Mixed Effects Spectral Vector Autoregressive Model

Application to brain connectivity in ADHD vs healthy children

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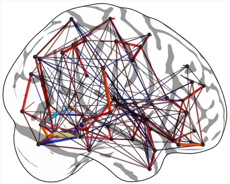
Introduction

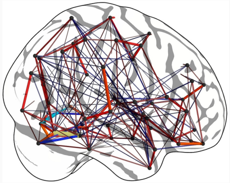
Effective connectivity

- Spatially distant brain regions often interact with each other during cognitive processing



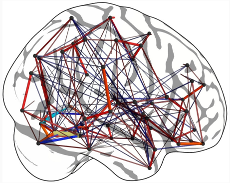
Effective connectivity

- Spatially distant brain regions often interact with each other during cognitive processing
- Effective connectivity ⇒ to study the direction and magnitude of interactions



Effective connectivity

- Spatially distant brain regions often interact with each other during cognitive processing
- Effective connectivity $\Rightarrow$ to study the direction and magnitude of interactions
- Models for effective connectivity are model-based and model-free: dynamic causal modelling [Friston, 2003], information theoretic [Hinrichs et al., 2008], Granger causality [Granger, 1980].



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- Many existing models of brain effective connectivity have certain limitations and different difficulty of implementation.
- None of the existing models accounts for variability of the parameters in different frequency bands $\leftarrow$ (NOVEL!).
- Fast and convenient implementation of the model allows us to investigate pathology specific features of brain functioning.

VAR model and Granger causality

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VAR model

Let Y_t be a vector of brain signals recorded at R spatial locations, where $Y_t = \left[Y_t^1, Y_t^2, ..., Y_t^R\right]$. **Vector autoregressive of order p:**

$$Y_t = \Phi_1 Y_{t-1} + \Phi_2 Y_{t-2} + \ldots + \Phi_p Y_{t-p} + \varepsilon_t, t = p, ..., T,$$

Φ_j - are coefficients matrices R by R dimension for each lag p,

$$\Phi_j = \begin{bmatrix} \phi_{11}^{(j)} & \ldots & \phi_{1R}^{(j)} \\ . & . & . \\ . & . & . \\ . & . & . \\ \phi_{R1}^{(j)} & \ldots & \phi_{RR}^{(j)} \end{bmatrix}, \varepsilon_t - \text{WN}(0, \Sigma_{diag})$$

Feature Y^j is said to Granger-cause Y^i, if auto-regressive model using **both** past values is statistically significantly more accurate than that based just on the past values of Y^i.

Mixed effects VAR

ME VAR model

$\mathbf{Y}^{(i)}(t) = [Y_1^{(i)}(t), Y_2^{(i)}(t), ..., Y_R^{(i)}(t)]$, where R is the number of EEG channels.

$$\mathbf{Y}^{(i)}(t) = \mathbf{F}^{(i)}(t) + \mathbf{E}^{(i)}(t), t = 1, \dots, T,$$

where $\mathbf{F}^{(i)}(t) = 0$ is the activity specific deterministic mean trend in preprocessed EEG.

$$\mathbf{Y}^{(i)}(t) \sim \text{VAR(p)},$$

p - lag order of autoregression.

$$\mathbf{Y}^{(i)}(t) = \sum_{k=1}^{P} \left[\Phi_{1,k}^{(i)} G_1(i) + \Phi_{2,k}^{(i)} G_2(i) \right] \mathbf{Y}^{(i)}(t-k) + \epsilon^{(i)}(t),$$

