# Linking functional connectivity to symptoms of borderline personality disorder in youth

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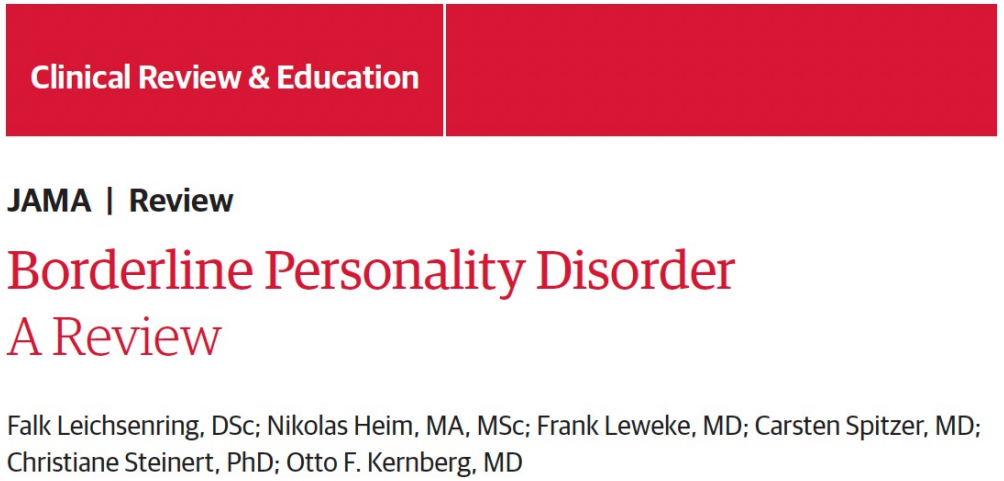
Internal Journal Club

June 20, 2023

Penn University of Pennsylvania

# Borderline Personality Disorder




- Borderline personality disorder (BPD) affects approximately **0.7% to 2.7% of adults in the US**.
- The disorder is associated with considerable **social and vocational impairments** and greater use of medical services.
- BPD is characterized by impulsivity, suicidality, self-harm, feelings of emptiness, intense anxiety and stress, and dissociative symptoms.
- BPD is also associated with disproportionately high rates of death by suicide (4% average rate) compared to other mental illness.
- **Psychotherapy** is the **treatment of choice for BPD** and reduces symptom severity more than usual care.
- **Psychoactive medications** do not improve the primary symptoms of BPD.

Leichsenring et al., 2023, *JAMA*

# Neurobiology of BPD

- Most diagnoses are made during late adolescence or early adulthood (at least 18 years old).
- Recognizable symptoms and traits of BPD manifest during adolescence (as early as at 12 years old).
- An **empirically supported model** of the **neurobiology of BPD** remains elusive.

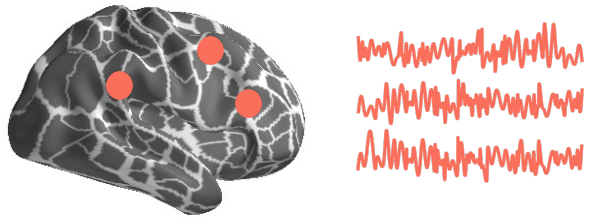

Leichsenring et al., 2023, *JAMA*

# Brain as a Complex Network

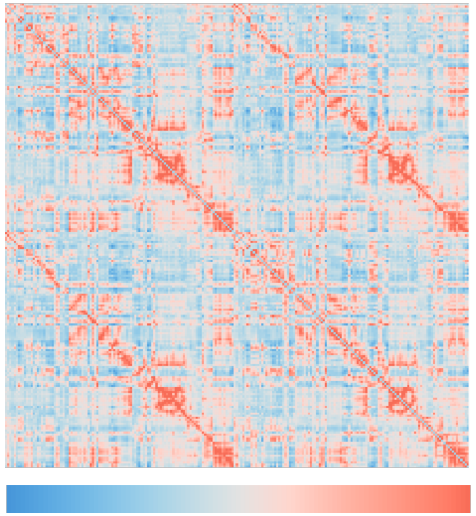
# Intrinsic Activity and Functional Connectivity

- Using neuroimaging techniques to quantify functional interactions between brain regions.
- Fundamentally shape the development and function of the brain, eventually manifesting as inter-individual variations in behavior and cognition.

