Modeling EEG Data at Increased Granularity in Autism Applications

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Outline

Introduction: EEG in Autism Studies

Analysis of EEG in the Time Domain (FDA)

- Dimension Reduction Techniques for High-dimensional EEG data
- Within-subject Response Variability

Analysis of EEG in the Frequency Domain

- Day-to-day Reliability of PSD (FDA)
- Synchronicity of PSD Across Electrodes (non-Euclidean)
- Contrastive Analysis of PSD: Wasserstein Boxplots (non-Euclidean)

Discussion

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Autism

- Autism (ASD) is an early-onset neurodevelopmental condition
  - Greater difficulties with social interaction and communication
  - More restricted and repetitive pattern of behaviors
  - Atypical response to sensory information
- As of 2025, the prevalence of autism in the U.S. is estimated to be 1 in 31 children (nearly 4 times more common among boys than among girls)
- To date, there are no established pharmacological treatments for the core symptoms of autism
- ASD is highly heterogeneous where individuals vary considerably in phenotype
- This heterogeneity limits the utility of one-size-fits-all treatment strategies and creates a critical need for biomarkers that can identify more homogeneous subgroups

EEG in Autism Studies

- EEG is a noninvasive and widely available modality that provides a unique opportunity to capture real-time neural functioning including measures of attentional and social-cognitive processes in autistic individuals
- It is the recording of electrical activity from electrodes placed on the scalp
- It measures voltage fluctuations resulting from ionic current flows within populations of neurons in the brain
- EEG well-suited for studying heterogeneity: EEG biomarkers can help identify subgroups of autistic individuals with more homogeneous neural response patterns
- Such neurobiologically informed subgroups may clarify variation in clinical presentation and support the development of more targeted interventions

Common Theme: Modeling EEG Data at Increased Granularity

Data reduction leads to loss of information

- Time domain analysis in stimulus-based paradigms
  - ERP signal averaged across trials
  - Collapsed across ERP time into numeric summaries
- Frequency domain analysis in resting state
  - Averaged across time
  - Scalp regions
  - Collapsed across frequency into numeric summaries
  - Within-group analysis (without a reference group)

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Analysis of EEG in the Time Domain (FDA)

Dimension Reduction Techniques for High-dimensional EEG data

Analysis of EEG from Stimulus-based Tasks in the Time Domain

- Traditional analysis considers summaries of the data in the time domain (after averaging across trials): e.g., latency and amplitude of ERP components
- Our group at UCLA made contributions to modeling of the entire ERP waveform (EEG response to presentation of each stimulus)
- Functional decomposition of the high-dimensional ERP signal across ERP time, experimental time, scalp regions, tasks and longitudinal visits
  - Hasenstab et al. (2015): Identifying longitudinal trends within EEG experiments
  - Hasenstab et al. (2017): A multidimensional FPCA of EEG data
  - Scheffler et al. (2020): Hybrid principle components analysis (HPCA) for region-referenced longitudinal functional EEG data
  - Campos et al. (2020): Principle ERP reduction and analysis
  - Campos et al. (2022): Multilevel HPCA
  - Scheffler et al. (2022): Covariate-adjusted HPCA
  - Boland et al. (2022): Longitudinal trends in TF transformations of EEG data
  - Dong et al. (2025): Multilevel multivariate FPCA of evoked and induced event-related spectral perturbations

Analysis of EEG in the Time Domain (FDA)

Within-subject Response Variability

Intra-individual Inter-trial Response Variability in Autism

- Recent studies suggest that instead of a general failure to synchronize neuronal activity, the disruptions in coordinated brain rhythms observed in autism may be related to a higher level of variability in neural responses (David et al. 2016, Milne 2011, Geurts et al. 2008)
- Neural responses captured by EEG show greater intra-individual inter-trial variability observed in autism
  - Dong et al. (2023): A functional model for studying common trends across trial time in eye tracking experiments
  - Dong et al. (2024): Modeling intra-individual inter-trial EEG response variability in Autism
- Inter-trial variability correlates with sensory processing scores and number of good trials retained (relating to attention)

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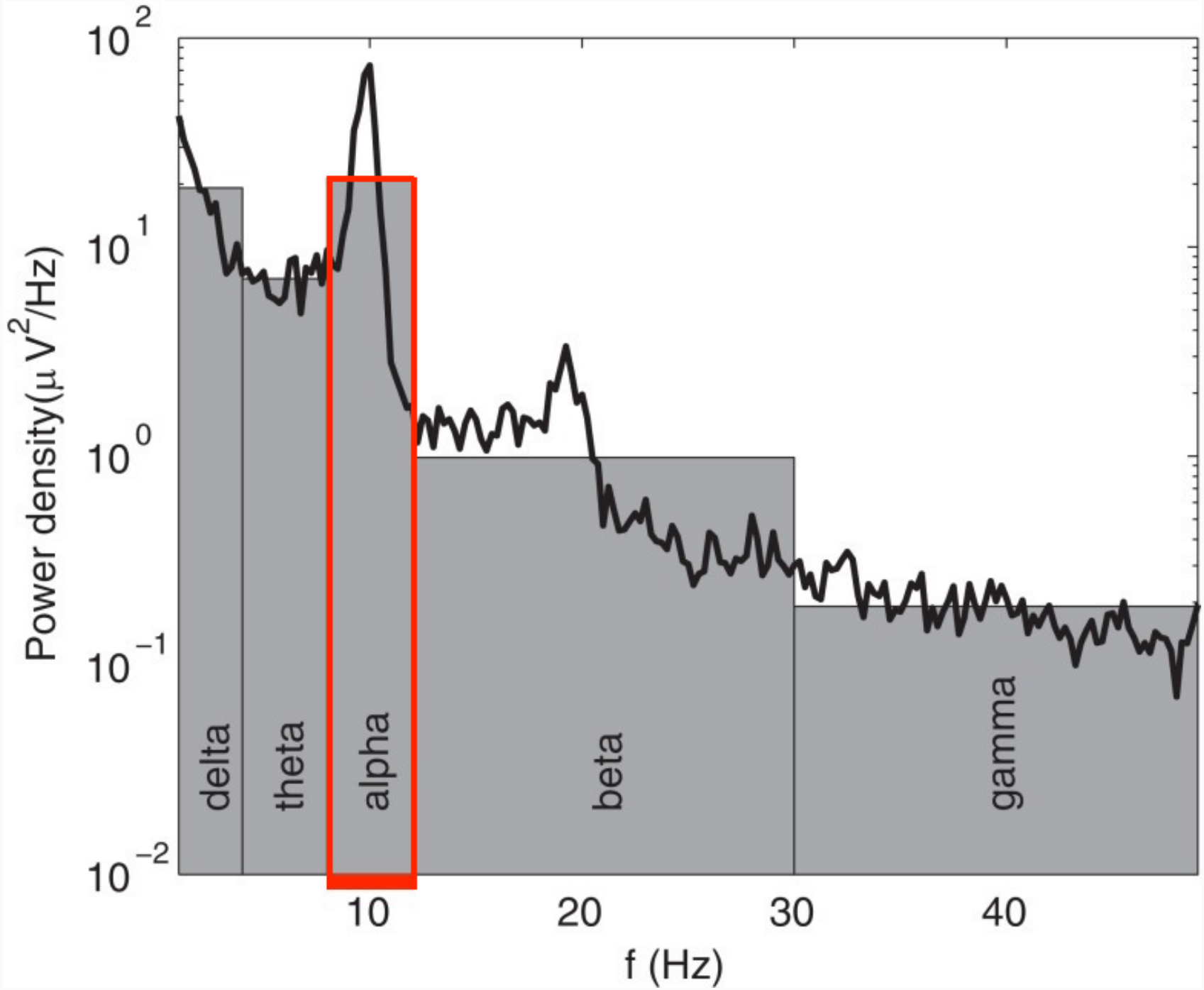
Analysis of EEG in the Frequency Domain