Mixed effects VAR

Mixed effects model [Gorrostieta et al., 2012] for the EEG signals for participant (i):

$$Y^{(i)}(t) = \sum_{k=1}^{P} \left[\Phi_{1,k}^{(i)} G_1(i) + \Phi_{2,k}^{(i)} G_2(i) \right] Y^{(i)}(t-k) + \epsilon^{(i)}(t),$$

$$G_1(i) = \begin{cases} 1, & \text{if } i = 1,\ldots,n_1 \\ 0, & \text{if } i = n_1+1,\ldots,n_2 \end{cases} \quad G_2(i) = \begin{cases} 1, & \text{if } i = n_1+1,\ldots,n_2 \\ 0, & \text{if } i = 1,\ldots,n_1 \end{cases}$$

$\Phi_{1,k}^{(i)}$ and $\Phi_{2,k}^{(i)}$ – connectivity matrices for each participant (i), for each lag k, depending on the group (1 or 2).

Mixed effects VAR

Mixed effects model [Gorrostieta et al., 2012] for the EEG signals for participant (i):

Connectivity matrices are decomposed into fixed and random effects:

$$\Phi_{1,k}^{(i)} = \Phi_{1,k} + b_k^{(i)}$$
$$\Phi_{2,k}^{(i)} = \Phi_{2,k} + b_k^{(i)},$$

where $\Phi_{1,k}$, $\Phi_{2,k}$ are the fixed connectivity components for groups 1 and 2; and $b_k^{(i)}$ are the participant-specific random effects for each lag k.

Spectral Decomposition

Spectral decomposition

- Electrical activity of neurons is essentially the summation of simultaneous neuronal firings, thus the resulting signal is a composition of underlying processes.
- Applying a 3rd orderButterworth filter we extract specific oscillatory activity.
- The commonly used $(\delta, \theta, \alpha, \beta, \gamma)$ frequency components of brain EEGs are linked to specific consciousness states and neural activity.

Frequency bands

- Slow waves as delta (0.5 - 4 Hz) and theta (4 - 8 Hz) are connected with sleep, learning and memory [Etard and Reichenbach, 2019].
- Alpha frequency at 8-12 Hz is mostly inherent to closed eyes alert state [Foster et al., 2017],
- Beta (12 - 30 Hz) is associated with thinking and active concentration [Baumeister et al., 2008],
- Gamma (30 - 50 Hz) is mostly correlated with high order cognitive functions such as memory, attention.

Spectral decomposition

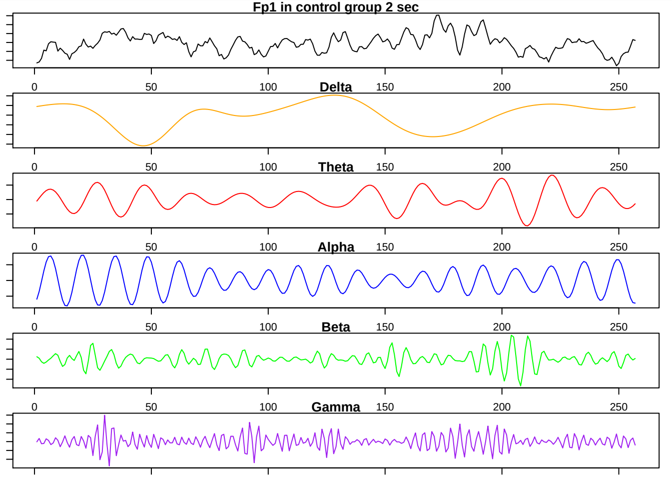


Figure 1: Spectral decomposition into $(\delta, \theta, \alpha, \beta, \gamma)$ frequency bands done by 3rd order Butterworth filter. Upper plot represents initial EEG signal from Fp1 channel for 2 sec.

Spectral decomposition

- For each participant (i) and for each channel R, we can decompose the signals into $(\delta, \theta, \alpha, \beta, \gamma)$ frequency bands using filter.
- Filtered signal is derived from linear combination of original signal and coefficients c_j corresponding to given frequency:

$$Y^{(i)}_{R,band}(t) = \sum_{j=0}^{10} c_j \mathbf{Y}^{(\mathbf{i})}_{\mathbf{R}}(t-j)$$

.