functional imaging & time series

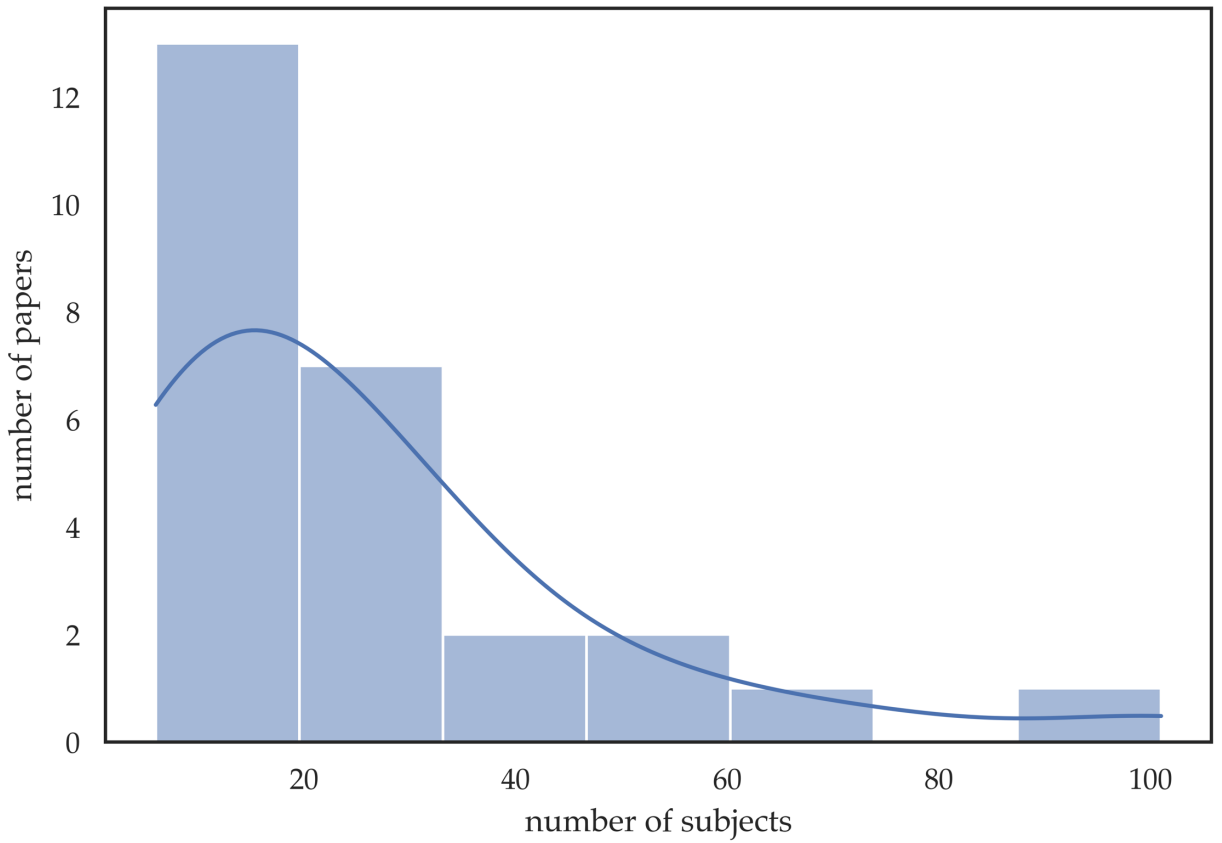


functional connectivity



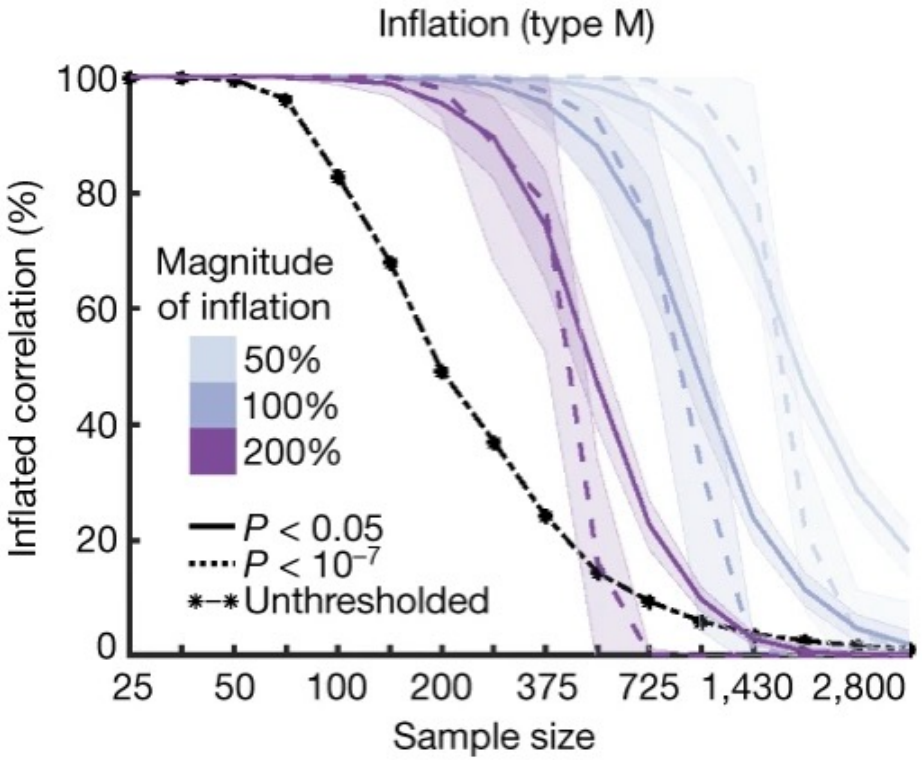
# Neuroimaging Studies of BPD

- There are not many neuroimaging studies of BPD available in the literature.