- Day-to-day Reliability of PSD (FDA)
- Synchronicity of PSD Across Electrodes (non-Euclidean)
- Contrastive Analysis of PSD: Wasserstein Boxplots (non-Euclidean)

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Resting State EEG as an Autism Biomarker

- Resting state EEG has promise as both a diagnostic and a predictive biomarker
- Individual features of the average power spectral density (PSD), band-specific power, slope or peak alpha frequency, have been studied for this purpose
- We present analysis on the use of the full morphology of the PSD in autism studies


Power density(μ V²/Hz)
10²
10¹
10⁰
10⁻¹
10⁻²
delta
theta
alpha
beta
gamma
10
20
30
40
f (Hz)

Analysis of EEG in the Frequency Domain

Day-to-day Reliability of PSD (FDA)

Day-to-day Reliability of PSD

- Crucial property of a biomarker especially for diagnostic or predictive contexts of use
- Reliability of the power spectral density (PSD) for resting EEG from the feasibility study of the Autism Biomarkers Consortium on 6-11 year olds
- Resting EEG eyes open recorded during 2 minutes of calm viewing of silent chromatic digital videos (non-social abstract moving images, similar to screen-savers)
- Study visit took place over 2 days, a median of 6 days apart
- 22 ASD and and 25 NT participants had resting EEG recorded on both days
- Reliability quantified via both parametric (FOOOF), and nonparametric functional method (functional ICC)

frontiers in Integrative Neuroscience

ORIGINAL RESEARCH
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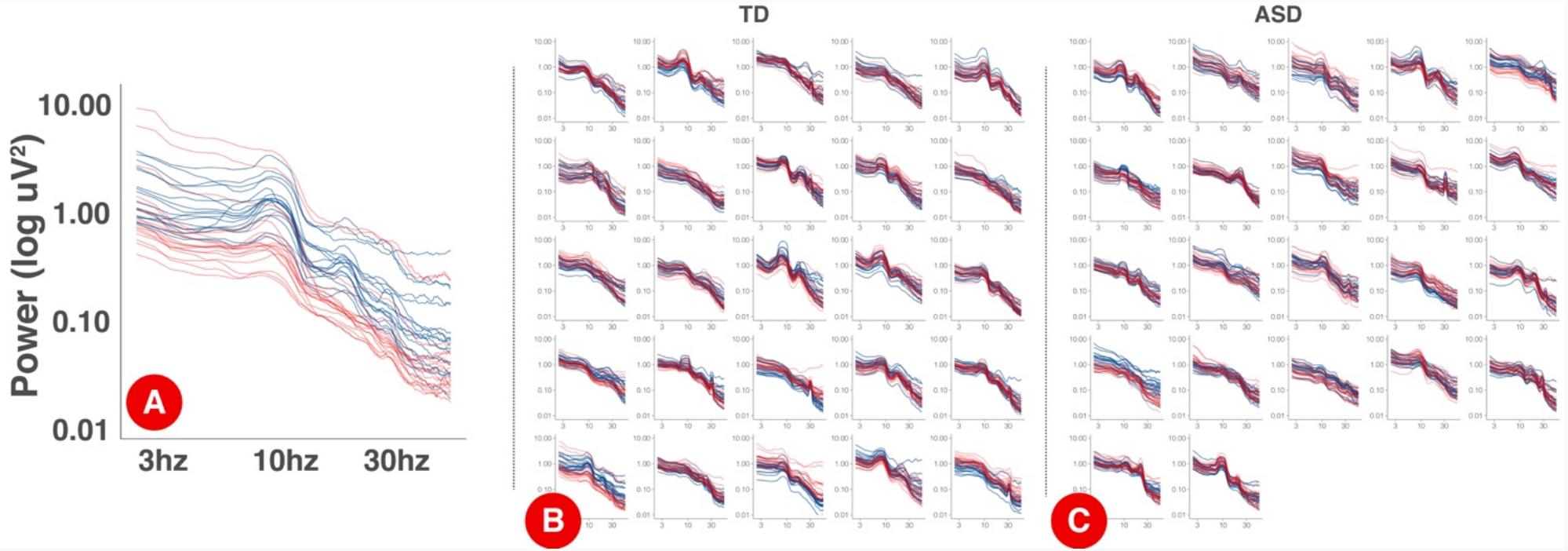
Check for updates

Day-to-Day Test-Retest Reliability of EEG Profiles in Children With Autism Spectrum Disorder and Typical Development

April R. Levin[1†], Adam J. Naples[2*†], Aaron Wolfe Scheffler[3], Sara J. Webb[4,5], Frederick Shic[4], Catherine A. Sugar[6,7], Michael Murias[8], Raphael A. Bernier[5], Katarzyna Chawarska[2], Geraldine Dawson[9,10,11], Susan Faja[12], Shafali Jeste[7], Charles A. Nelson[12], James C. McPartland[2*] and Damla Şentürk[6*] and the Autism Biomarkers Consortium for Clinical Trials*

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John A. Sweeney,
University of Cincinnati, United States


TD
ASD
Power (log uV²)
10.00
1.00
0.10
0.01
3hz
10hz
30hz
A
B
C

Analysis of EEG in the Frequency Domain

Synchronicity of PSD Across Electrodes

(non-Euclidean)

