# *Enhanced inference of network structure from functional connectivity*

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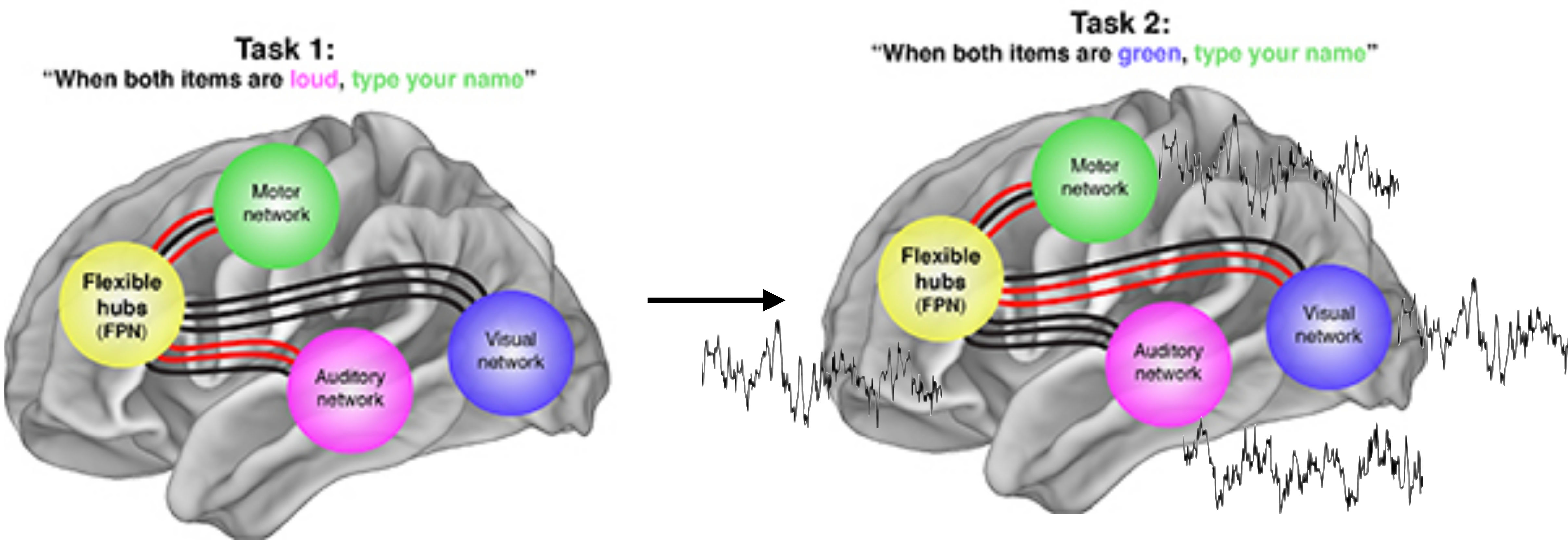
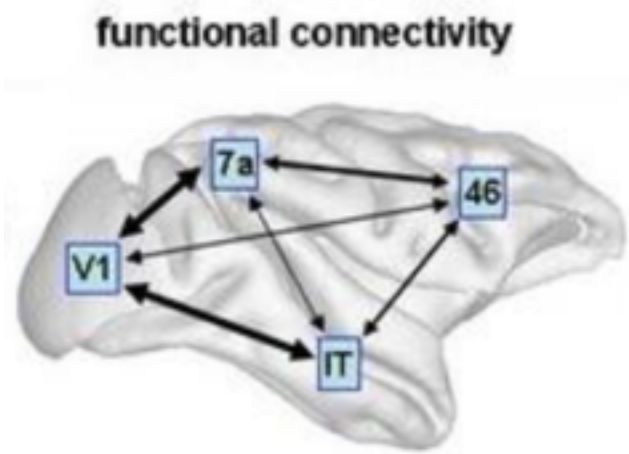
# Brain connectivity in functional neuroimaging

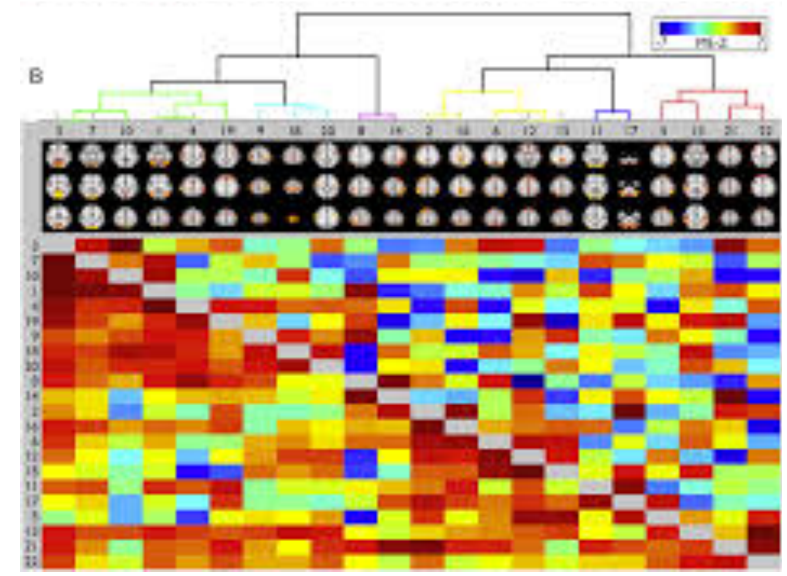


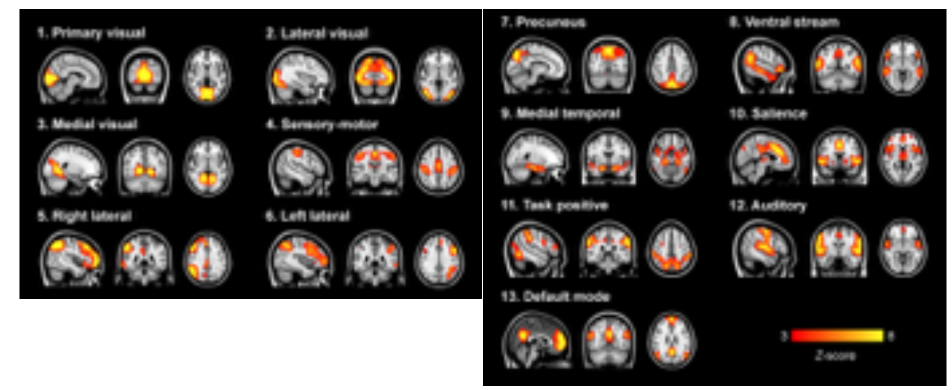

Cole, Nature Neuroscience, 2013

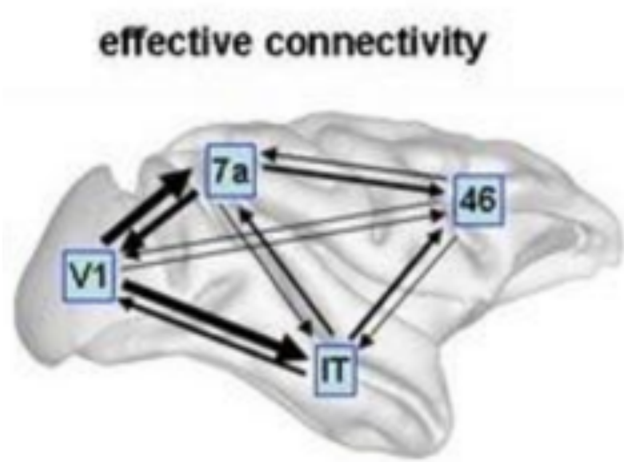
# Brain connectivity in functional neuroimaging



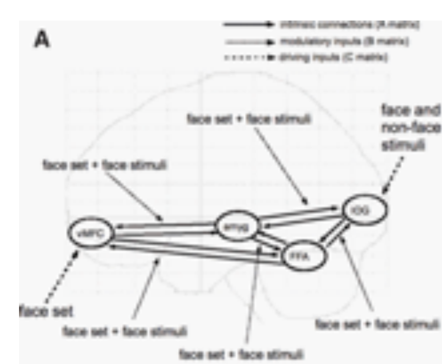

- Correlation (network matrices)
- Power/frequency analysis
- PPI
- Mutual Information
- Coherence

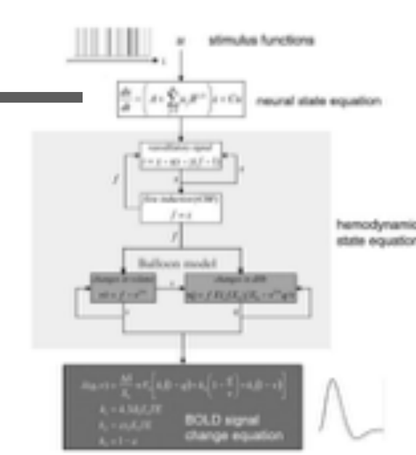


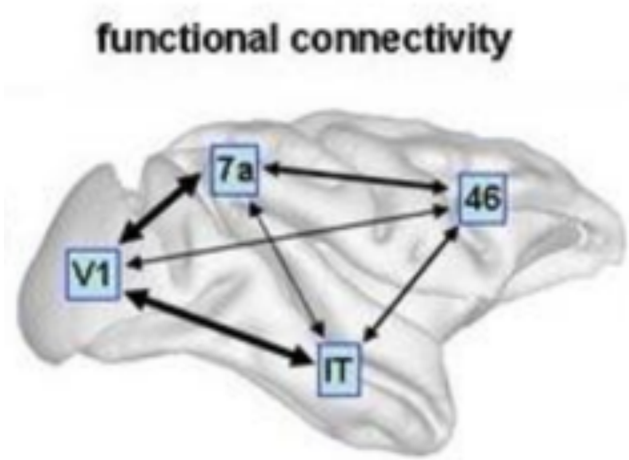




- Partial correlation
- Dynamic Causal modelling
- Structural Equation modelling
- Granger
- Graph models



# *Brain connectivity in functional neuroimaging*




Correlation (network matrices)

Power/frequency analysis

PPI

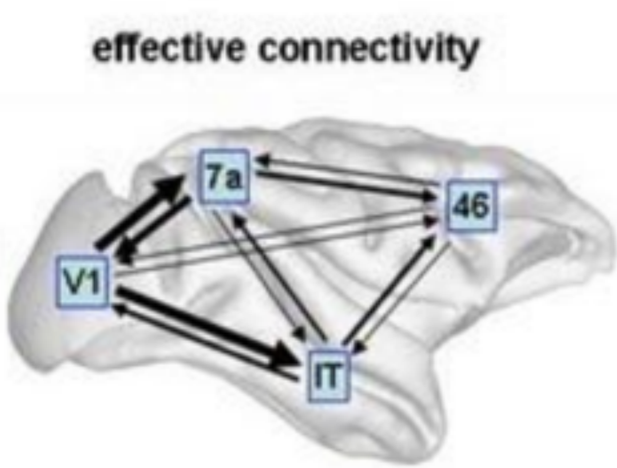
Mutual Information

Coherence

**Pros:**
- Simple pairwise measures permit, comprehensive characterisation.
- Computationally efficient.

**Cons:**
- Can be sensitive to a wide range of effects: ambiguous interpretation
- Do not estimate neurophysiological parameters

How to use FC to inform EC model structure?