- Translational studies of BPD have small sample sizes.



# Brain-wide association studies require large samples

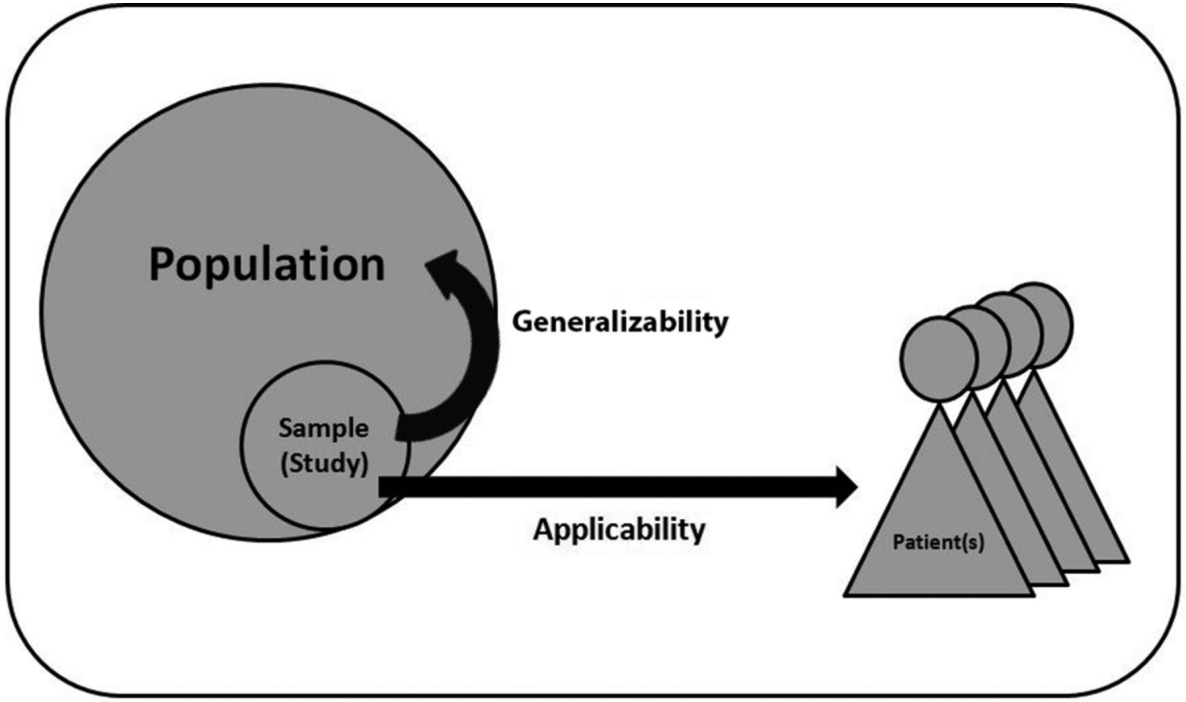
- Small samples produce inflated results by overfitting to data.
- Results are not reproducible: inconsistent findings, sometimes even contradictory.