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Inferring Brain Signals Synchronicity from a Sample of EEG Readings

Qian Li[1], **Damla Şentürk**[1,2], **Catherine A. Sugar**[1,2,3], **Shafali Jeste**[3], **Charlotte DiStefano**[3], **Joel Frohlich**[3], **Donatello Telesca**[1,*]

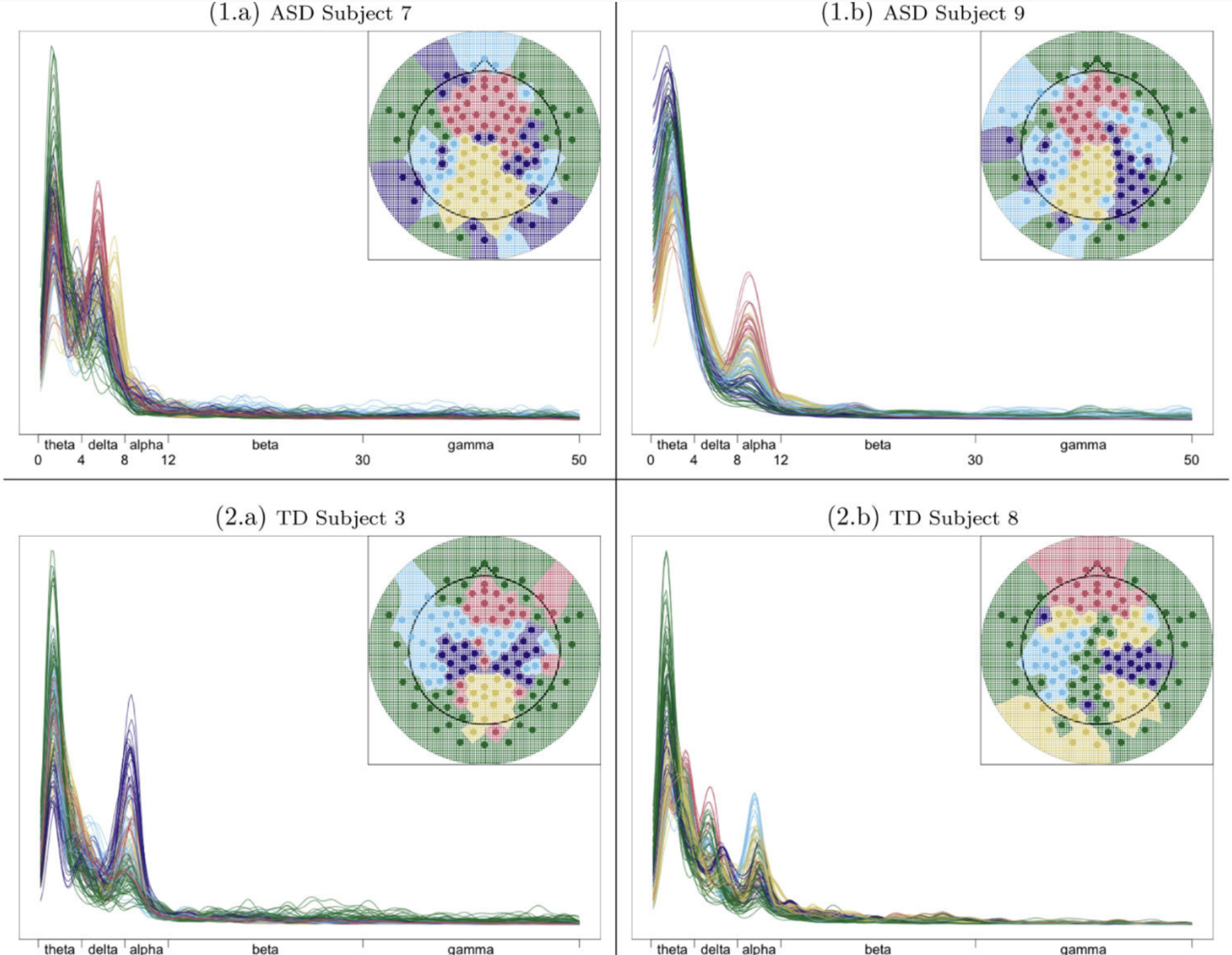
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Synchronicity of Power Spectra Across Electrodes

- Resting state EEG data is not necessarily aligned across time or subjects
- Hence, pooling information across time or subjects to study recurrent patterns of brain activation is challenging.
- Clustering electrodes according to PSD synchronicity
  - PSD is estimated in 1024ms epochs for each subject
  - Desynchronicity between PSD from two electrodes is quantified by total variation distance (distance metric for densities)
  - Affinity matrix is derived from the desynchronicity distances across electrodes
  - Spectral clustering of electrodes is achieved based on eigenvectors of the graph-Laplacian of the affinity matrix
  - Bayesian multilevel clustering borrows information across epochs and subjects (on cluster labels) in modeling eigenvectors of the graph-Laplacian


(1.a) ASD Subject 7
theta
delta
alpha
beta
gamma
0
4
8
12
30
50
(1.b) ASD Subject 9
theta
delta
alpha
beta
gamma
0
4
8
12
30
50
(2.a) TD Subject 3
theta
delta
alpha
beta
gamma
(2.b) TD Subject 8
theta
delta
alpha
beta
gamma

