Resting-state functional connectivity differences in memory networks of autism spectrum disorder

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Background

Autism spectrum disorder (ASD) is traditionally characterized by impaired social interaction/ communication, and restricted and repetitive behaviors. Recent studies employing resting-state fMRI (rs-fMRI) have further shown that ASD can be associated with differences in brain functional connectivity.[1,2]

Individuals with ASD also exhibit a variety of long-term memory impairments. The specific nature of these impairments is becoming increasingly clear, with some findings demonstrating that episodic memory is affected more than semantic memory,[3] and other studies narrowing down the episodic retrieval deficits to recollection (as opposed to familiarity).[4]

Given that a network of posterior medial and anterior temporal brain regions—collectively, the **PMAT network**—has been proposed to differentially support the content and quality of episodic versus semantic memory,[5] understanding altered connectivity within this network may help to further elucidate the nature of memory deficits in ASD.

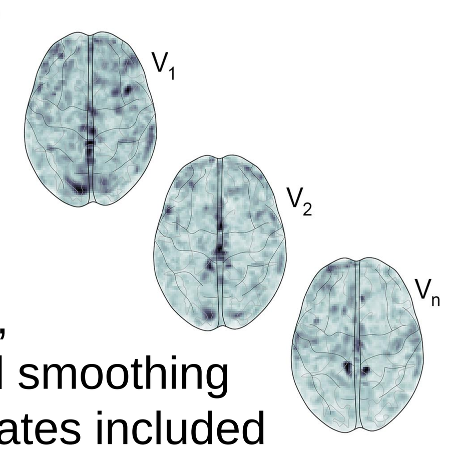
Here, we used rs-fMRI data to identify differences in functional connectivity within the PMAT network for individuals with ASD and matched controls. A multivariate pattern analysis (MVPA) approach was then used to classify individuals from the two groups, revealing that connectivity within the posterior medial (PM) sub-network was particularly informative to diagnosis.

Methods

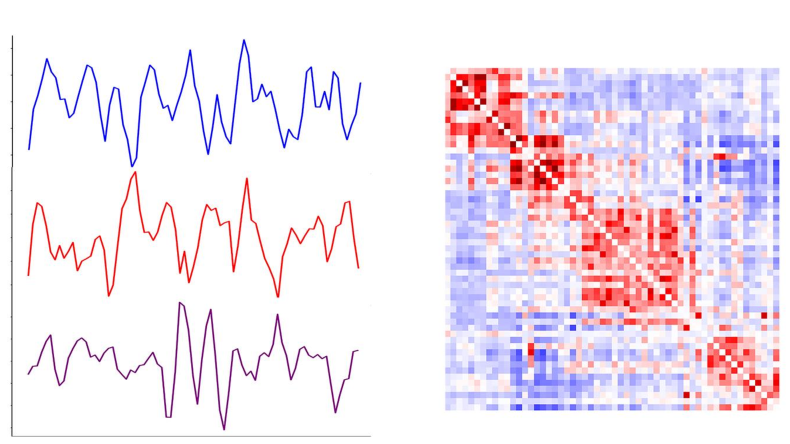
57 subjects (24 ASD, 33 controls)