Marek et al., 2022, *Nature*

# What is the solution?

- Rigorous Type I Error Correction:
  - **Large** sample size
  - **Multiple** datasets
  - Testing the models on **unseen** data
  - **Multivariate** analysis
  - **Cross-Validation (CV)** analysis



# Reliable and Validated Measure of BPD

- **Explicit BPD measures** are designed for specialized studies with **small sample size** and are not available in large-scale neruoimaging studies.
- We use a **validated measure of BPD liability for large-scale studies** (validated on 6 datasets)
- Calculates a BPD proxy score from a **widely-used personality instrument** (NEO-FFI)
- Not designed to explicitly assess diagnostic BPD symptoms, but rather variation in general personality traits associated with increased liability to BPD symptomatology
- Available in **both Human Connectome – Young Adult & Human Connectome – Development**
- Highly correlated with BPD-specific scales ($r$ = 0.89)

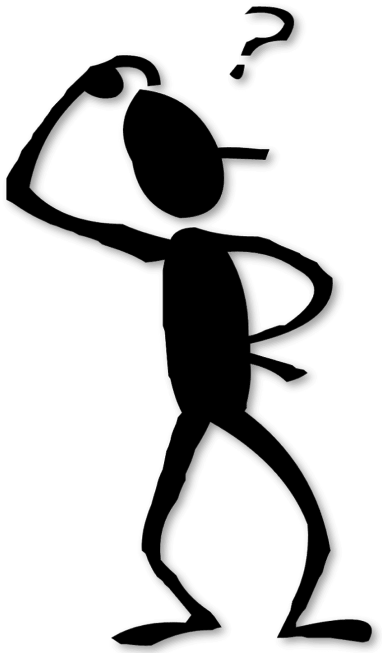
> Psychol Assess. 2016 Jan;28(1):39-50. doi: 10.1037/pas0000142. Epub 2015 May 18.

**Trait-based assessment of borderline personality disorder using the NEO Five-Factor Inventory: Phenotypic and genetic support**

Lauren R Few [1], Joshua D Miller [2], Julia D Grant [1], Jessica Maples [2], Timothy J Trull [3], Elliot C Nelson [1], Thomas F Oltmanns [4], Nicholas G Martin [5], Michael T Lynskey [6], Arpana Agrawal [1]

# Project Goals

- Conduct a **large-scale neuroimaging** analysis on the association between **functional brain networks** and symptoms of **borderline personality disorder**
- Identify **unique patterns of functional interactions** that contribute to BPD symptoms
- **Cross-validated predictive** analysis using 2 **large datasets** (young adults and development)
- **Validated** trait-based measure of **BPD liability**
- High-quality **data curation** and **preprocessing**