Partial correlation

Dynamic Causal modelling

Structural Equation modelling

Granger

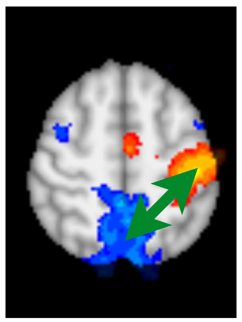
Graph models

**Pros:**
- Can estimate more biologically meaningful variables
- Can model out uninteresting variables

**Cons:**
- Often overparameterised, can only compare limited set of model structures
- Difficult to estimate for many nodes
- Strong assumptions for ROIs, connectivity patterns, signal dynamics, noise sources
- All parameters/regions interdependent

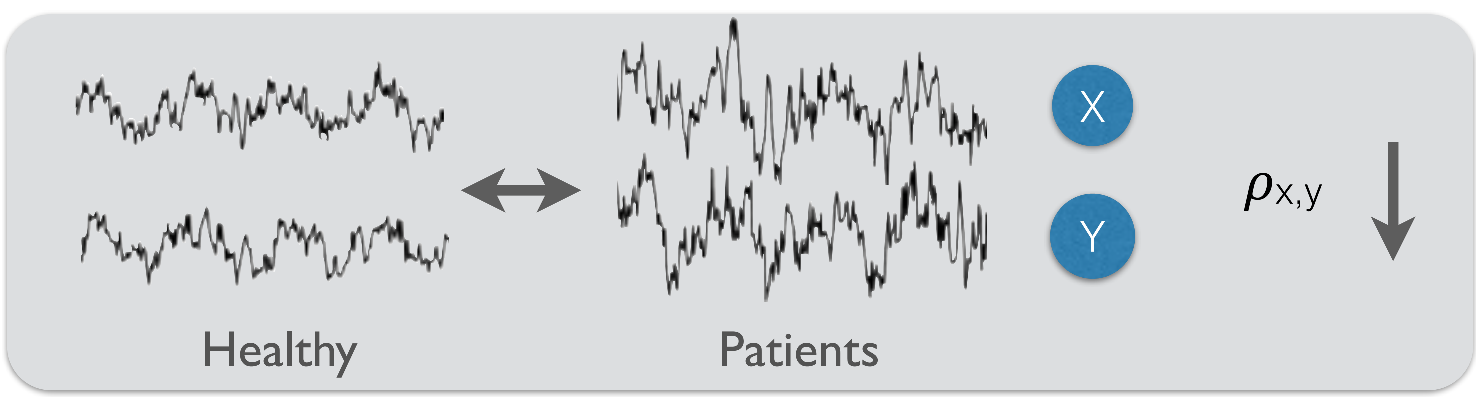
# *What causes changes in correlations?*

Typical assumption is some sort of change in level of interaction between brain regions:



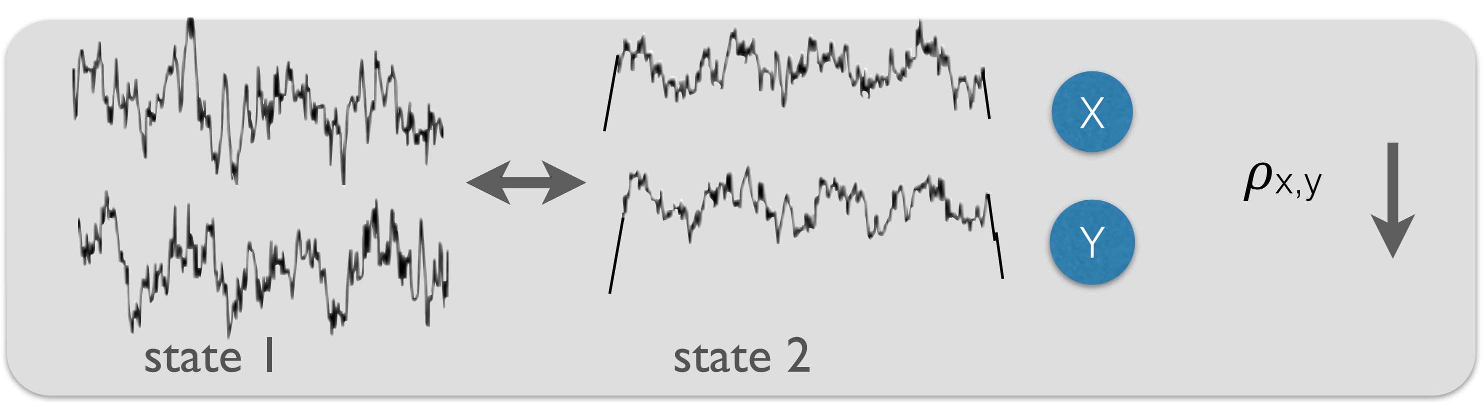

- Strength of interaction
- Extent of interaction
- Activity level of network

With no model of signal, analyses will be sensitive to variations in noise:




- Increase in noise level

e.g. Differences in patient group, due to vascular tone.




- Reduction in signal

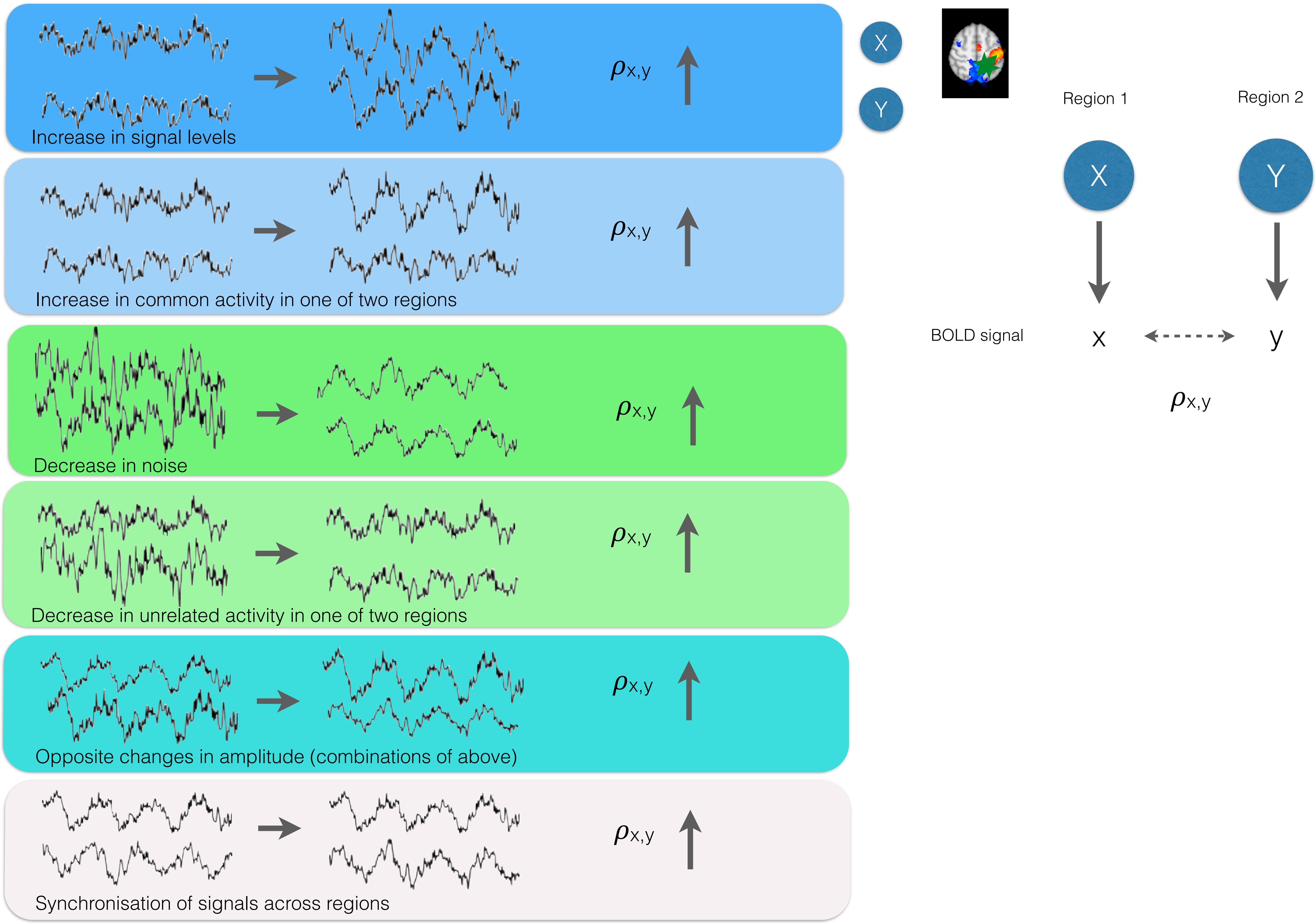
e.g. Differences across activation states due to BOLD ceiling effect

# *Aims*

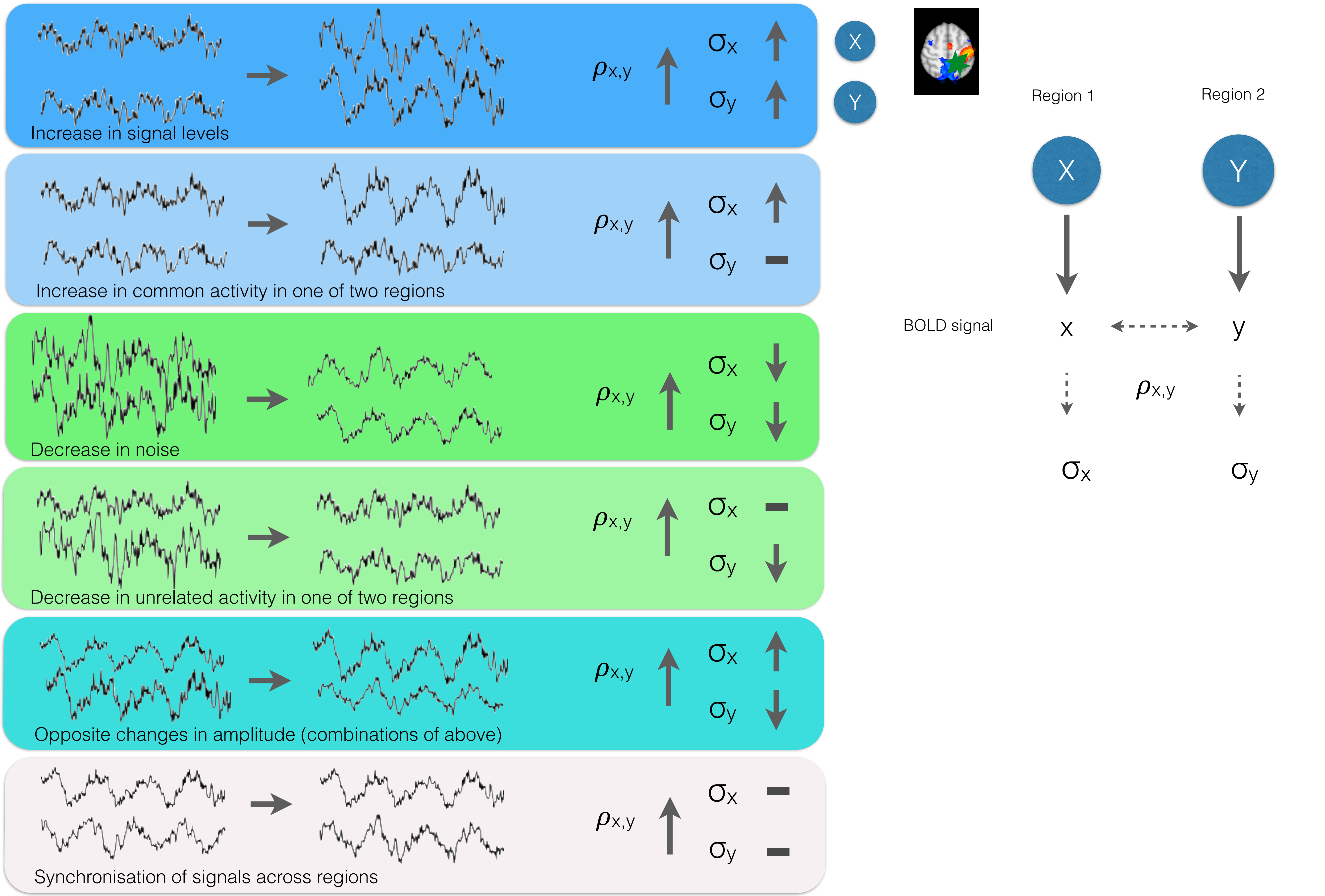
To identify a simple approach to characterising functional connectivity:

- that is less ambiguous
- remains a bivariate function for mapping and flexible implementation
- provides insight into effective connectivity network modelling methods (e.g. DCM, causal methods)

# Signal changes affecting correlations

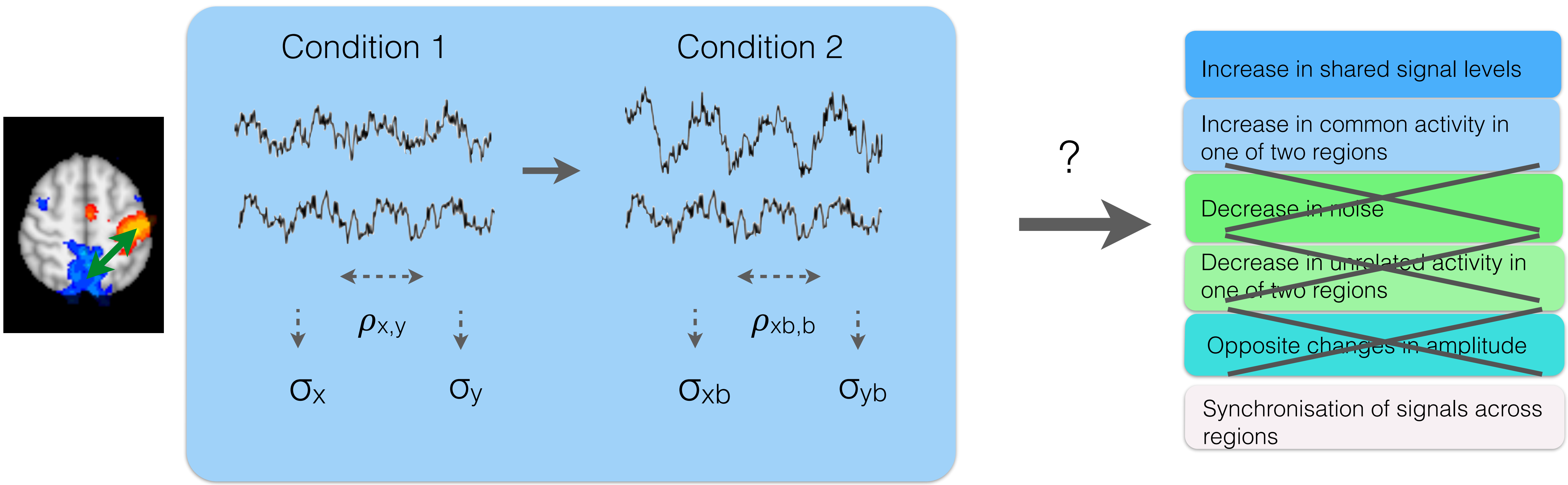


# Signal changes affecting correlations



# *Potential dynamics affecting connectivity*

By observing variances, we can eliminate the possibility of certain changes..



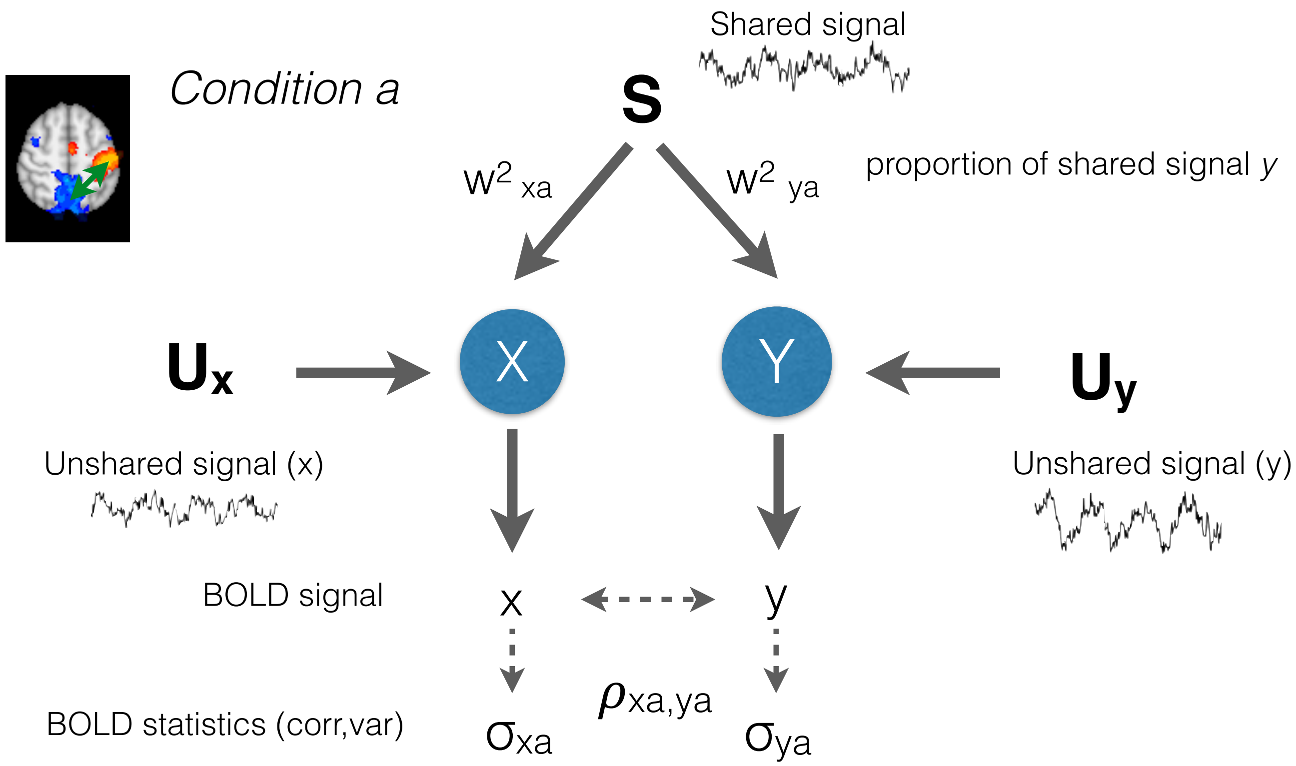

But the necessary extent of a change required to explain a specific change in correlation is unclear.

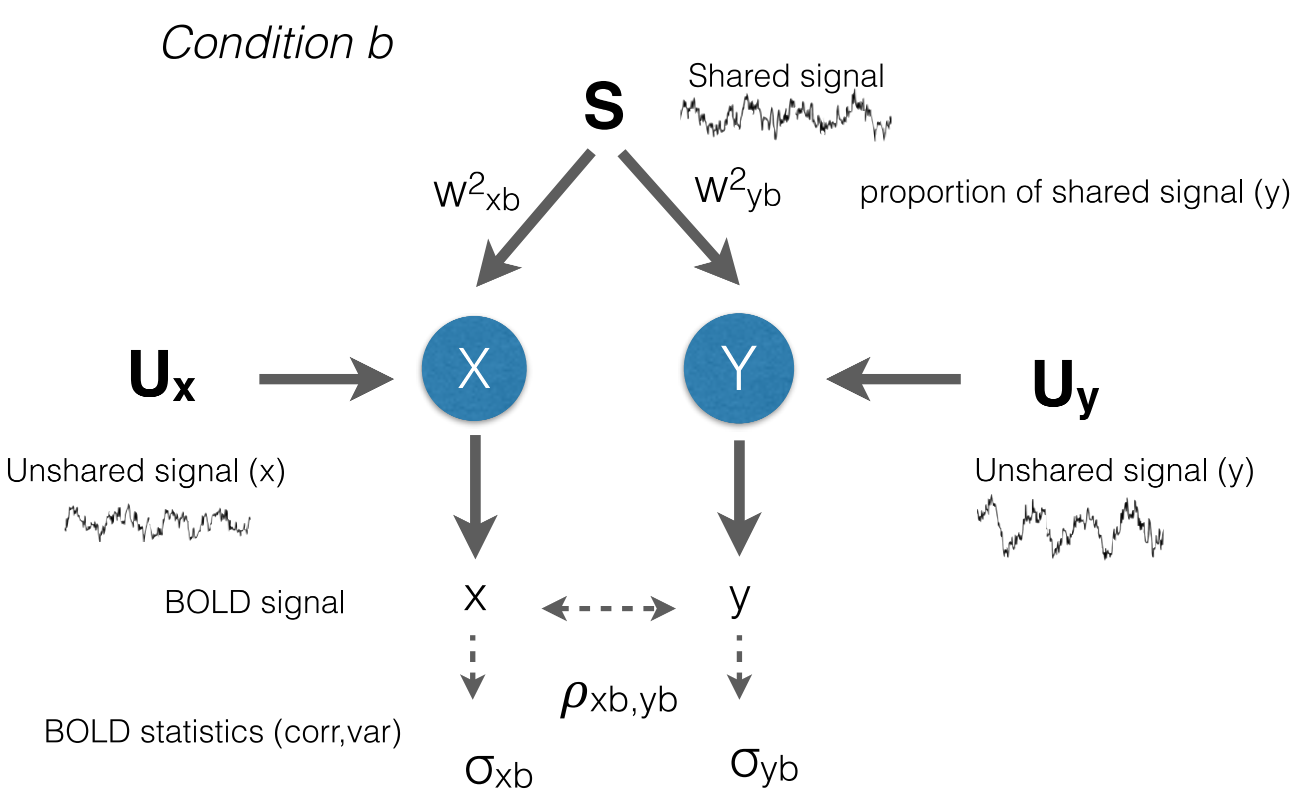
**Can we determine if certain variance changes explain a particular observed change?**

$$\rho_{x,y} \quad \sigma_x, \sigma_{xb} \; \sigma_y, \sigma_{yb} \longrightarrow a < \rho_{xb,yb} < b$$

# Shared/Unshared Signal Model

## Pairwise model linking regions X and Y.




## Model Formulation

BOLD signal for condition a as a function of S and Ux Uy.

$$x_a = \sigma_{x_a}(w_{x_a}\boldsymbol{S} + \sqrt{1 - w_{x_a}^2}\,\boldsymbol{U_x})$$

$$y_a = \sigma_{y_a}(w_{y_a}\boldsymbol{S} + \sqrt{1 - w_{y_a}^2}\,\boldsymbol{U_y})$$