ME-SpecVAR

ME-SpecVAR

Fit Mixed effects VAR model for each frequency band separately using filtered signals

$\downarrow$

Delta Theta Alpha Beta Gamma

$\downarrow\downarrow\downarrow\downarrow\downarrow$

Fixed connectivity structure and standard deviations of random effects for each band.

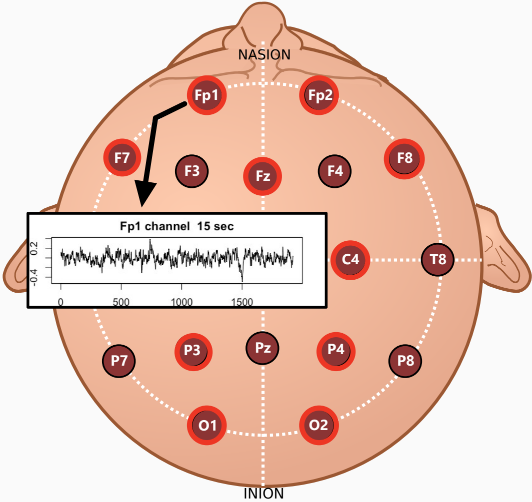
Advantages of the proposed model

- The model for random fluctuation $\mathbf{Y}^{(i)}(t)$ can vary for number of groups, lag values and accounting for random part in connectivity structure. $\Rightarrow$ discriminate connectivity structure between groups and detect differences of variance of random effects in two groups.
- Conduct EASILY statistical inference on the connectivity parameter $\Phi_{g,l}(r, r') = 0$ where g = group, l = lag values from 1...p, (r,r') - two arbitrary channels. Using Welch-Satterthwaite T-Test or likelihood ratio test (LRT).
- Filtered signals allow to obtain new meanings and interpretations.
- Can be implemented using existing software with Mixed Effects Linear Models.

ADHD Dataset

ADHD children EEG data

- EEG recording by 19 channels at 128 Hz sampling frequency [Ekhlasi et al., 2021]
- Preprocessed data for 53 control children and 51 ADHD medicated children
- Perform visual attention task for about 90 seconds counting cartoon characters
- The following channels were used: (Fp1, Fp2, F7, F8, Fz, C3, C4, P3, P4, O1, O2) and 15 seconds of data.



Model implementation results

Results

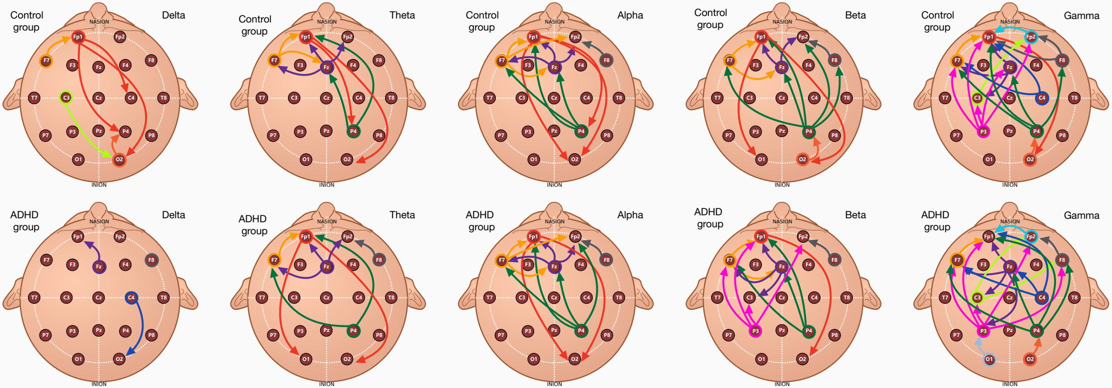


Figure 2: Fixed connectivity parameters in each group and frequency band. Arrows represent significant connections with p-value less than 10^{-6}.