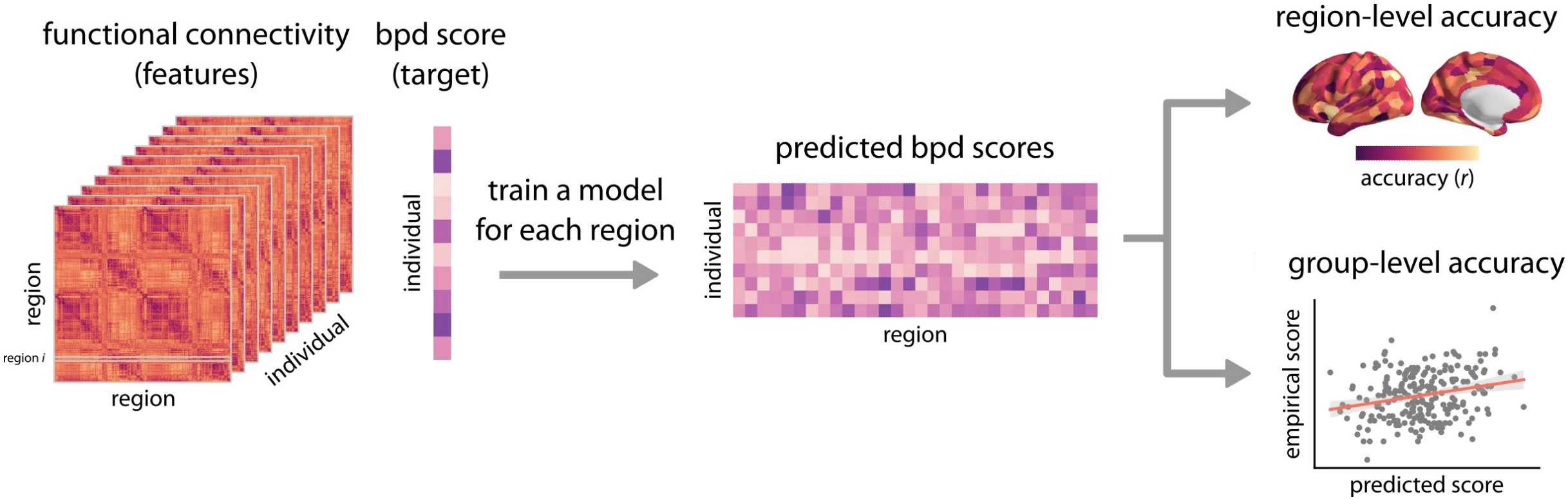
# Data

- **High-quality neuroimaging data:** high resolution; 2 hours of functional MRI
- **High-quality behavioral data:** used to estimate the BPD liability score
- **Human Connectome Project – Young Adult:**
  - N = 870, age range 22-37, 457 female and 413 male
  - All have BPD liability score
- **Human Connectome Project – Development:**
  - N = 610, age range 5.6-21.9, 331 female and 279 male
  - Subset with BPD liability score: N = 223, age range 16-21, 121 female and 102 male


Van Essen et al., 2013, *Neuroimage*

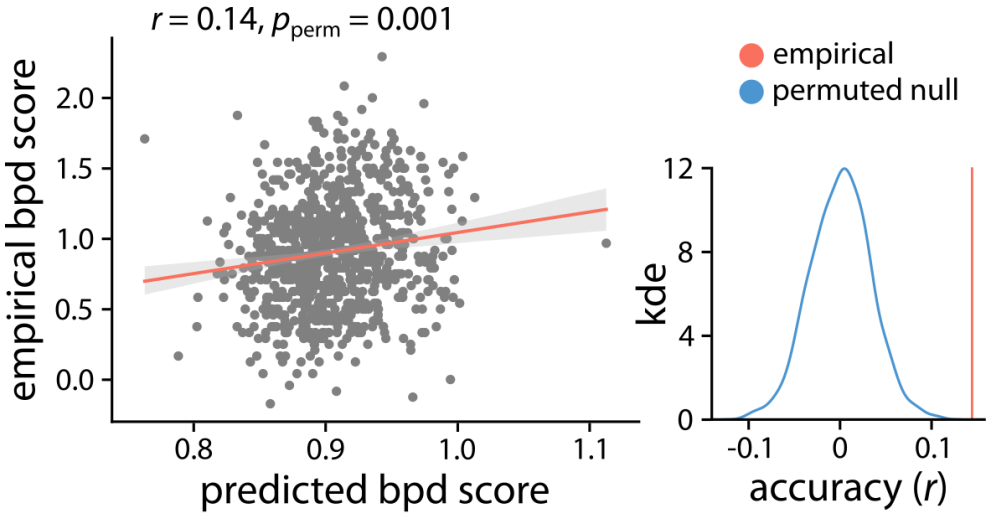
# Predictive Modeling

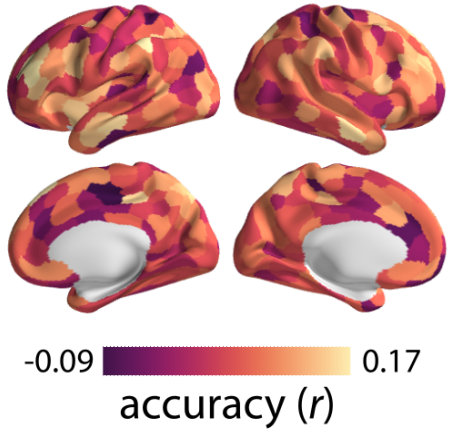
- Cross-validated model trained and tested in unseen data.



# Result: HCP Young Adults

- Functional connectivity significantly predicts BPD liability score in young adults.
- Regional heterogeneity in predictive capacity of functional connectivity profiles.