Proportion of shared signal in each region is bounded by correlation

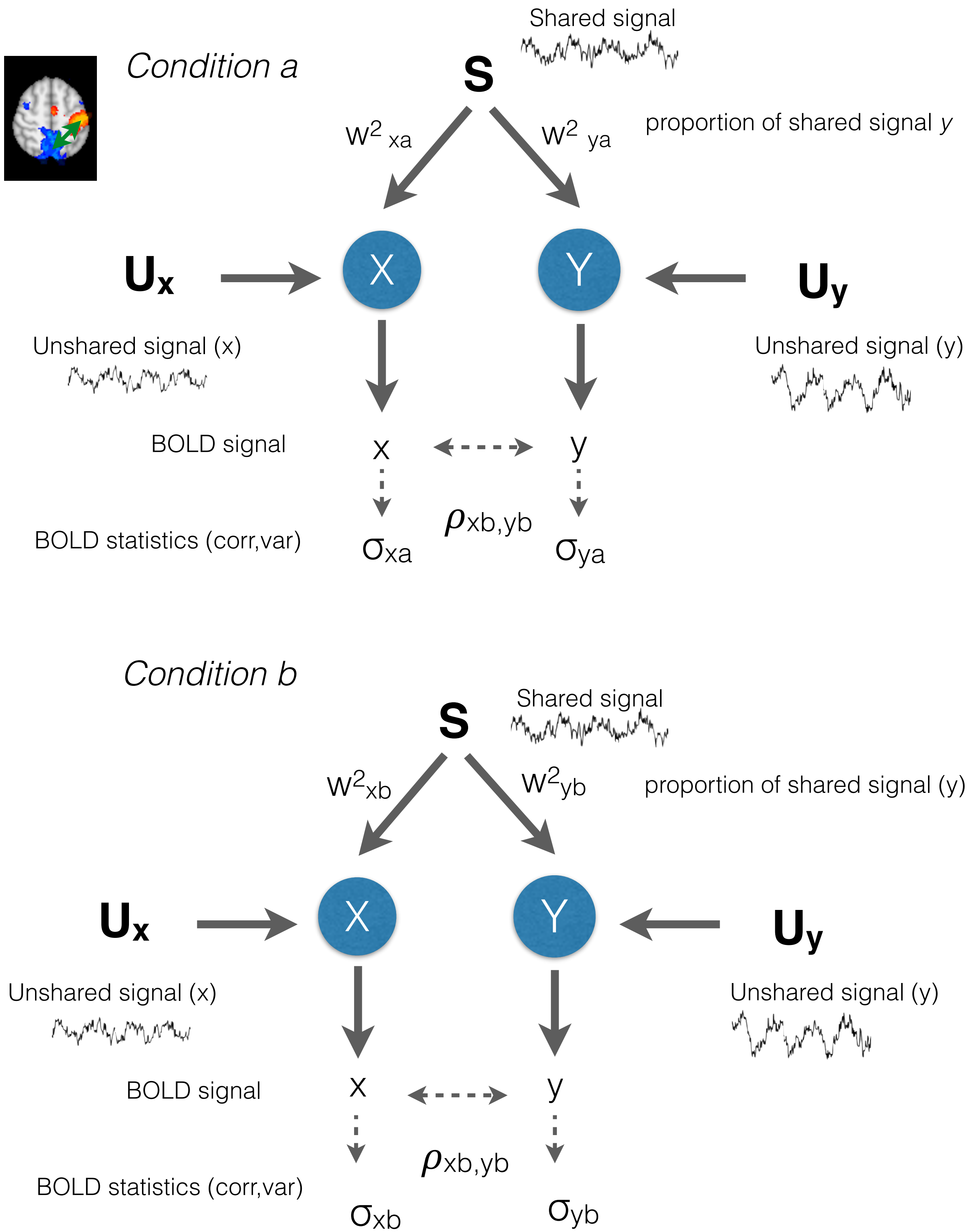
$$\rho_{x_a,y_a} = \frac{cov\left(x_a, y_a\right)}{\sigma_{x_a}\sigma_{y_a}}$$

$$\rho_{x_a,y_a} = \frac{w_{x_a}\sigma_{x_a}w_{y_a}\sigma_{y_a}}{\sigma_{x_a}\sigma_{y_a}}$$

$$\rho_{x_a,y_a} = w_{x_a}w_{y_a} \quad \longrightarrow \quad \rho_a < w_{x_a} < 1$$

# Shared/Unshared Signal Model

**Pairwise model linking regions X and Y.**




Condition b produces some change in levels of shared and unshared signals - $w_{xb} = c_x w_x$, $w_{yb} = c_y w_y$. , matching the total change in variance:

$$x_b = \sigma_{x_a}\left(c_x w_{x_a} \boldsymbol{S} + u_x \sqrt{1 - w^2_{x_a}} \cdot \boldsymbol{U_x}\right)$$
$$= \sigma_{x_b}\left(\frac{\sigma_{x_a}}{\sigma_{x_b}} c_x w_{x_a} \boldsymbol{S} + \frac{\sigma_{x_a}}{\sigma_{x_b}} u_x \sqrt{1 - w^2_{x_a}} \cdot \boldsymbol{U_x}\right)$$

New observed variance can be expressed:

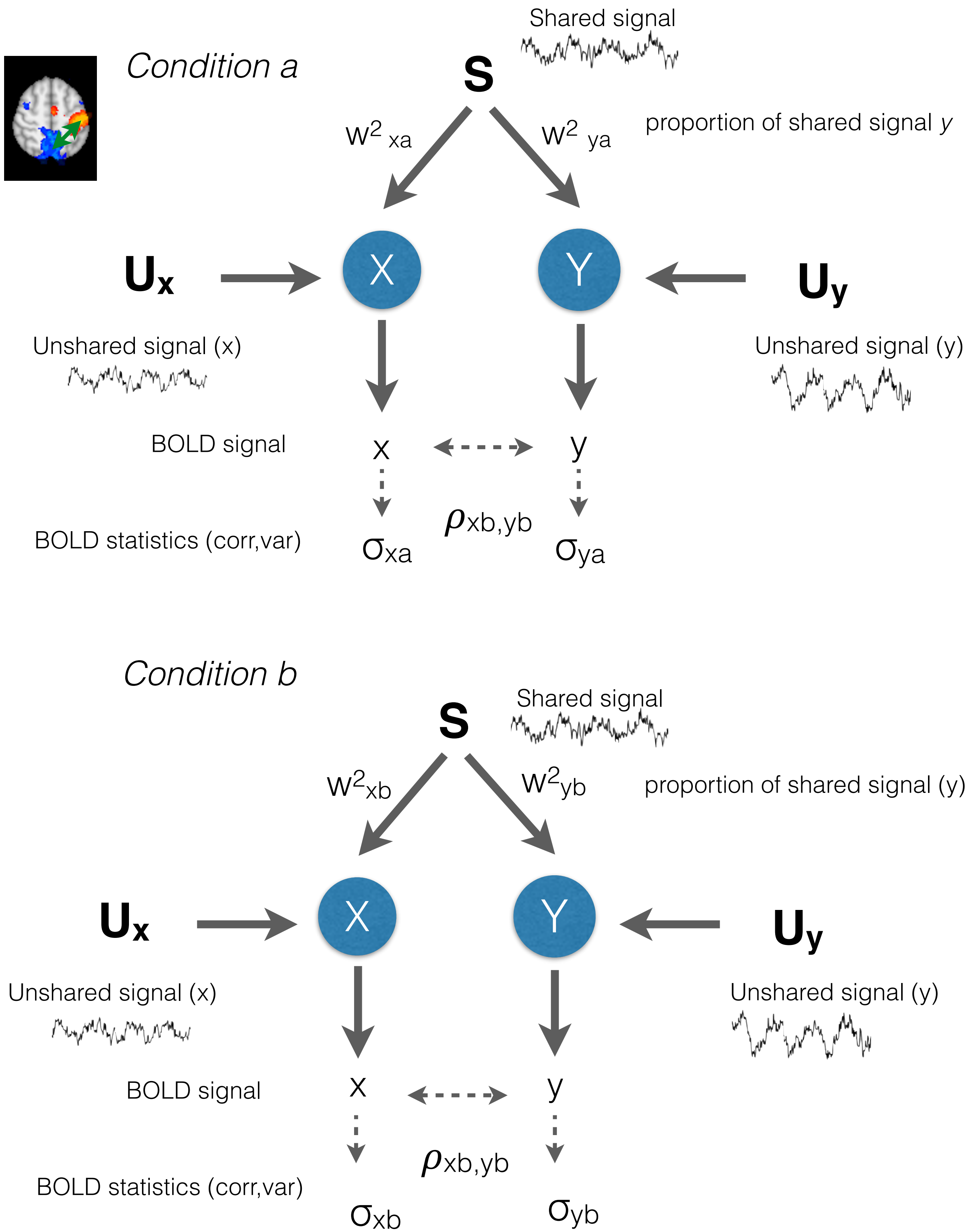
$$\sigma^2_{x_b} = \sigma^2_{x_a}\left(c_x^2 w^2_{x_a} + u_c^2\left(1 - w^2_{x_a}\right)\right)$$

And correlation:

$$\rho_b = \rho_a \frac{\sigma_{x_a}}{\sigma_{x_b}} \frac{\sigma_{y_a}}{\sigma_{y_b}} c_x c_y$$

