

Motor cortex functional connectivity signatures of autism

Mary Beth Nebel^{1,2}, Ani Eloyan³, Anita Barber^{1,2}, Brian Caffo³, James Pekar^{1,2}, and Stewart Mostofsky^{1,2}

¹Kennedy Krieger Institute, Baltimore, MD, United States, ²Johns Hopkins School of Medicine, Baltimore, MD, United States, ³Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States

Introduction: Motor impairments are prevalent in children with autism spectrum disorders (ASD), relate to the communicative/social deficits at the core of their diagnosis, and may reflect abnormal connectivity within brain networks underlying motor control and learning. Resting state (rs) functional connectivity (FC) analysis is a potentially powerful tool to estimate brain organization within clinical populations like ASD but also poses challenges for quantitative image analysis, mainly related to the comparison of noisy signals from a large number of sources. Recently, several groups have proposed parceling the brain prior to FC analysis to reduce the dimensionality of the data and to enable rapid calculation of inter-parcel FC signatures for individual subjects.¹⁻³ Motivated by these potentially scalable methods to investigate brain organization, the aim of this study was to estimate how well FC between subregions of the motor cortex (M1) discriminate individuals with ASD from typically developing (TD) participants using a large, heterogeneous sample of resting state data.

Methods: rs fMRI and anatomical images from the Autism Brain Imaging Data Exchange (ABIDE) were used (539 ASD and 573 TD). Gender, age and full-scale intelligence quotient (FIQ) data for the ABIDE sample are shown in Fig 1. Analyses were limited to data from males between 6 and 40 years of age with an FIQ of at least 80 and whose data were collected from ABIDE-contributing sites that provided information regarding slice

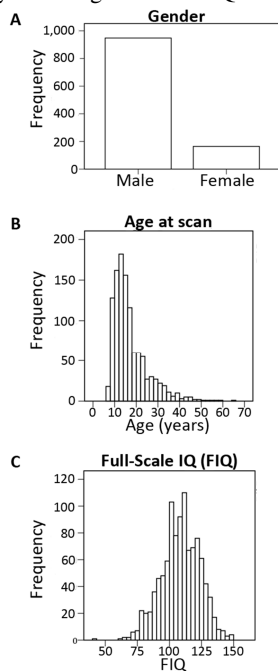


Fig 1. Demographic characteristics of the ABIDE sample including A) gender, B) age at the time of image collection, and C) full-scale IQ.

acquisition order (368 ASD and 412 TD). Image processing was performed using SPM8 and custom MATLAB scripts run on a high performance computing system. Anatomical images were registered to the first functional volume and normalized to MNI space using unified segmentation (SPM8). Functional data were adjusted for slice acquisition order and participant motion and were then transformed to MNI space. Nuisance covariates from white matter and CSF were estimated using CompCor⁴ and regressed from the data along with motion estimates, their derivatives, global mean signal, and linear trends. Data were then spatially smoothed (6-mm kernel) and band-pass filtered (.01-0.1 Hz).

The five-region M1 parcellation used to estimate FC signatures for each subject was derived from test-retest rs data collected from an independent sample of 20 neurotypical adults and reflects the general organization of the motor homunculus.⁶ For each subject, correlations between the 10 pairs of mean parcel time courses were computed. Group differences were assessed using a multinomial logistic regression model. Demographic factors and M1 correlations were used as predictors, disease status as the outcome. Two image quality measures were also included as predictors: 1) framewise displacement (FD), a measure of between-volume motion,⁵ and 2) the spatial correlation between each subject's MNI-registered data and SPM's EPI template to assess the influence of variability in the consistency of spatial normalization across subjects. To account for possible confounds among the many variables, generalized boosted methods were used to estimate model parameters.

Results and Discussion: Preliminary analysis suggests that FIQ had a high relative influence in predicting disease status (35%) when all demographic variables and M1 parcel correlations were included. The correlation of the dorsomedial-most (DM) region, normally reserved for lower limb/trunk control, and the posterior lateral (PL) region (near the hand area) had the second highest relative influence in the prediction model (24.6%). The third most influential factor also involved PL FC, but with the dorsolateral (DL)/upper limb region.

Conclusion: We identified potentially predictive FC signatures of ASD. FC disruptions between the DM/DL regions and the brain outside of M1 have been previously implicated in ASD⁶. Here, we showed that FC between these regions and other parts of M1 (PL) may also be abnormal, and these FC differences within M1 are consistent with deficits in complex multi-joint coordination that are associated with ASD.

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