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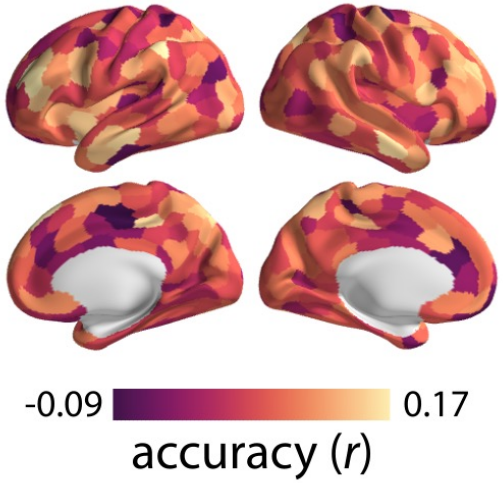
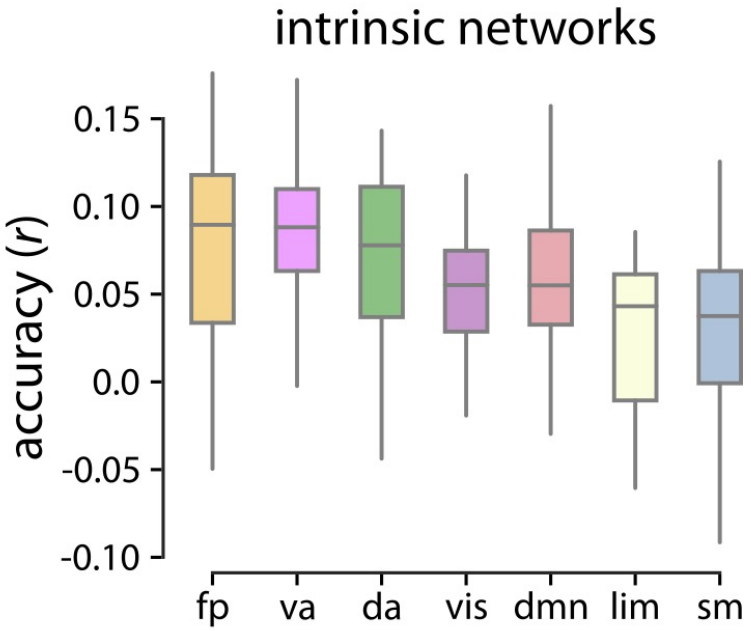
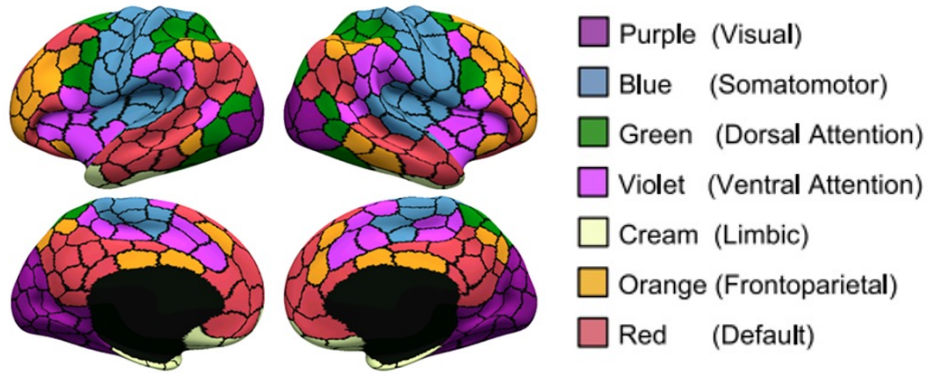
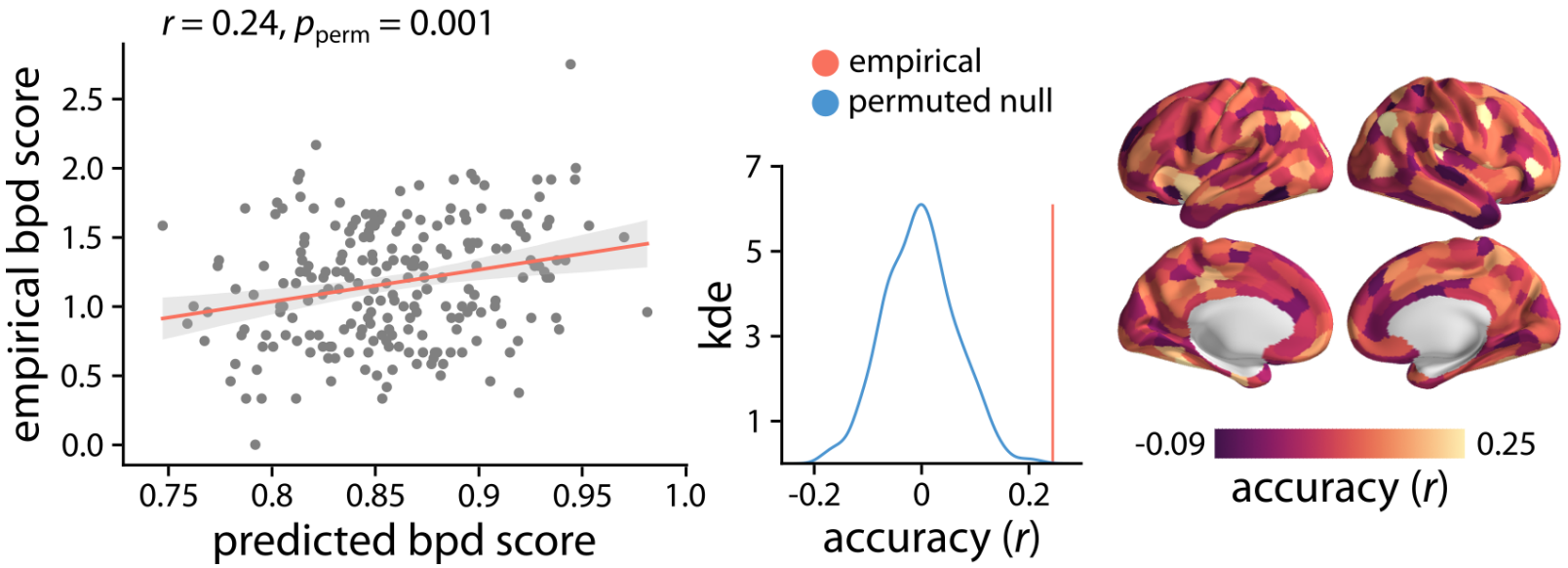