Differences of connections in Control and ADHD groups

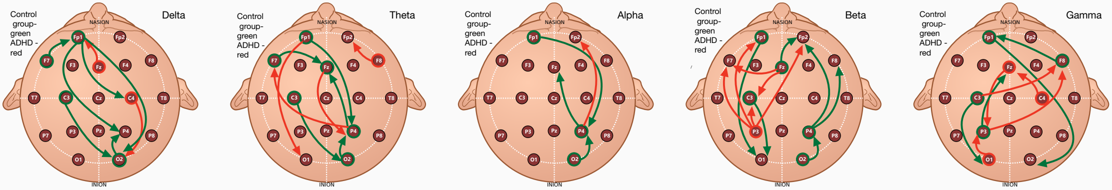


Figure 3: Differences in fixed effects in two groups, green arrows represent significant connection with corrected p-value$< 10^{-6}$ that are ONLY in control, red represents connections that are ONLY in ADHD.

Model implementation results

Standard deviations of random effects

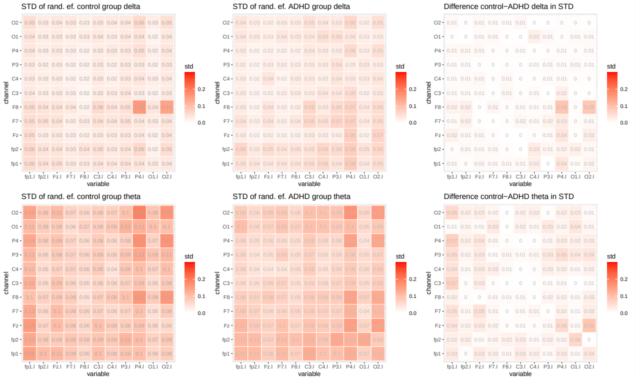
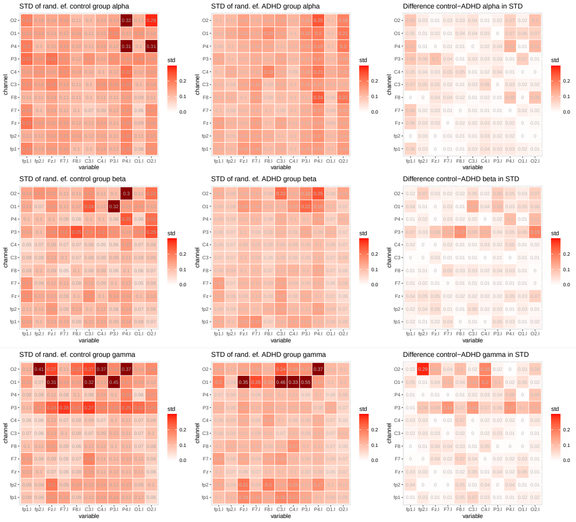


Figure 4: Standard deviations of random effects. Darker color corresponds to higher difference.

Model implementation results

Standard deviations of random effects



Discussion

Novel results

- Control group has more effective connectivity connections in all frequency bands, especially in low frequencies.
- Differences in fixed effects are more concentrated in connections between frontal part and parietal-occipital part (Cognitive control and attention connections).
- The variability of random effects is also higher in control group, especially in O2-F8, P4-F8 in slow wave oscillations.
- Various channels influence on P3, O1 and O2 is higher in control group at fast frequencies beta and gamma.

Connections to existing studies

- The finding of Parietal-Occipital brain region connection is associated with control of selective and focused visual attention [Gottlieb and Balan, 2010].
- The results are consistent with decreased anterior-posterior connectivity in children with ADHD compared to healthy controls [Fair et al., 2010].
- Results are consistent with finding that ADHD patients showed a reduction in slow waves across the whole brain compared to healthy controls [Furrer et al., 2019].

For more details look arxiv version of the paper:

https://arxiv.org/abs/2210.03017

Thank you!

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