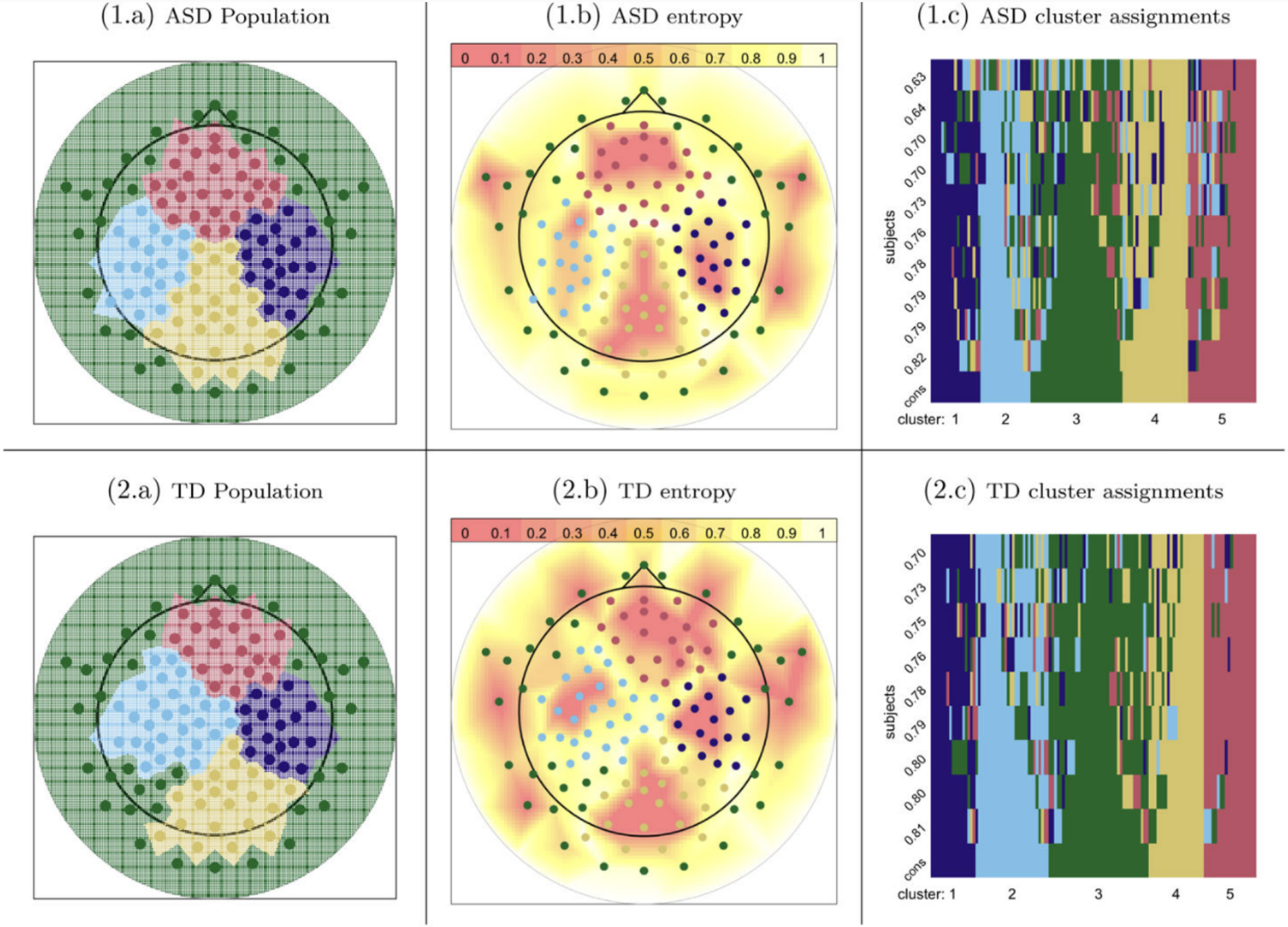


Figure 4. Group contrasts, ASD (1) vs TD (2)

Analysis of EEG in the Frequency Domain

Contrastive Analysis of PSD: Wasserstein Boxplots (non-Euclidean)

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Wasserstein Boxplots for the Analysis of EEG Power Spectral Densities with Applications to Autism

Puyuan Liu[1], **Donatello Telesca**[1], **Abigail Dickinson**[2], **Shafali Jeste**[3], **Damla Şentürk**[1]

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Wasserstein Boxplots

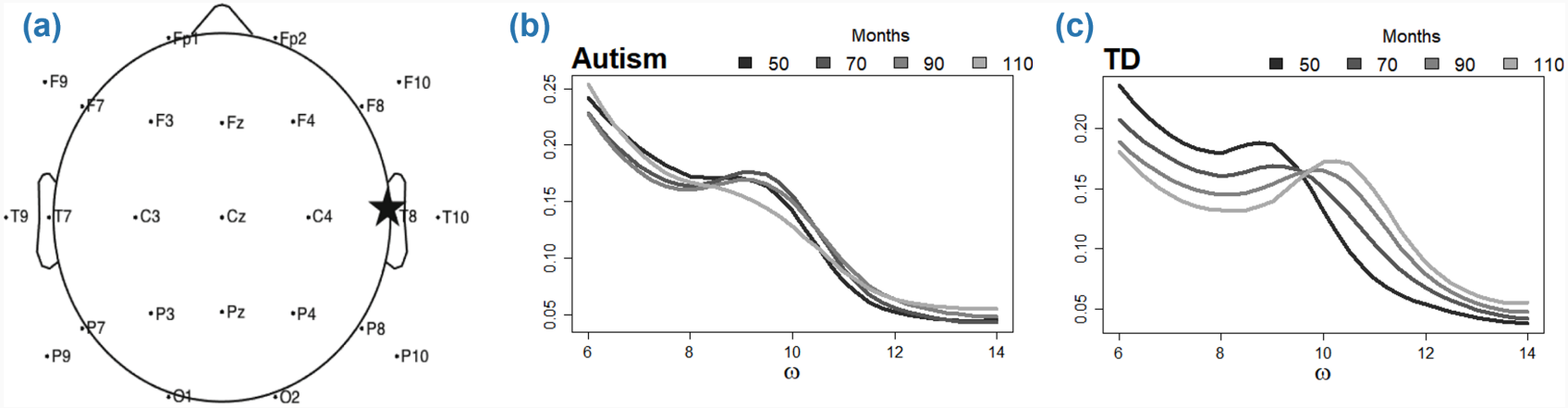
- Boxplots provide a concise summary of central tendency, spread, and potential outliers
- Functional boxplots provide an analogous visual summary for a sample of curves (Sun and Genton, 2011)
  - Curves are ordered from center outward using band depth or modified band depth
  - Central envelopes display the spread of the sample
- Density functions differ from unconstrained curves
- They must be nonnegative and integrate to one
- Their comparison should respect these constraints
- Existing functional boxplots primarily describe one sample of functions
- Our setting also requires target (autism) –reference (NT) comparisons
- The reference distribution may change with age or other covariates
- We utilize the 2-Wasserstein metric to quantify distances between EEG PSDs