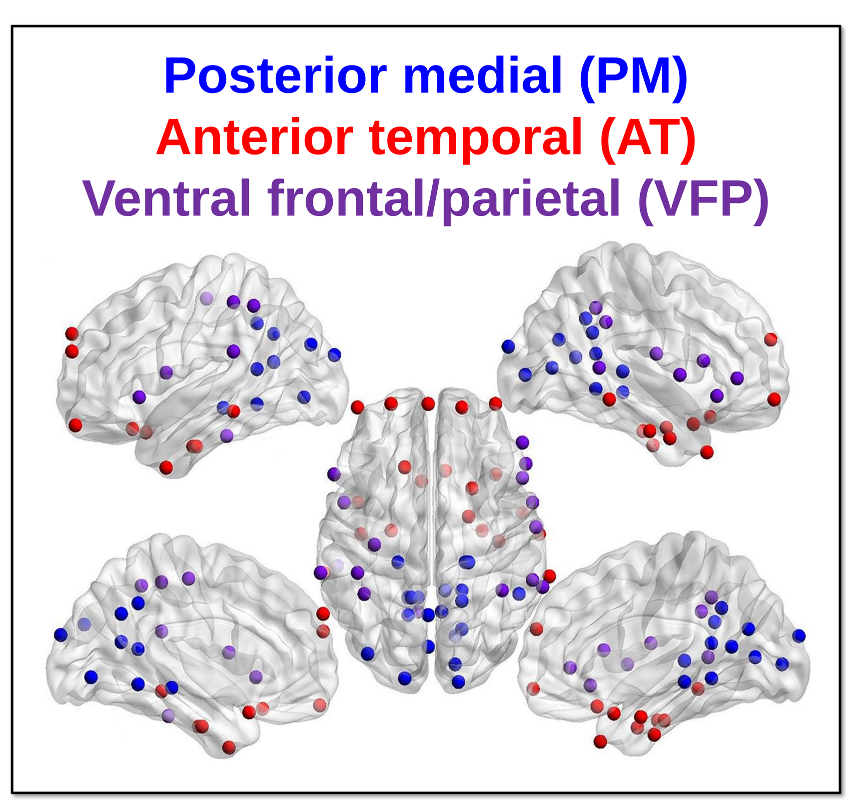
344 subjects (164 ASD, 180 controls)

- *rs-f*MRI data were obtained from subjects with/without ASD at MU and from ABIDE I/II.[6]
- Preprocessing largely followed the Human Connectome Project (HCP) pipeline, using a combination of *FSL*, *AFNI*, and *ANTs* within the *nipype* module (in Python v.3.6.1).
  - **Structural:** bias field correction, skull-stripping, CSF/WM/GM segmentation, and registration.
  - **Functional:** motion censoring (>0.2 mm FD), motion correction, slice-timing correction, co-registration and normalization, spatial smoothing (6-mm FWHM), and band-pass filtering (0.01<*f*<0.1 Hz). Covariates included motion parameters, global signal, and ventricle/WM signals (plus derivatives).

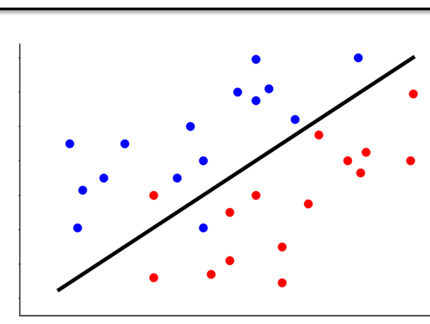


- 56 6-mm spherical ROIs were defined using MNI coordinates of the PMAT framework.[7]
- Functional connectivity matrices for each subject were constructed by correlating the time series of each ROI pair (Pearson's *r*, *z*-transformed).



