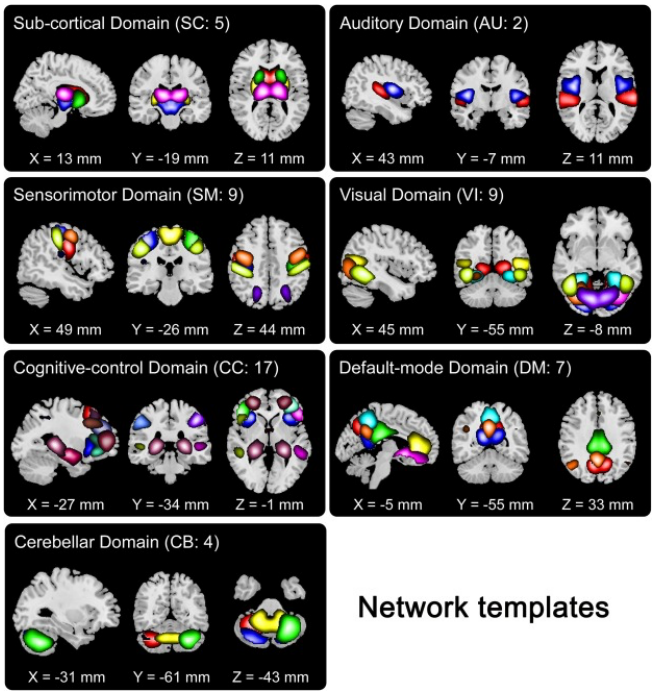

Figure 2: Visualization of Neuromark network template [14]

For component 2, we observe decreasing functional connectivity coupling between default mode domain (DMN) and SMN with age. The associated T-value (of 11.47) is positive for component 2 meaning this FCP is strongly (positively) expressed in the data. We also see increased functional coupling between the CBN and DMN regions over the two-year period.

We plotted the loading scores using a raincloud plot to show the distribution of data, and their relationship to one another at a glance via medians and confidence intervals. From figure 4, we see that the variance of loading parameter is higher for component 4, and it also shows a (significantly) negative mean value.

Finally, we also performed a two-sample t-test on each loading parameters using sex information. We observed that male and females show negative effects on component 4 and 5, with the directionality being the opposite (males show smaller FCP changes for component 4 and females show smaller FCP changes for component 5).

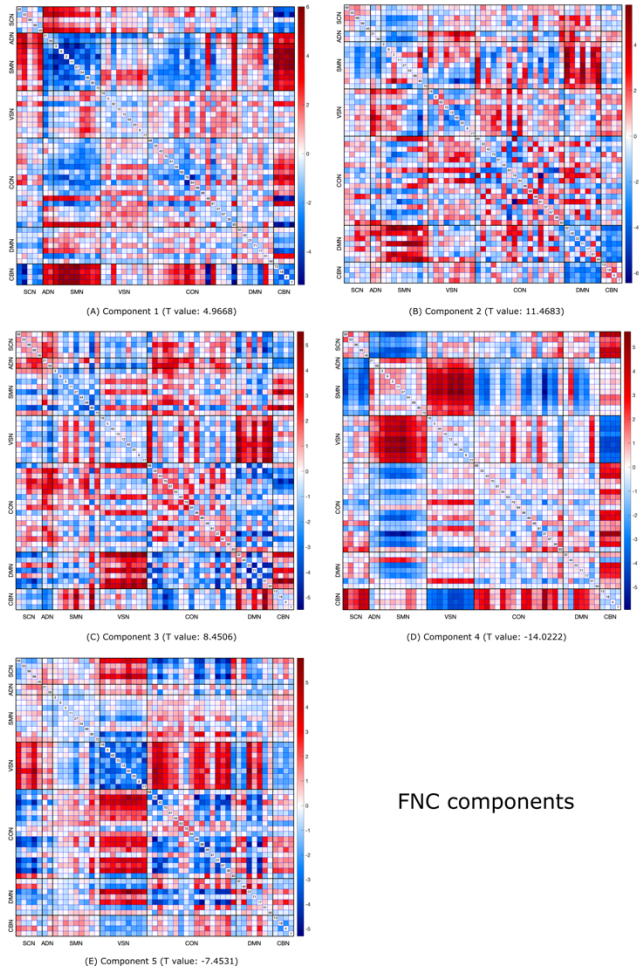

Figure 3: FNC component plot. In the figure, we observe the FCPs for components 2 and 4 have the highest positive (component 2) and negative (component 4) T-values.

4. DISCUSSION AND CONCLUSION

In this paper, we introduce a novel approach to compute multiple overlapping brain functional change patterns using FNC matrices. We take delta FNC matrix to show brain functional connectivity change with age. Our findings show that several FCPs showing a significant change over a two-year period and stronger functional connectivity coupling between the VSN and SMN domains and decreasing anticorrelation between sensorimotor and cognitive/default mode network domains with increasing age. We also find both shared and distinct brain functional pattern changes between male and female where male and female exhibit negative effects on component 4 and 5 with the opposite directionality. Our approach shows promise to be a powerful

tool to evaluate whole brain functional changes longitudinal studies

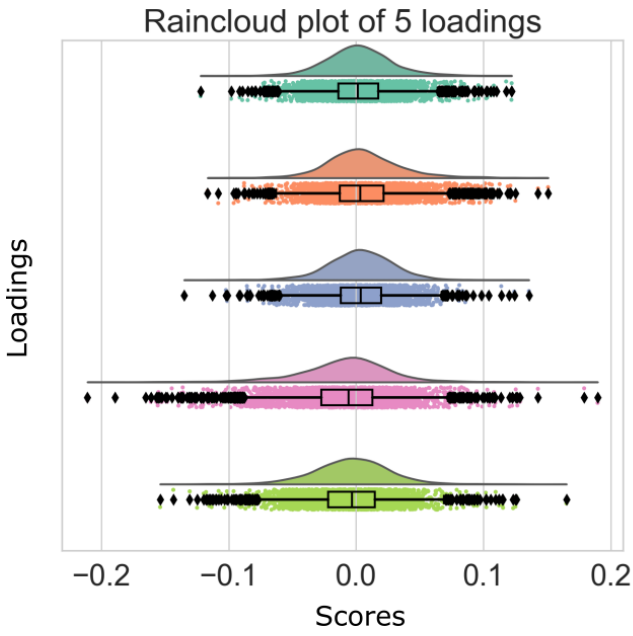

Figure 4: Scatter plot of loadings parameters. In Y axis, we present five loading and in X axis, we present the scores of the corresponding loadings.

5. ACKNOWLEDGMENTS

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