# Shared/Unshared Signal Model

**Pairwise model linking regions X and Y.**



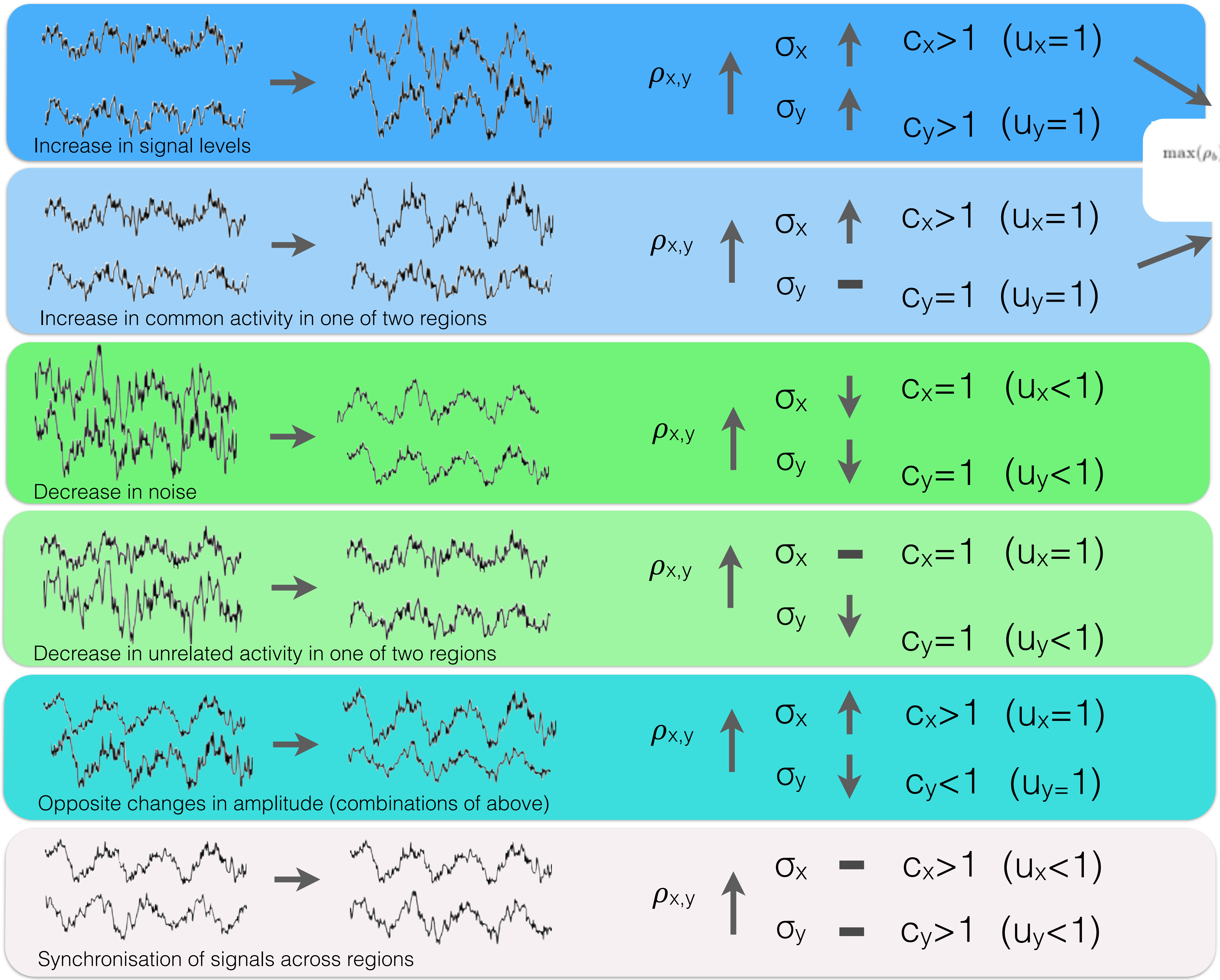

$$
\begin{aligned}
\rho_b &= \rho_a \frac{\sigma_{x_a}}{\sigma_{x_b}} \frac{\sigma_{y_a}}{\sigma_{y_b}} c_x c_y \\
&= \rho_a \frac{\sigma_{x_a}}{\sigma_{x_b}} \frac{\sigma_{y_a}}{\sigma_{y_b}} \sqrt{\frac{\sigma_{x_b}^2}{\sigma_{x_a}^2} - u_x^2\left(1 - w_{x_a}^2\right)} \cdot \frac{1}{w_{x_a}} \sqrt{\frac{\sigma_{y_b}^2}{\sigma_{y_a}^2} - u_y^2\left(1 - w_{y_a}^2\right)} \cdot \left|\frac{w_{x_a}}{\rho_a}\right| \\
&= \operatorname{sign}(\rho_a) \sqrt{1 - \frac{\sigma_{x_a}^2}{\sigma_{x_b}^2}\left(u_x^2 - w_{x_a}^2\right)} \sqrt{1 - \frac{\sigma_{y_a}^2}{\sigma_{y_b}^2}\left(u_y^2 - \frac{\rho_a^2}{w_{x_a}^2}\right)}
\end{aligned}
$$

Given the limits on $w_{ay}$, the effects of particular changes in signal and noise on $\rho_{xb,yb}$ can be determined based on variance changes.

E.g. if there was no change in signal levels (variance was associated with unshared signal):

$$
\rho_b = \rho_a \frac{\sigma_{x_a}}{\sigma_{x_b}} \frac{\sigma_{y_a}}{\sigma_{y_b}}
$$

# *Identifying bounds on correlation*

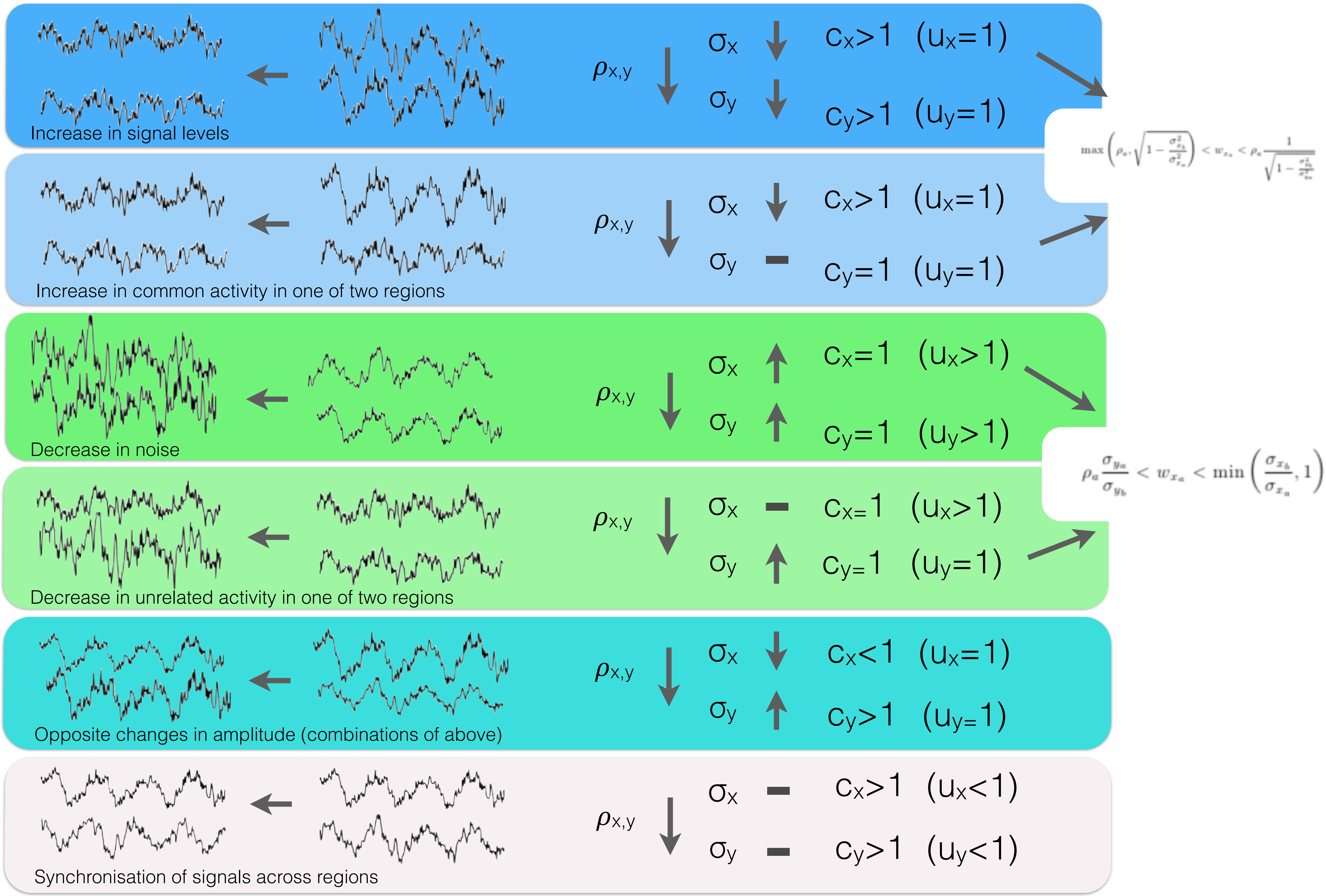



$$\max(\rho_b) = \mathrm{sign}(\rho_a)\sqrt{1 - m\,(1-\rho_a^2)},$$

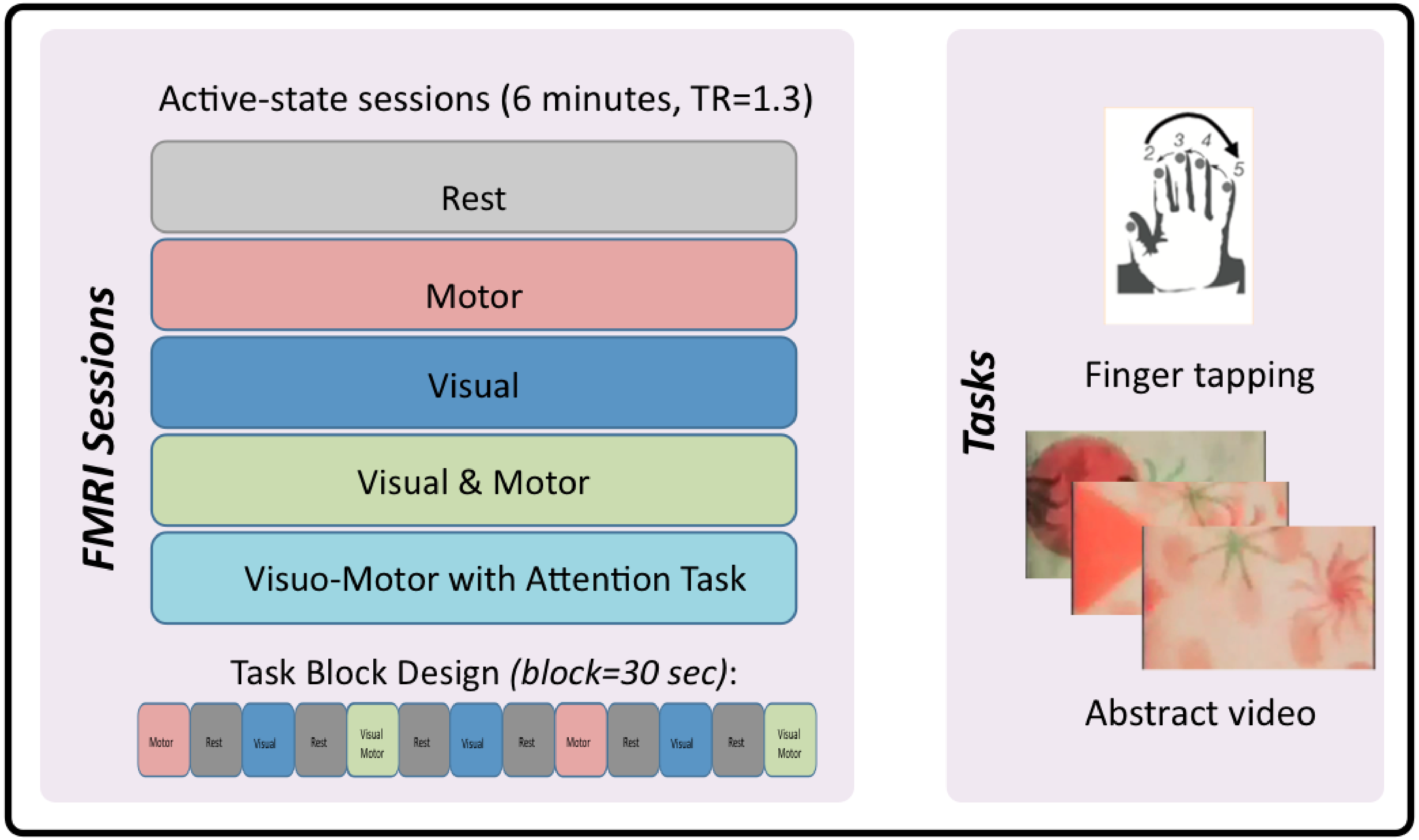
$$\text{where} \quad m = \min\left(\frac{\sigma_y^2}{\sigma_y^2}, \frac{\sigma_x^2}{\sigma_x^2}\right)$$

$$\rho_b = \rho_a \frac{\sigma_{x_a}}{\sigma_{x_b}} \frac{\sigma_{y_a}}{\sigma_{y_b}}$$