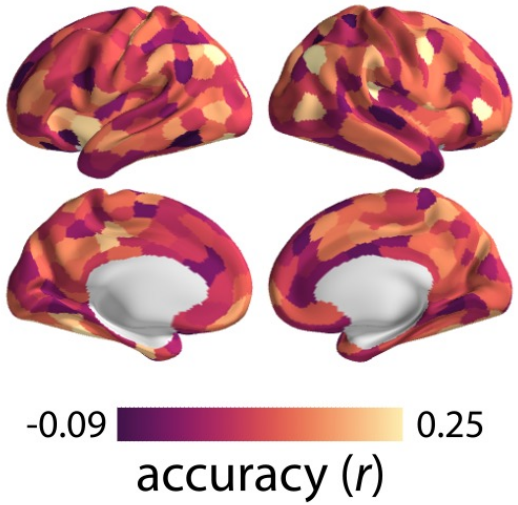
# Result: HCP Development

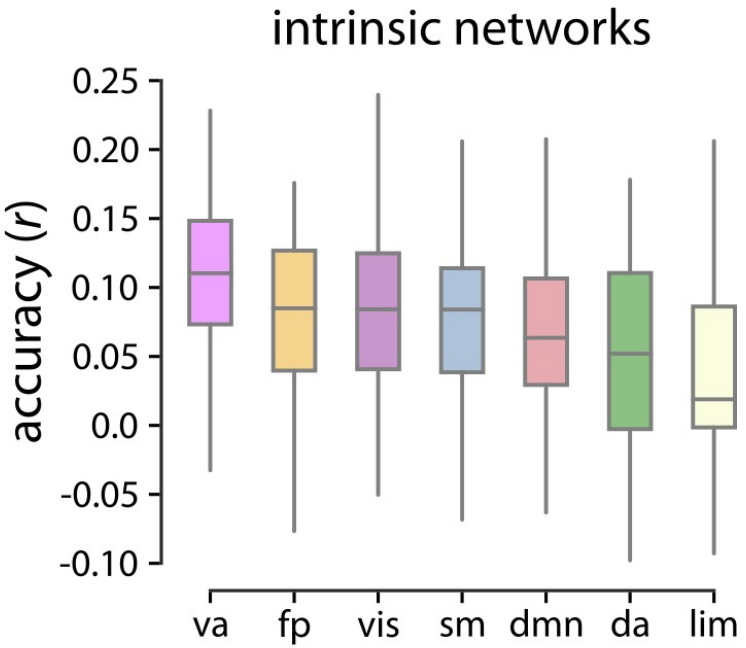
- Functional connectivity significantly predicts BPD liability score in **youth** in a separate, **unseen dataset**.

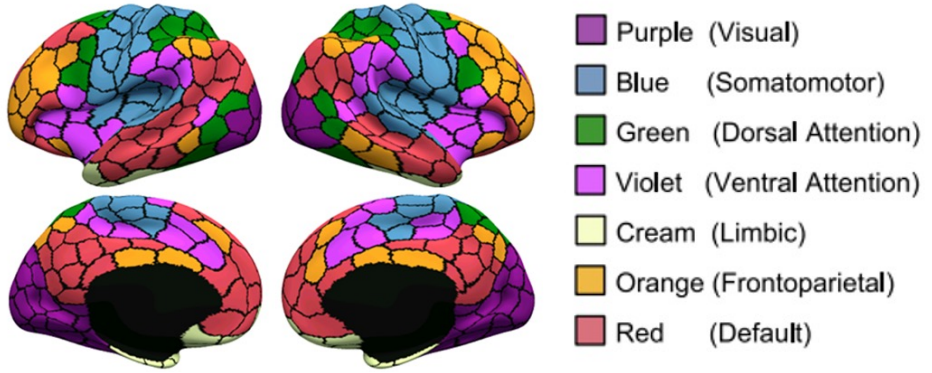


# Result: HCP Development

- Functional connectivity significantly predicts BPD liability score in youth in a separate, unseen dataset.
- Highest contribution from ventral attention and frontoparietal networks.