Resting-state EEG data in the alpha frequency domain

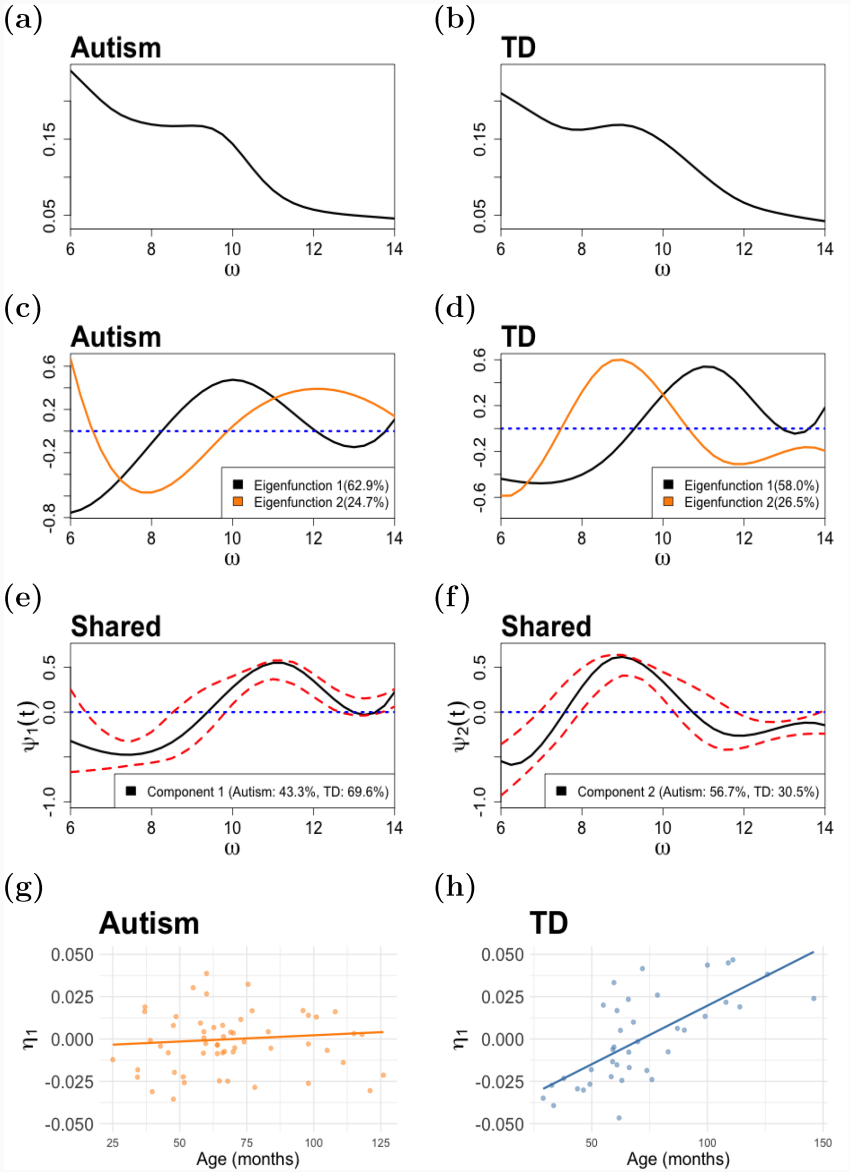
- Peak alpha frequency (PAF), defined as the location of a prominent peak in the spectral alpha frequency band, is widely used to study neural processes in young children
- Studies have shown that PAF moves to higher frequencies as children age, while this developmental shift may be altered in children with **autism**

Resting-state EEG data

- Studying developmental changes in neural networks and cognitive function of children with autism
- 39 children diagnosed with **autism** vs 58 **TD** children aged 25 to 144 months old
- Measured at 25 electrodes, transformed into the alpha frequency band (6 – 14 Hz) with resolution of .25 Hz
- Features of interest: peak alpha frequency (PAF) and amplitude of the alpha peak

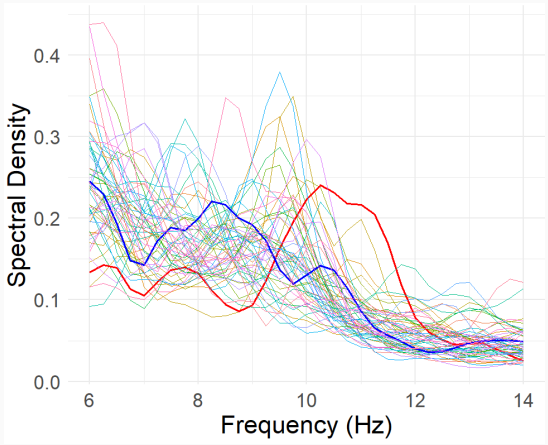


Contrastive FPCA on PSD (Bai et al. 2026)

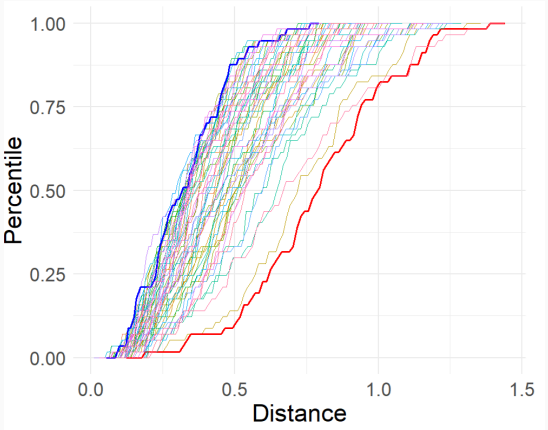


- Shared component:
  1. First component (e) highlights variation in the PAF
  2. Second component (f) highlights variation in the power of alpha peak
- Difference in dominant patterns of variation across two groups emphasizes the development shift in PAF across different age groups in TD children, while it is absent or delayed in children with autism
- Scatter plots (g) and (h) showcase the association between the children's age and the subject-level scores of the first shared latent component

How to rank the densities?



Power spectral densities



Empirical distance profiles

Density functions are constrained to be nonnegative and integrate to one.

- **2-Wasserstein distance:** the 2-Wasserstein distance between μ and ν is the L^2 distance between their quantile functions,

$$d_W(\mu,\nu) = \left[\int_0^1 \{F_\mu^{-1}(u) - F_\nu^{-1}(u)\}^2\, du\right]^{1/2} = d_{L^2}(F_\mu^{-1}, F_\nu^{-1}).$$

- **Distance Profiles (Dubey et al., 2024):** For a density ω, its distance profile

$$F_\omega(t) = \Pr\{d_W(\omega, Z) \le t\}, \qquad Z \sim P,$$

characterizes how other distributions are distributed around ω in Wasserstein space.

How to rank the densities?

