Prediction of Age Using Resting-State Functional and Effective Connectivity

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INTRODUCTION In combination with multivariate pattern analysis algorithms such as Support Vector Machines (SVM) [1] or Support Vector Regression (SVR) [2], functional connectivity offers a powerful tool for brain classification. With this approach, several groups have successfully identified and predicted brain characteristics using resting-state MRI data [3-5]. Specifically, Dosenbach et al. have recently reported high prediction accuracy of brain maturity [3]. However, temporal correlations (CORR) alone do not contain information about the directional or causal influences that brain regions exert over one another (effective connectivity). Including such information may allow for greater prediction accuracy and sensitivity than is possible with functional connectivity alone. Using subjects with a broader age range than those used by Dosenbach et al., here we use Correlation-Purged Granger Causality (CPGC) [6] to calculate effective connectivity, and then compare the age prediction accuracy between CORR and CPGC features in SVM and SVR.

METHODS Resting-state fMRI data (1.5T SonataVision Siemens scanner, TR=2s, Matrix=64x64, nSlices=23 Axial, nTimePoints=128) for 51 subjects (29F22M, ages: 19-85, mean=45.1) were obtained from the International Consortium for Brain Mapping [7]. All scans were corrected for slice timing and motion effects, spatially smoothed (Gaussian kernel, FWHM=5mm) and spatially normalized into the standard MNI space. The head motion parameters and cerebrospinal fluid signal were regressed out, temporal signal fluctuations were scaled to the same range across subjects, and the data were band pass filtered between 0.009Hz and 0.08Hz. Following these pre-processes, BOLD signal time series were extracted from 142 cerebral regions of interest as defined in [3], and then fed into both pair-wise Pearson correlation and CPGC analysis [6]. The resulting 10011 CORR and 20022 CPGC coefficients were the “features” used for SVM age group classification of old (N=16, age>=60 yrs.) vs. young (N=19, age<=30 yrs.), and SVR age prediction (all 51 subjects). SVM and SVR were implemented using the Spider Machine Learning Library [8] for MATLAB. As in [3], a group t-test identified the 200 most reliably different features between young and old and these features were used for group classification in SVM. Similarly, the 200 features with the highest correlation between feature value and chronological age were used for age prediction in SVR. Both the SVM and SVR were conducted using “leave one out” cross validation with model parameters identical to those in [3].

RESULTS Group classification (young vs. old) with SVM was highly accurate for both CORR (97%) and CPGC (100%) when using the top 200 features as described above. Age prediction using SVR also performed well, with the top 200 features yielding correlation coefficients of r=0.88 (CORR) and r=0.95 (CPGC) between real and predicted age. Figure 1 shows predicted age vs. actual age for CPGC (left) and CORR (right).

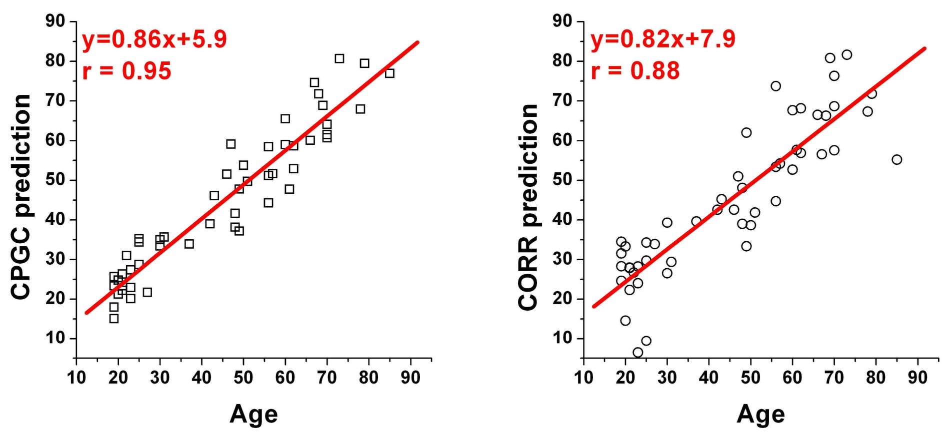

Figure 1. Actual and SVR-predicted ages based on CPGC (left) and CORR (right). CPGC-based SVR provides higher accuracy.

DISCUSSION SVM and SVR prediction of age using CORR alone has recently been applied to developing subjects of ages 7–30 years [3]. Our results build on this work in two ways. First, we have shown that SVM and SVR based on CPGC (effective connectivity) offers improved performance compared to that based on CORR (functional connectivity). This could be because the direction-of-influence information provided by CPGC possesses more power in characterizing the development of neural networks than undirected correlation does. Second, our preliminary data show that these techniques work over the whole range of adulthood with important connectivity changes in prefrontal-parietal and prefrontal-subcortical networks.

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