# Potential dynamics affecting connectivity



# Active-state experiment

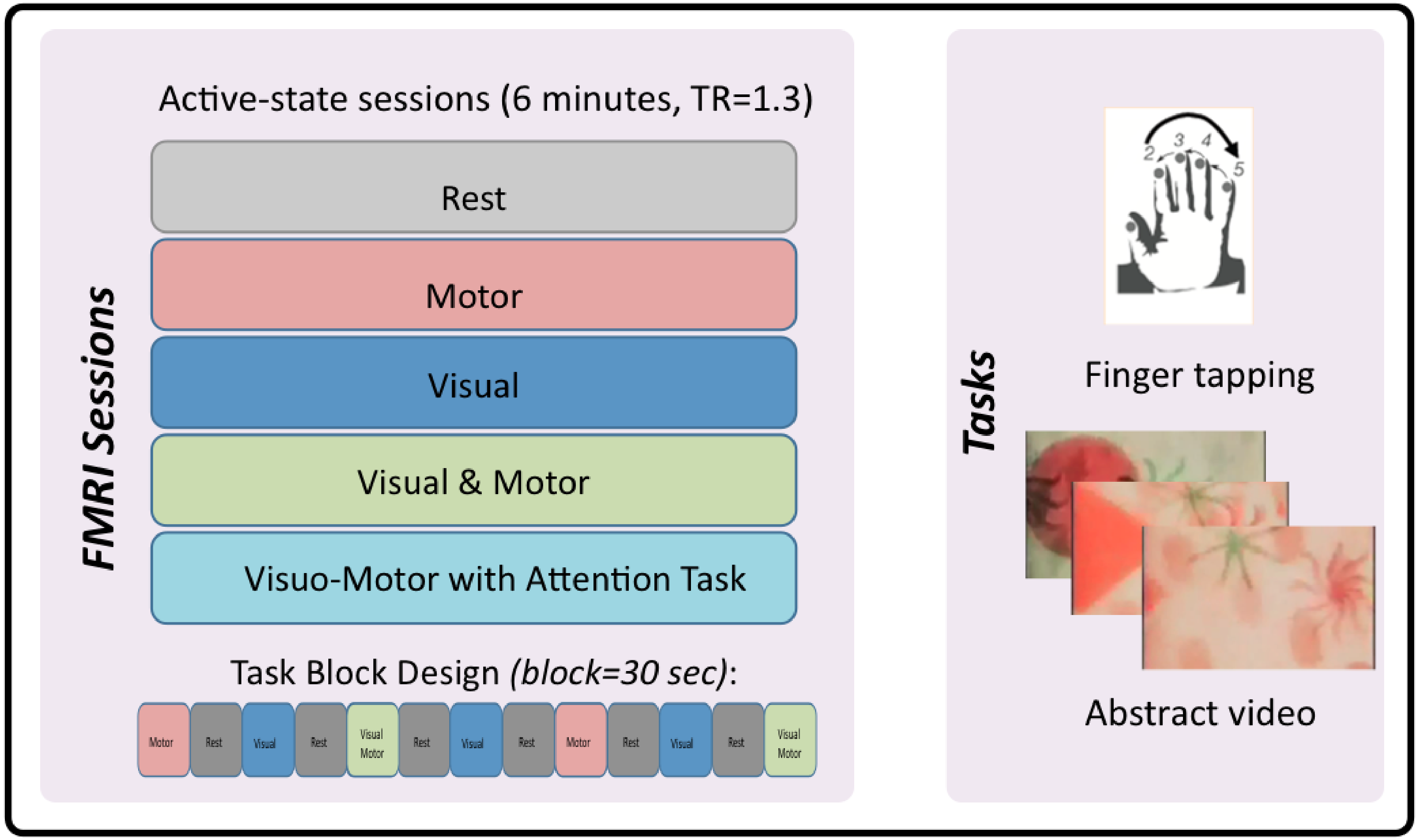



16 Subjects

Multiband-6 TR: 1.3, 2x2x2mm voxels

Five active-state conditions produce robust changes in ongoing dynamics providing a good testing set for connectivity measures.

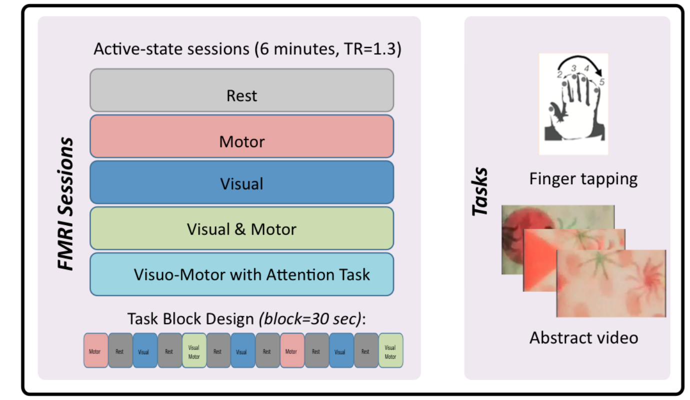
# Active-state experiment

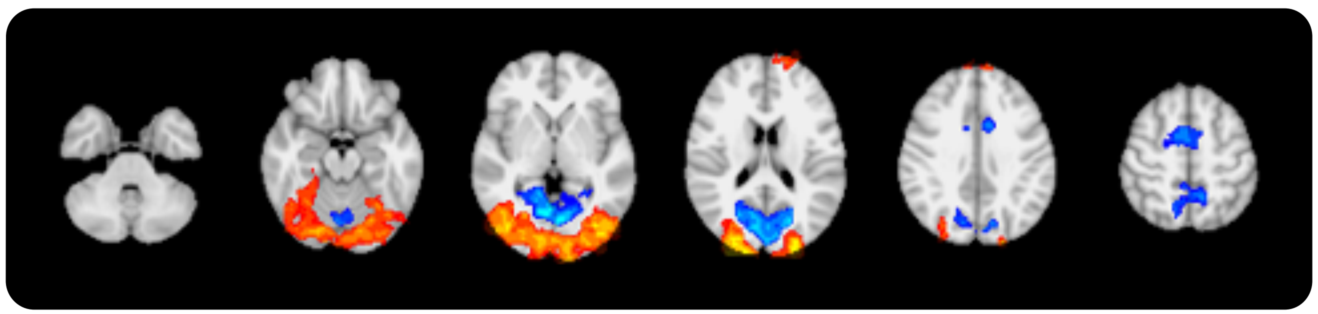



Are changes in connectivity across associated with variance changes?

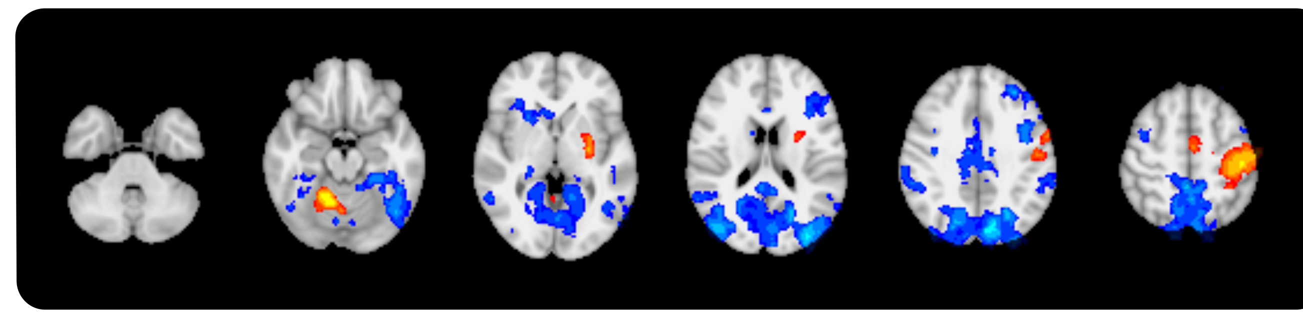
Do these changes correspond to particular types of changes in connectivity - are they predicted by model?

# *Activation, variance, and correlation changes*

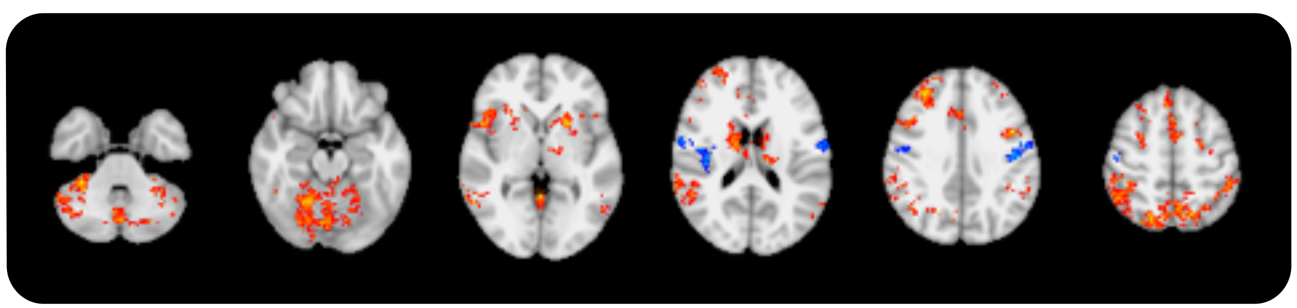


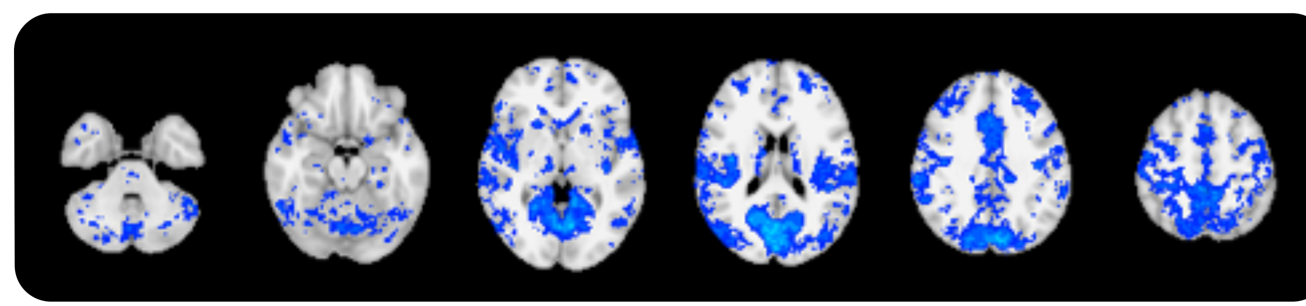
Visual task activation



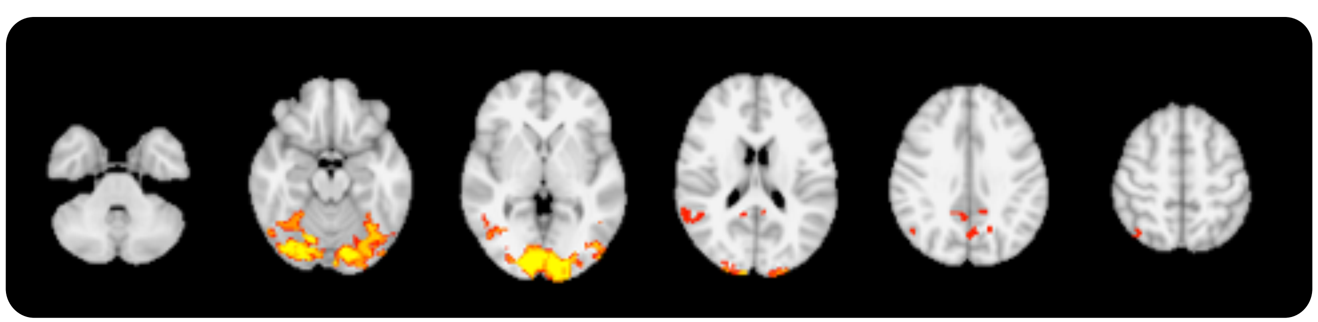
Motor task activation



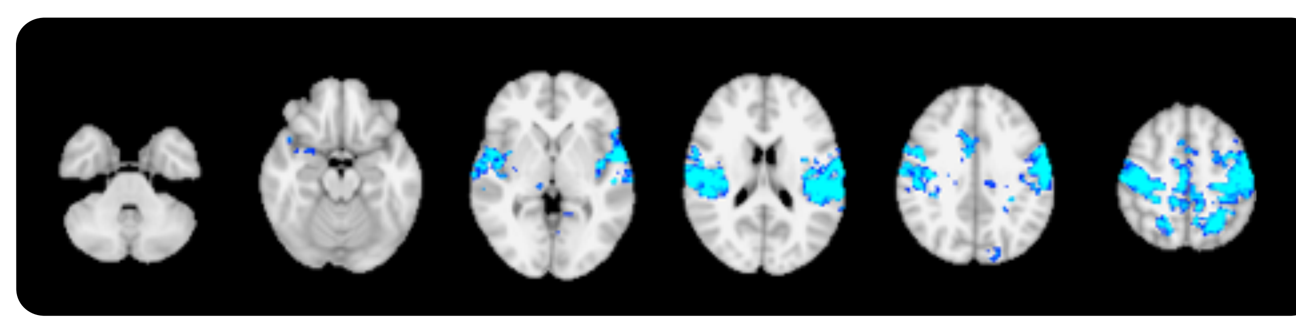
Connectivity change from rest for visual condition (V1 seed)