To compare two densities ω and Z, their distance profiles F_ω and F_Z are aligned via the monotone **optimal transport map**

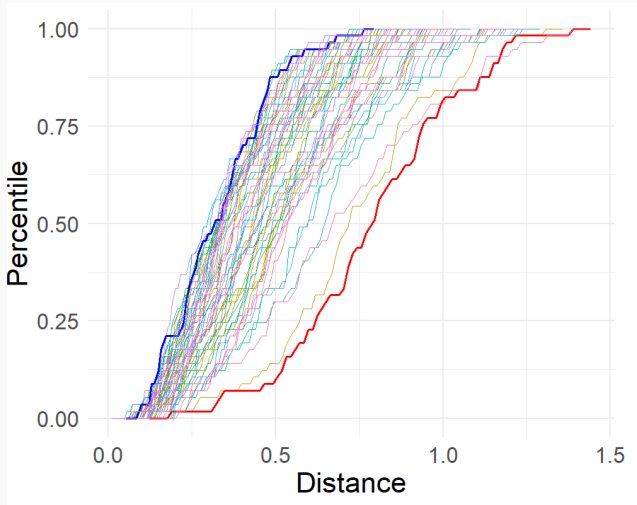
$$H_{Z,\omega}(v) = F_Z^{-1}\{F_\omega(v)\} - v,$$

which quantifies the pointwise adjustment needed to morph F_ω into F_Z. The integral

$$\int H_{Z,\omega}(v)\, dF_\omega(v) = \int_0^1 \{F_Z^{-1}(u) - F_\omega^{-1}(u)\}\, du$$

summarizes the **total transport cost**.

Positive values indicate ω is more central than Z (mass shifts to the right to align F_ω with F_Z); negative values imply the opposite.



How to adjust for covariates?

Fréchet regression (Peterson and Mueller, 2019)

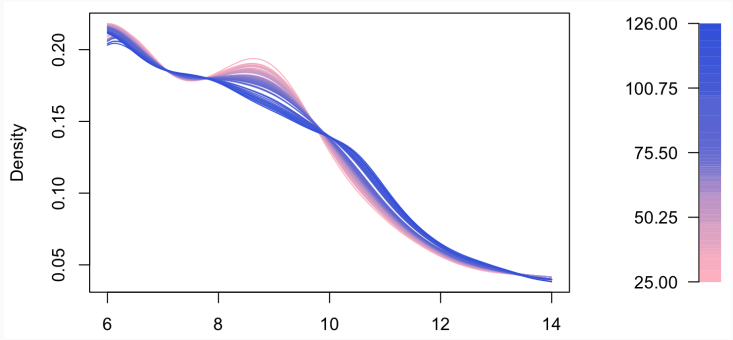
Let (X, Y) denote covariates $X \in \mathbb{R}^p$ and distributional outcomes $Y \in (\Omega, d_W)$, the Fréchet mean is defined as

$$\omega_\oplus = \arg\min_{\omega \in \Omega} E\{d^2(Y, \omega)\}.$$

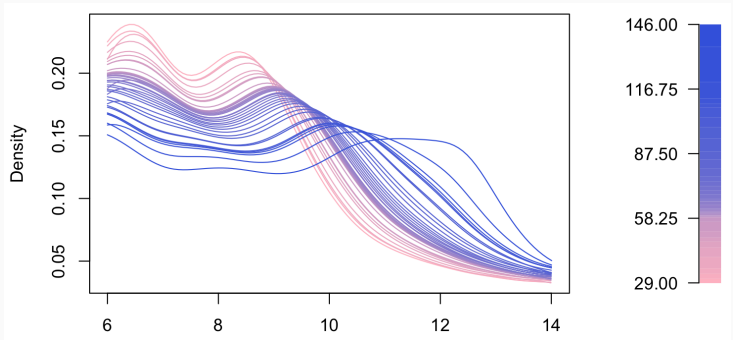
The Fréchet regression function of Y given $X = x$ was introduced based on the above concepts,

$$M_\oplus(\cdot, x) = E\{d^2(Y, \cdot) \mid X = x\},$$
$$m_\oplus(x) = \arg\min_{\omega \in \Omega} M_\oplus(\omega, x),$$

where $M_\oplus(\cdot, x)$ is referred to as the conditional Fréchet function and $m_\oplus(x)$ is the conditional Fréchet mean.



Conditional Fréchet means across age in ASD

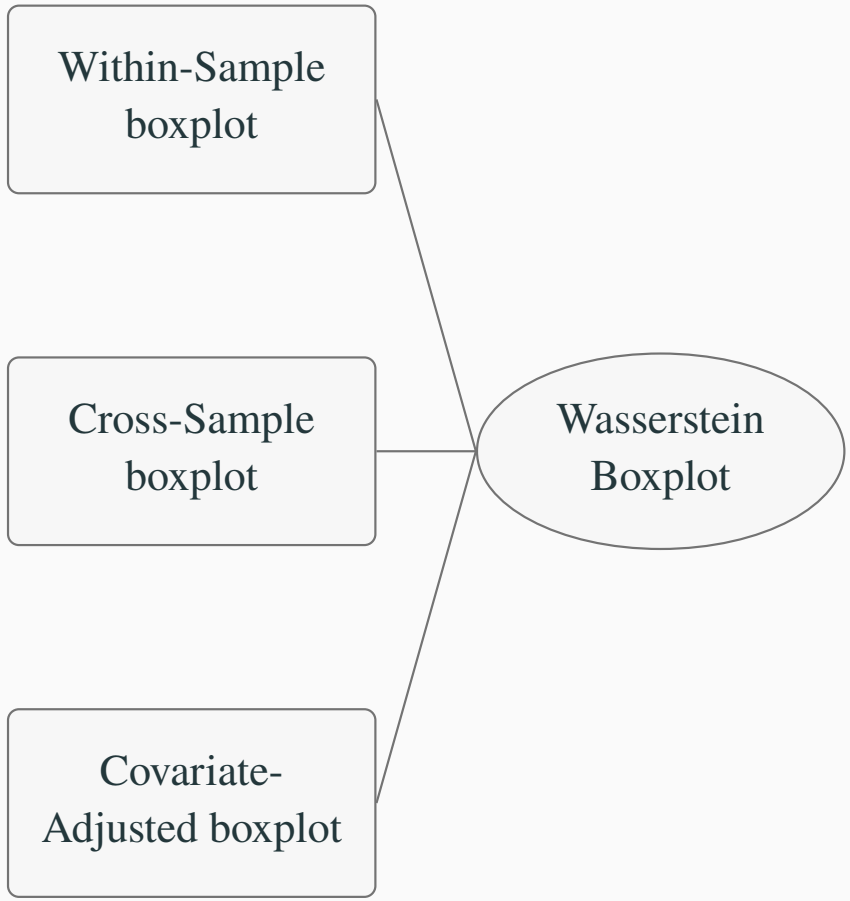


Conditional Fréchet means across age in NT

Methods: *Proposed Wasserstein Boxplot Framework*

Motivated by providing a visual summary of EEG PSDs while highlighting differences between autistic and neurotypical groups.