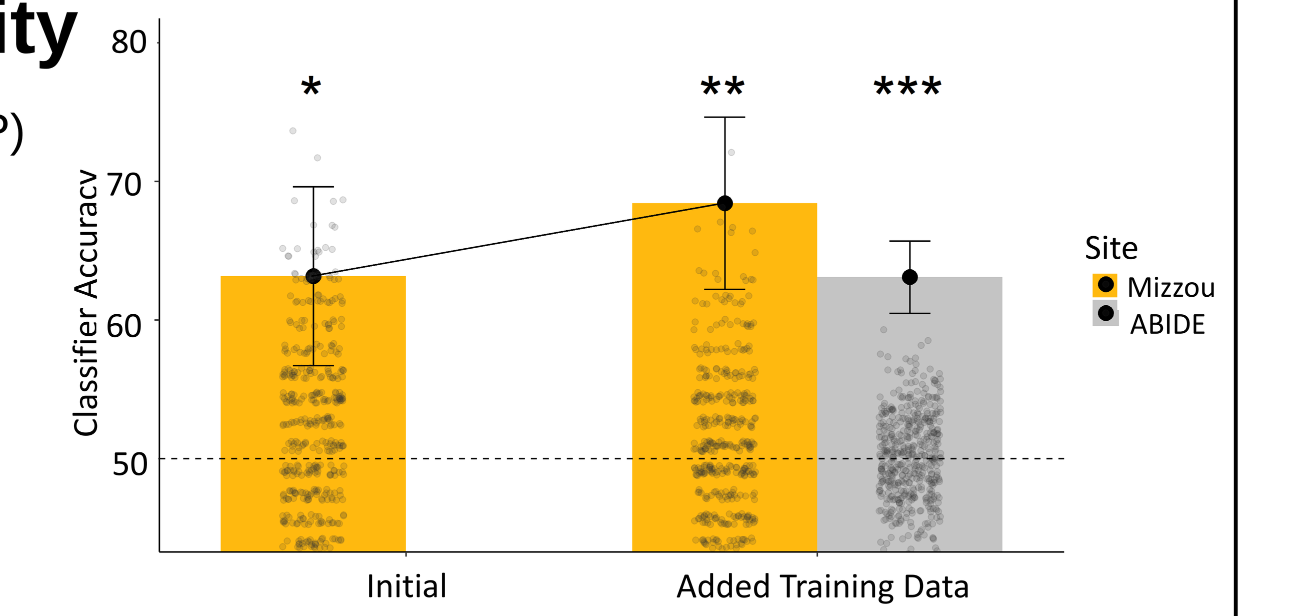


- Multivariate pattern analysis (MVPA; *nilearn*/*scikit-learn*) was used to classify **ASD vs. control** using FC values as input features. Logistic regression models (L_2 penalty = 0.1) were built and cross-validated (10-fold), and feature selection (*top F-values*) was implemented within each fold of training data.



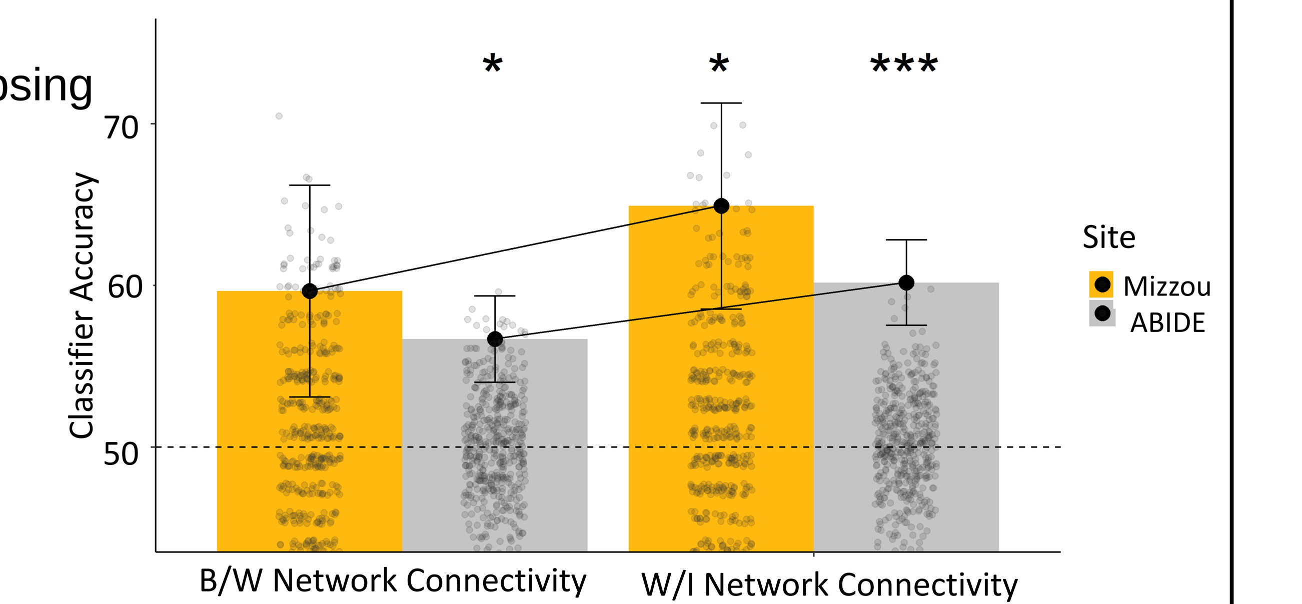
Overall memory network (PMAT) connectivity