Connectivity change from rest for visual condition (V1 seed)

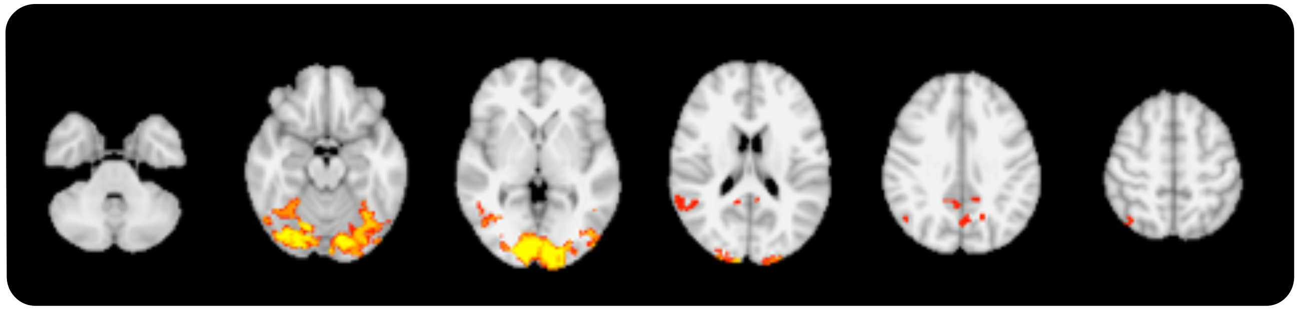


Variance changes from rest for visual condition

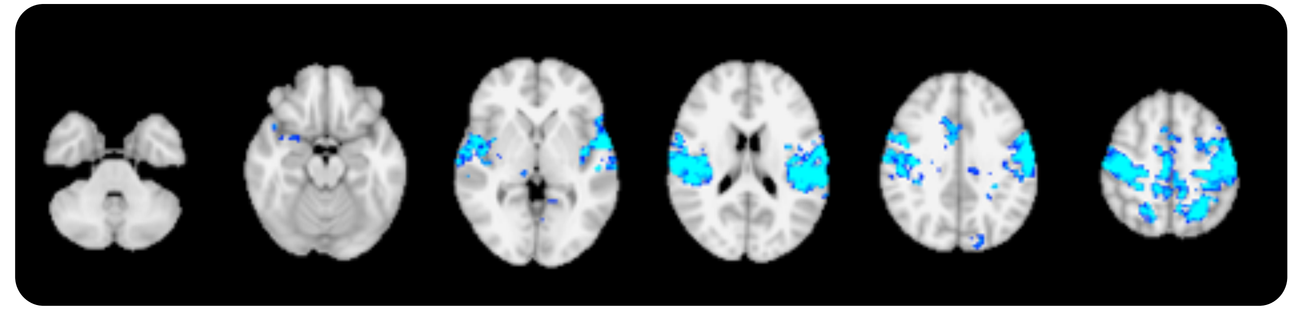


Variance changes from rest for motor condition

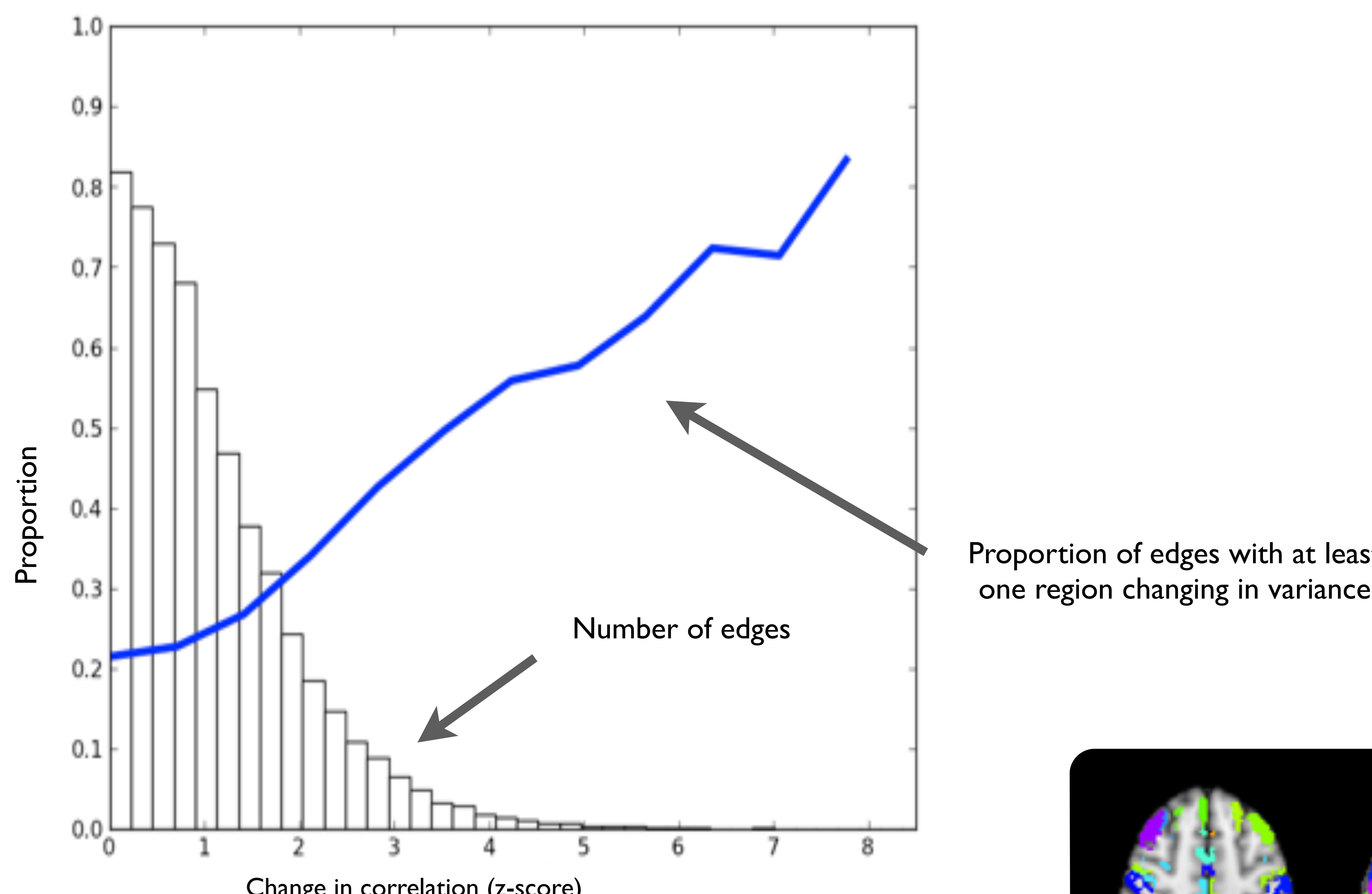
# Activation, variance, and correlation changes