- Provide a visual summary of a sample of densities ⇒ **Within-Sample boxplot**
- Extend to contrastive settings with a target and a reference group ⇒ **Cross-Sample boxplot**
- Consider covariate adjustments ⇒ **Covariate-Adjusted boxplot**



Methods: *Within-Sample Boxplot*

The estimated distance profile $\widehat{F}_{x_i}$ for subject i can be computed by

$$\widehat{F}_{x_i}(t) = \frac{1}{n_x - 1} \sum_{i' \neq i} \mathbb{I}\{d_W(x_i, x_{i'}) \leq t\}, \qquad t \geq 0.$$

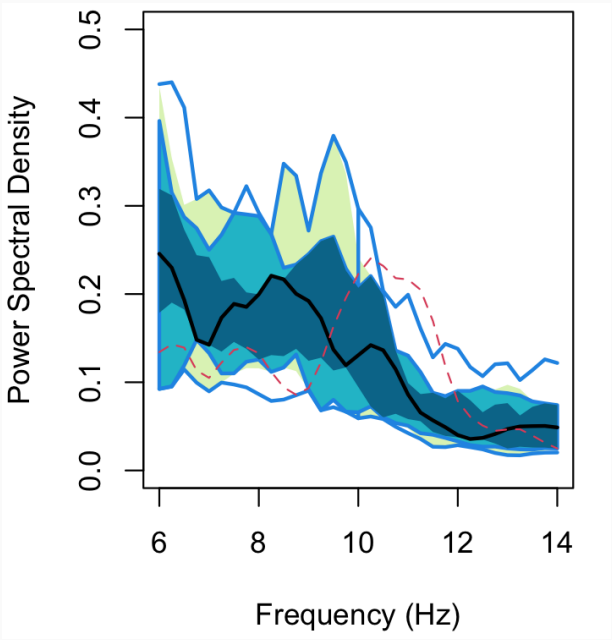
A **raw centrality score** for each spectra is computed by averaging the integrated mass transfer of its distance profile to those of all other spectra,

$$\widehat{C}_{x_i} = \frac{1}{n_x - 1} \sum_{i' \neq i} \left[\int_0^1 \{\widehat{F}^{-1}_{x_{i'}}(u) - \widehat{F}^{-1}_{x_i}(u)\}\, du \right], \quad u \in [0, 1].$$

The expit function $\text{expit}(x) = e^x/(1 + e^x)$ scales the **transport ranks** to $(0, 1)$,

$$\widehat{R}_{x_i} = \text{expit}(\widehat{C}_{x_i}).$$

Methods: *Within-Sample Boxplot*



Within-sample Wasserstein boxplot

The within-sample boxplot visualizes ordered densities by highlighting the **median**, defining the **central envelopes** and **interquartile range (IQR)**, and flagging potential **outliers**.

- In the Wasserstein boxplot, IQR is redefined as the range (max – min) of the top 50% raw centrality scores.
- Outliers are identified using a threshold:

$$L_b = Q_2(\{\widehat{C}_{x_i}\}) - 3 \cdot \text{IQR}.$$

- For more conservative outlier detection, we offer a skewness-adjusted threshold that scales the IQR multiplier according to distributional asymmetry.

Methods: *Cross-Sample Boxplot*

- The proposed cross-sample Wasserstein boxplots extend the framework to **contrastive settings** involving a **target** and a **reference group**. The goal is to characterize subject-specific deviations within the target group from the reference sample.

- Each individual's density in the target group is evaluated relative to the reference group by computing the Wasserstein distance between the target density x_i and each density y_j in the reference group.

- The cross-sample distance profile function for a target density x_i is

$$\widehat{F}'_{x_i}(t) = \frac{1}{n_y} \sum_{j=1}^{n_y} \mathbb{I}\{d_W(x_i, y_j) \leq t\}, \qquad t \geq 0.$$

Methods: *Cross-Sample Boxplot*

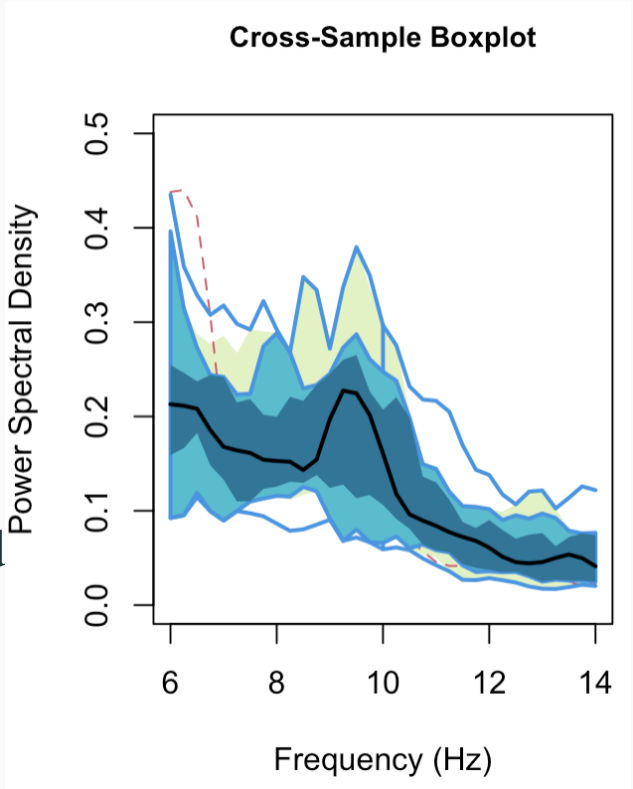
Similarly, a **raw centrality score** for each spectrum is computed by averaging the integrated transfer mass of its distance profile to those of all other spectra, specifically,

$$\widehat{C}'_{x_i} = \frac{1}{n_x - 1} \sum_{i' \neq i} \left[\int_0^1 \{ \widehat{F}'^{-1}_{x_{i'}}(u) - \widehat{F}'^{-1}_{x_i}(u) \} \, du \right]$$

Expit function $\text{expit}(x) = e^x/(1+e^x)$ is applied to raw centrality scores to ensure that the **transport ranks** are scaled to $(0, 1)$,

$$\widehat{R}'_{x_i} = \text{expit}(\widehat{C}'_{x_i}).$$

Cross-sample boxplots are constructed based on the obtained cross-sample transport ranks.



