Machine Learning Approaches to Brain Connectivity in Autism

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Autism spectrum disorder (ASD) is a neurodevelopmental condition affecting many areas of life. Resting-state functional MRI (rs-fMRI) measures functional connectivity between brain regions and may provide a biological perspective to complement behavioral assessment. This project investigated whether individuals with ASD exhibit altered brain connectivity and whether these differences can be detected above chance using machine learning. We analyzed ABIDE rs-fMRI data from 679 males ages 5-30 (319 ASD, 360 controls) across 24 sites. Functional connectivity was computed among 200 brain regions, yielding 19,900 features per participant. Group-average heatmaps showed slightly weaker and distributed connectivity in ASD. PCA and UMAP revealed stronger clustering by site than by diagnosis. Site confounds were quantified by a site-classification model (accuracy=0.831; macro-F1=0.780) and per-edge variance explained, with site effects exceeding diagnosis effects across essentially all edges (median ?²(site)=0.0915 vs median ?²(dx)=0.0027). A logistic regression classifier evaluated with leave-one-site-out validation achieved mean accuracy of 0.700, with aggregated accuracy 0.675, balanced accuracy 0.674, and ROC-AUC 0.738. A 1,000-iteration permutation test confirmed the LOSO result was unlikely by chance (z=4.57, p=0.001). Model interpretation showed distributed predictive signal, with the strongest network-level interactions centered on limbic connections with somatomotor, attention/control, and default mode networks, supporting ASD-related differences in emotion regulation, sensory-motor processing, and attentional shifting. These results support subtle ASD-related connectivity differences while showing site effects remain a major barrier to reliable clinical prediction.

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