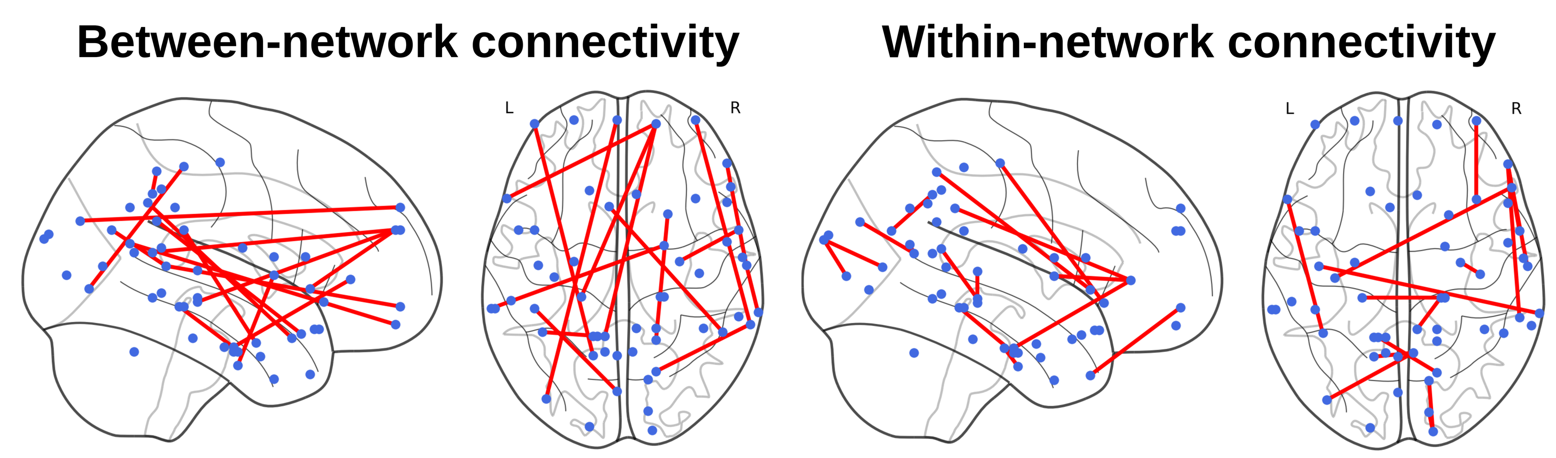
- ASD vs. control classification of the MU data, based on all PMAT (and VFP) ROIs, was **63.2%** and significantly above chance performance (50%; permutation-based p < .05).
- Adding the ABIDE data at the classifier training stage improved overall accuracy to **68.4%** (p < .01). Figures to the right show mean classification accuracy along with individual permutation test scores.



Within vs. between PMAT sub-network connectivity

- Based solely on connectivity between sub-networks of the PMAT(i.e. collapsing classifier accuracy was not significantly above chance for the MU dataset (**59.7%**, p > .05) but was for the ABIDE dataset (**56.7%**, p < .05).
- When considering connectivity within the PMAT sub-networks, accuracy improved to above-chance levels for both the MU (**64.9%**, p < .05) and ABIDE data (**60.2%**, p < .001).