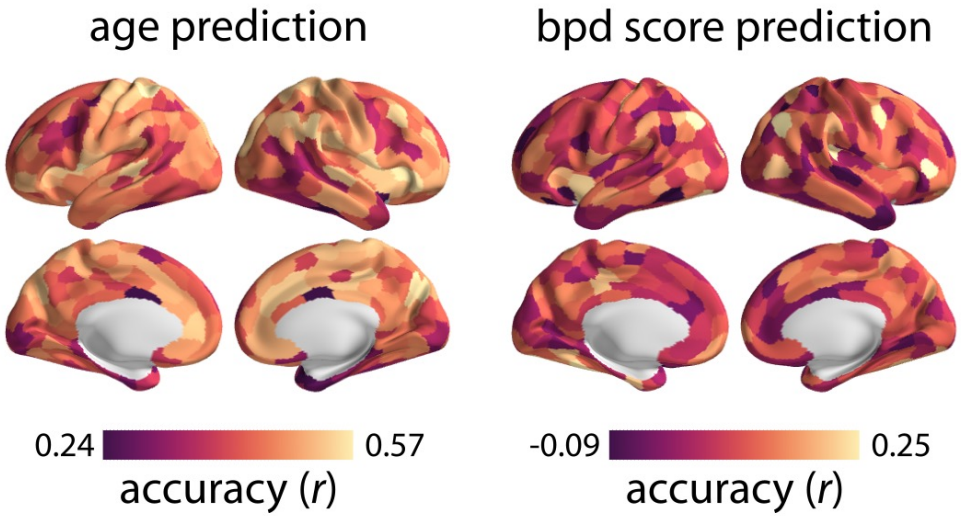



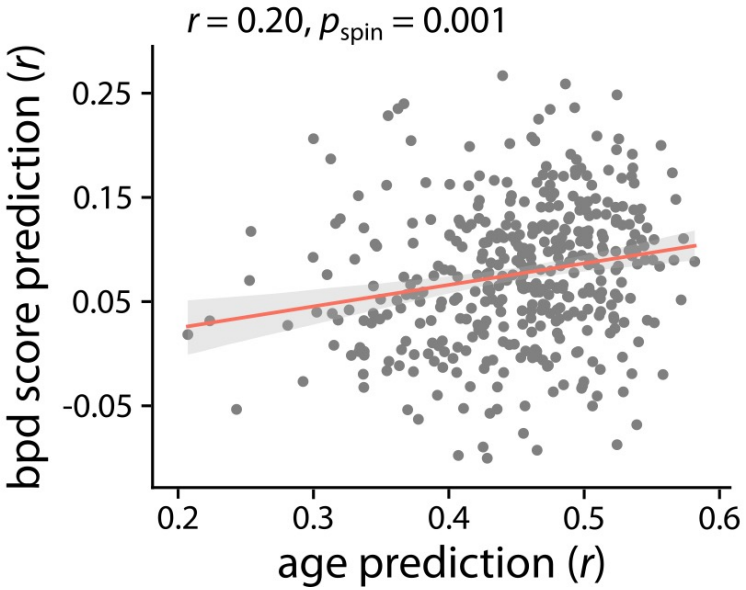
# Result: Developmental Changes in Connectivity

- Regional predictive capacity is associated with developmental changes in functional connectivity.
- Regions that are highly predictive of BPD symptoms are also affected most during development.

a | Age prediction in HCP-D




b | Age *vs* BPD score prediction



# Summary

- Functional connectivity **significantly predicts** BPD liability score in **unseen data** from both **adults (HCP-YA)** and **adolescents (HCP-D).**
- **Heterogenous predictive capacity** of brain regions: **localized and specialized** effects
- **Highest contributions** from functional systems responsible for **emotion regulation** and **executive function**.
- **Functional connectivity** patterns of **regions** that **undergo the most development in youth** highly contribute to prediction of BPD liability score.

# Significance

- **Largest study** of **functional connectivity** linked to symptoms of **borderline personality disorder (BPD).**
- Provides insight into understanding **BPD as a neurodevelopmental disorder**.