Cross-sample Wasserstein boxplot

Methods: *Covariate-Adjusted Boxplot*

Main idea: Adjust for covariate effect

- A younger autistic subject should be compared to neurotypical spectra with an earlier PAF.
- Older autistic subjects should be compared to spectra with higher PAFs.
- Our approach: for each subject in the target group, we identify the corresponding conditional Fréchet mean estimated in the reference group at the covariate value of the subject.
- To obtain the conditional Fréchet mean, the Fréchet regression is performed in the reference group with $y \in \Omega$

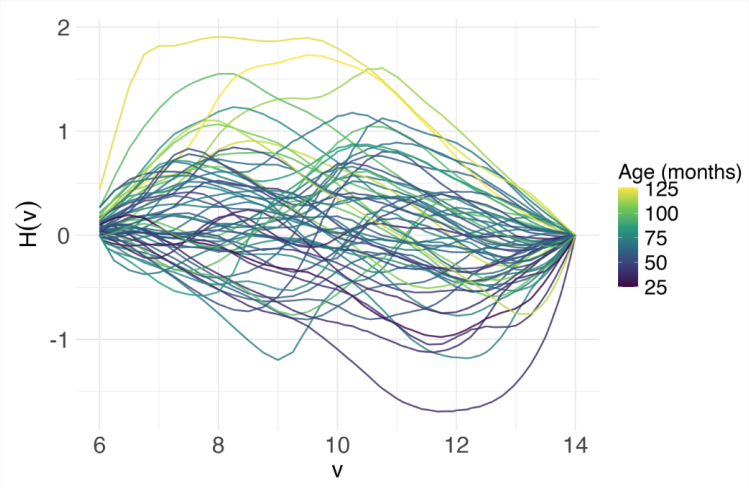
$$M_{\oplus}(\cdot, a_i) = E\{d^2(y, \cdot) \mid a = a_i\}, \qquad m_{\oplus}(a_i) = \arg\min_{\omega \in \Omega} M_{\oplus}(\omega, a_i).$$

Methods: *Covariate-Adjusted Boxplot*

Fréchet regression residual: the optimal transport map moving mass from the CDF of the observed distribution x_i to the CDF of the conditional Fréchet mean $m_{\oplus}(a_i)$:

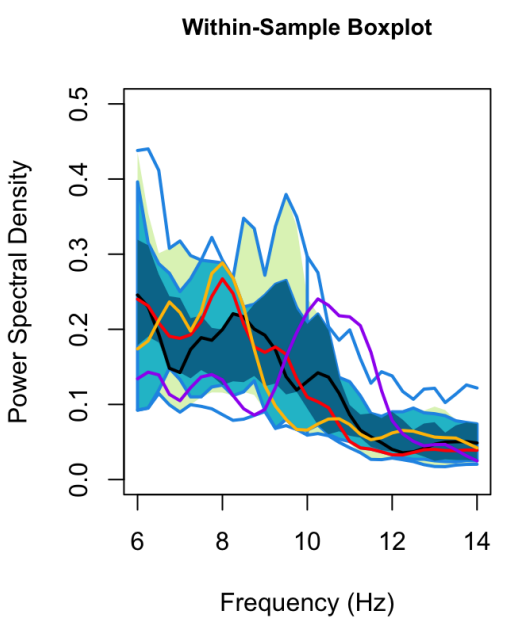
$$H_{m_{\oplus}(a_i),x_i}(v) = F^{-1}_{m_{\oplus}(a_i)}\{F_{x_i}(v)\} - v.$$

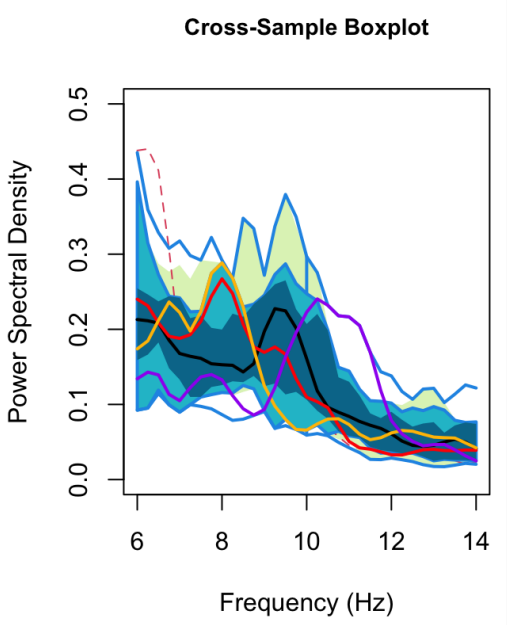
The residuals are no longer densities. The covariate-adjusted boxplot is the functional boxplot of Fréchet regression residuals.

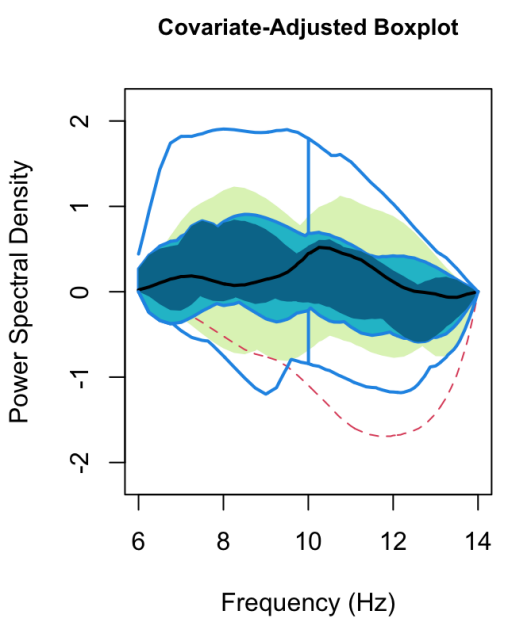


Fréchet regression residuals, color-coded by age

Wasserstein Boxplots of Subject-specific PSD







- Two patients with similar spectral patterns and a shared PAF of 8 Hz are highlighted in red (126 months) and yellow (34.2 months).
- In the within-sample boxplot, their order statistics are 23rd (red) and 20th (yellow) out of 58; in the cross-sample boxplot, they shift to 38th and 28th, respectively. Their residuals differ significantly.
- The observation colored in purple (98 months): peripheral in within and cross-sample boxplots, but normal in covariate adjusted boxplot.

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Discussion

Discussion

- non-Euclidean methods can incorporate contextual information from the EEG signal
  - Determination of the data object
  - Choice of appropriate metric
  - 2-Wasserstein distance for EEG PSDs
  - ERP components have specific convex/concave shape features
  - EEG coherence matrices can be modeled using distance metrics for positive definite matrices
- Euclidean methods only target different features of the signal one at a time (leading to complex and cumbersome modeling)
- non-Euclidean methods can model contextual signal information (e.g., amplitude vs. phase variability, mass transformation in densities, concavity and convexity) jointly.
- Hence, analysis in non-Euclidean metric spaces has the potential to accentuate results on diagnostic group differences or phenotypic correlations with autism-specific EEG traits

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Thank You!