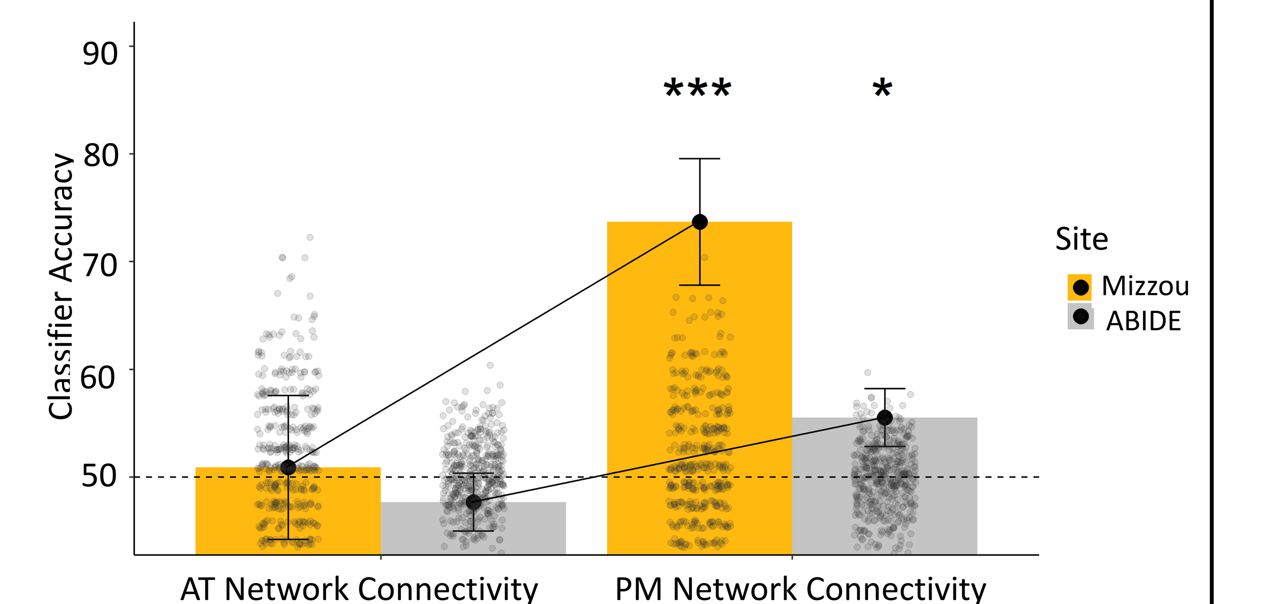


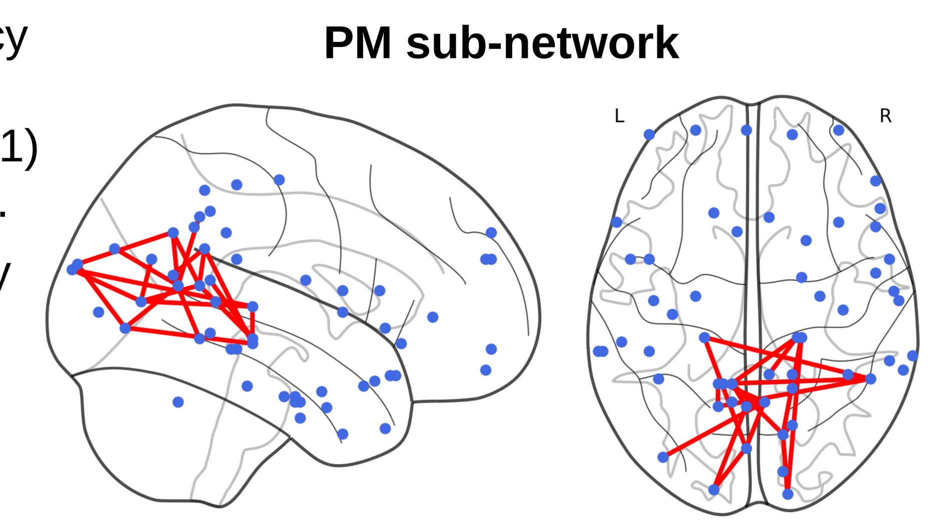
Top features: post. mid. temporal, ant. inf. temporal, precuneus, orbitofrontal, sup. temporal, inf. frontal, angular gyrus, retrosplenial, dorsolateral PFC, post. hippocampus, med. PFC

Top features: precuneus, med. occipital, fusiform, post. hippocampus, mid. temporal, retrosplenial, inf. frontal, temporoparietal junction, angular gyrus, ant. inf. temporal

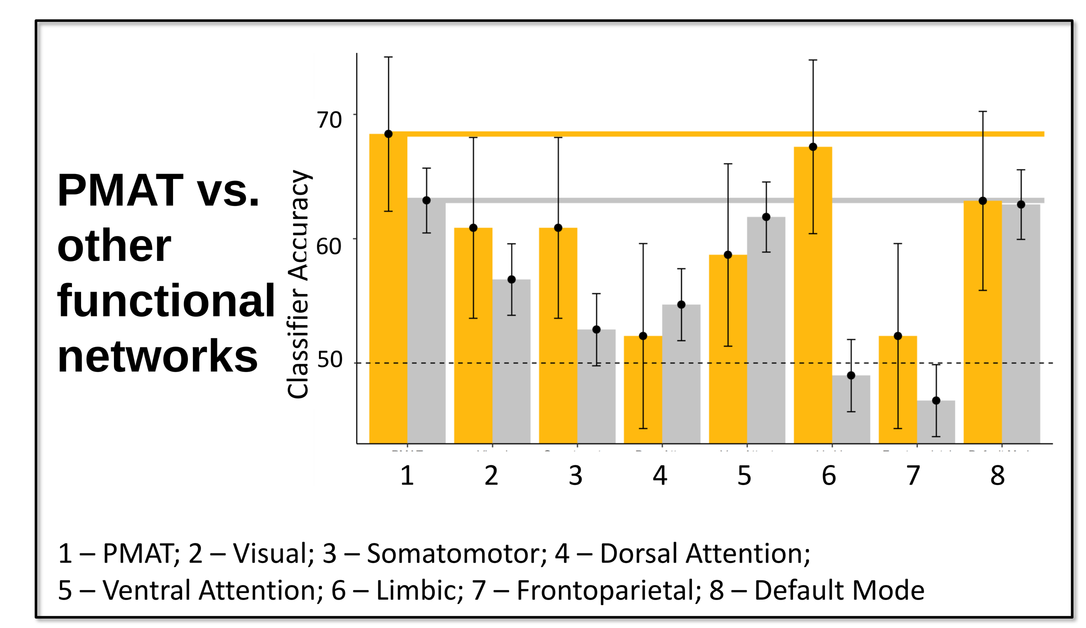
Connectivity within PMAT sub-networks

- For the PM sub-network, accuracy was significantly above chance with both the MU (**73.7%**, p < .001) and ABIDE data (**55.5%**, p < .05).
- For the AT sub-network, accuracy was at chance in both cases (MU: **50.9%**, p > .05; ABIDE: **47.7%**, p > .05).





Top features: occipital, med. occipital, precuneus, retrosplenial, angular gyrus



Summary & conclusions

- The memory-centric PMAT network[5] exhibits differences in intrinsic functional connectivity (via rs-fMRI) that may be informative about ASD diagnosis.
- The enhanced classification performance of the posterior-medial (PM) sub-network help guide our focus of memory deficits in ASD toward those that are episodic (spatiotemporal/contextual) as opposed to semantic (conceptual) in nature.[4,7]
- The PMAT-based classifier appears to perform as well as, and sometimes better than, traditional rs-fMRI networks that span the whole brain.

References

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