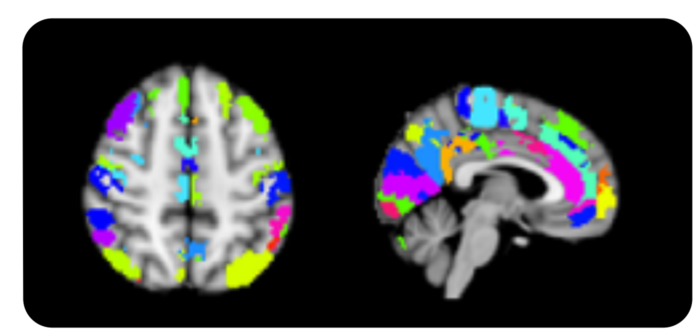


Variance changes from rest for visual

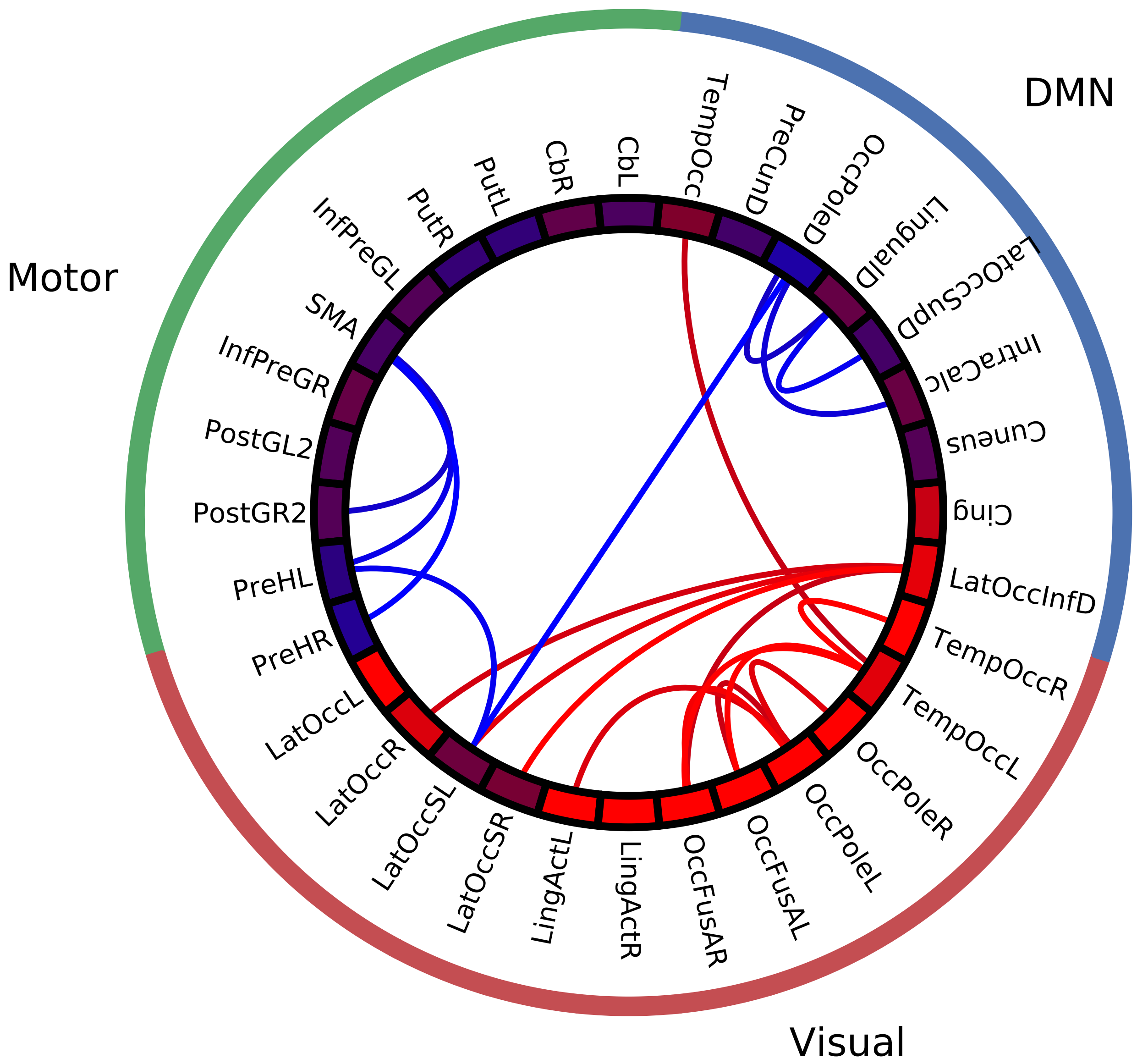


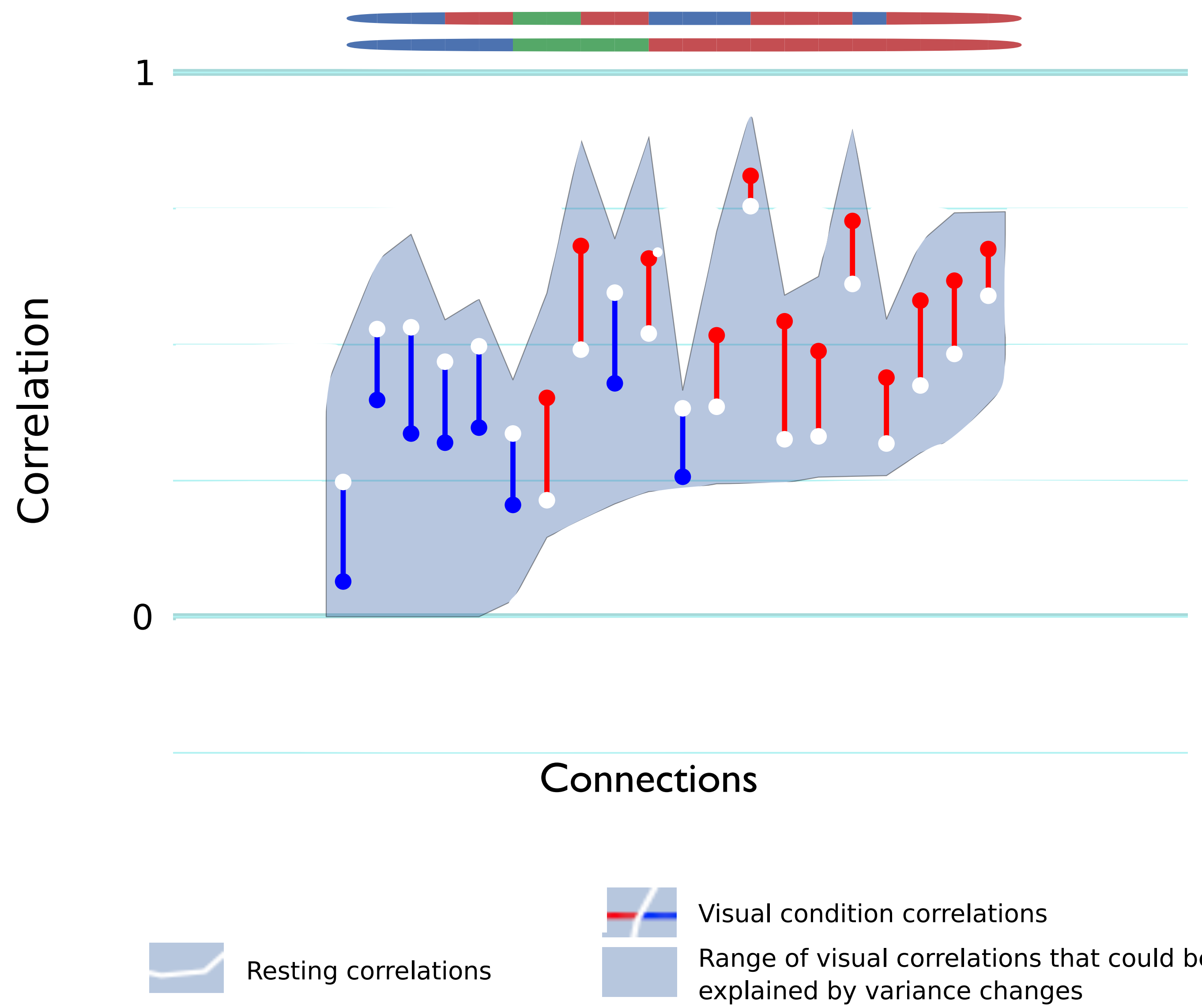
Variance changes from rest for motor



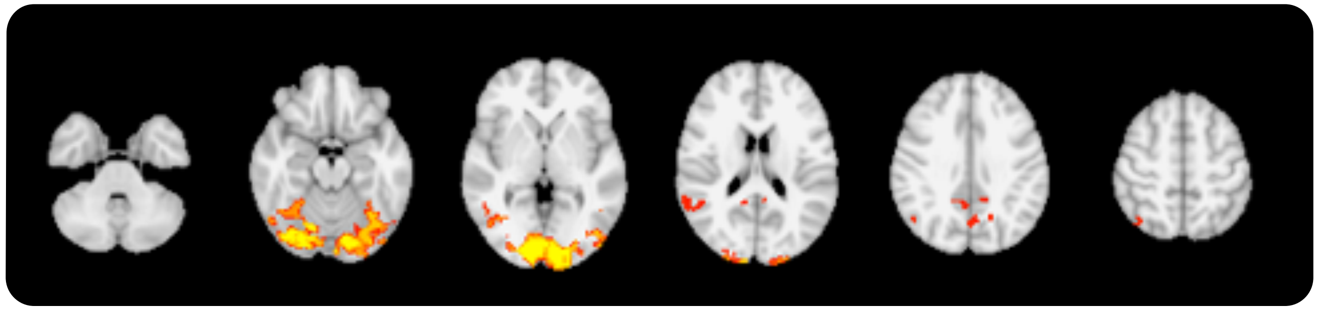



# Representing connectivity changes

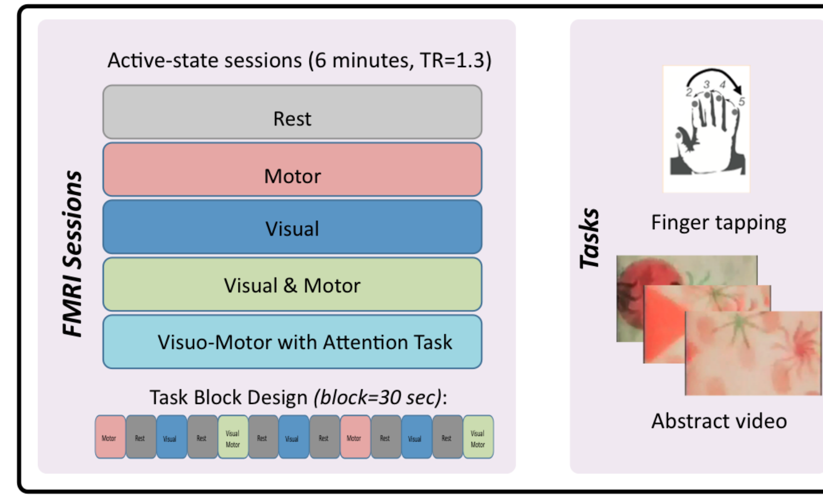


# Changes between visual condition and rest



Variance changes from rest for visual condition

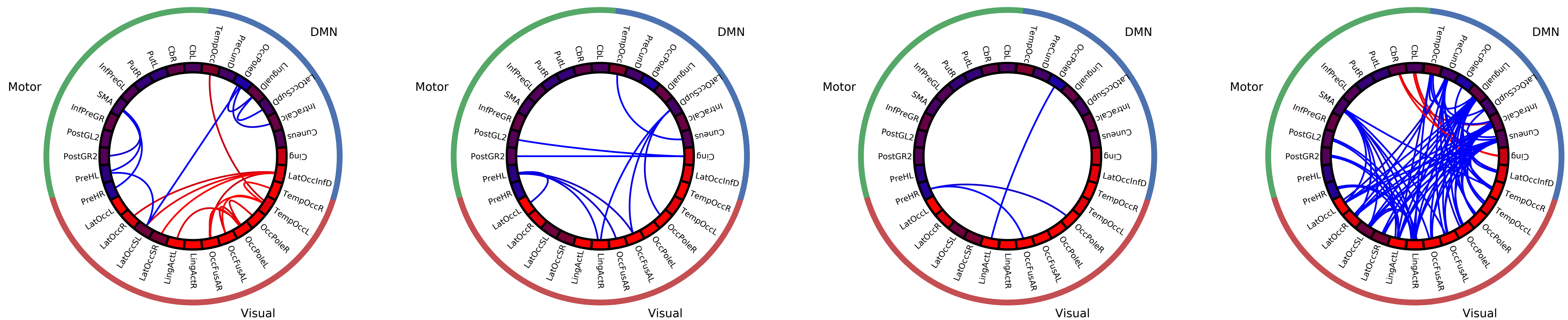


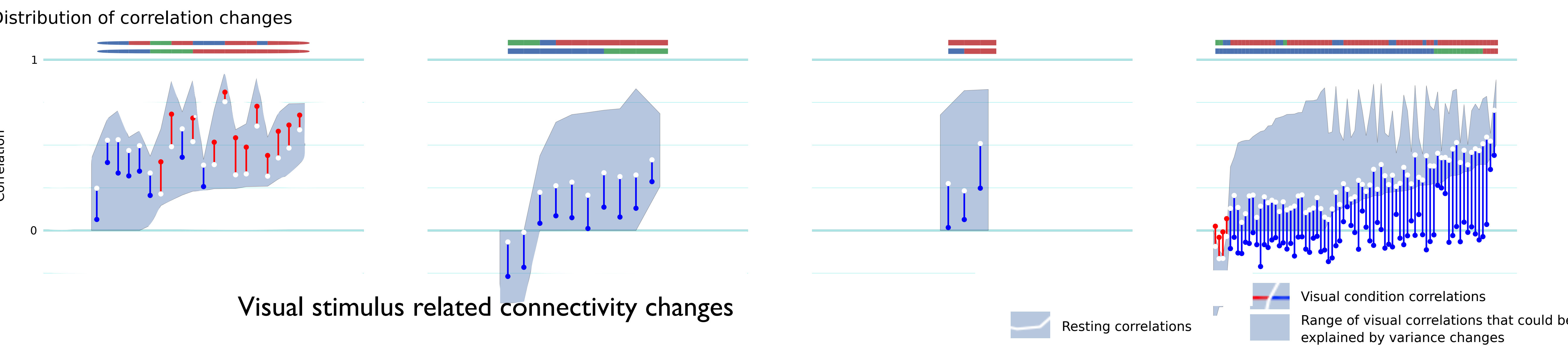

Change in Shared Signal

Change in Unshared Signal

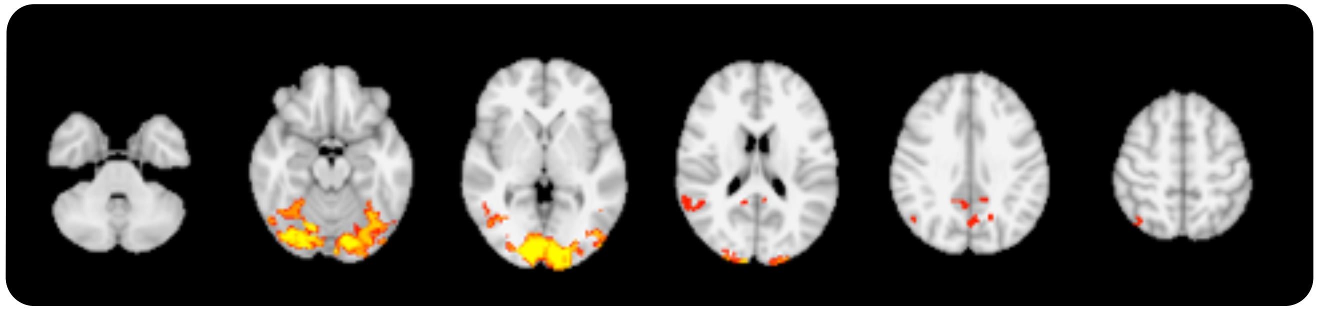
Change in Shared Signal

Changes that can't be explained by SNR changes

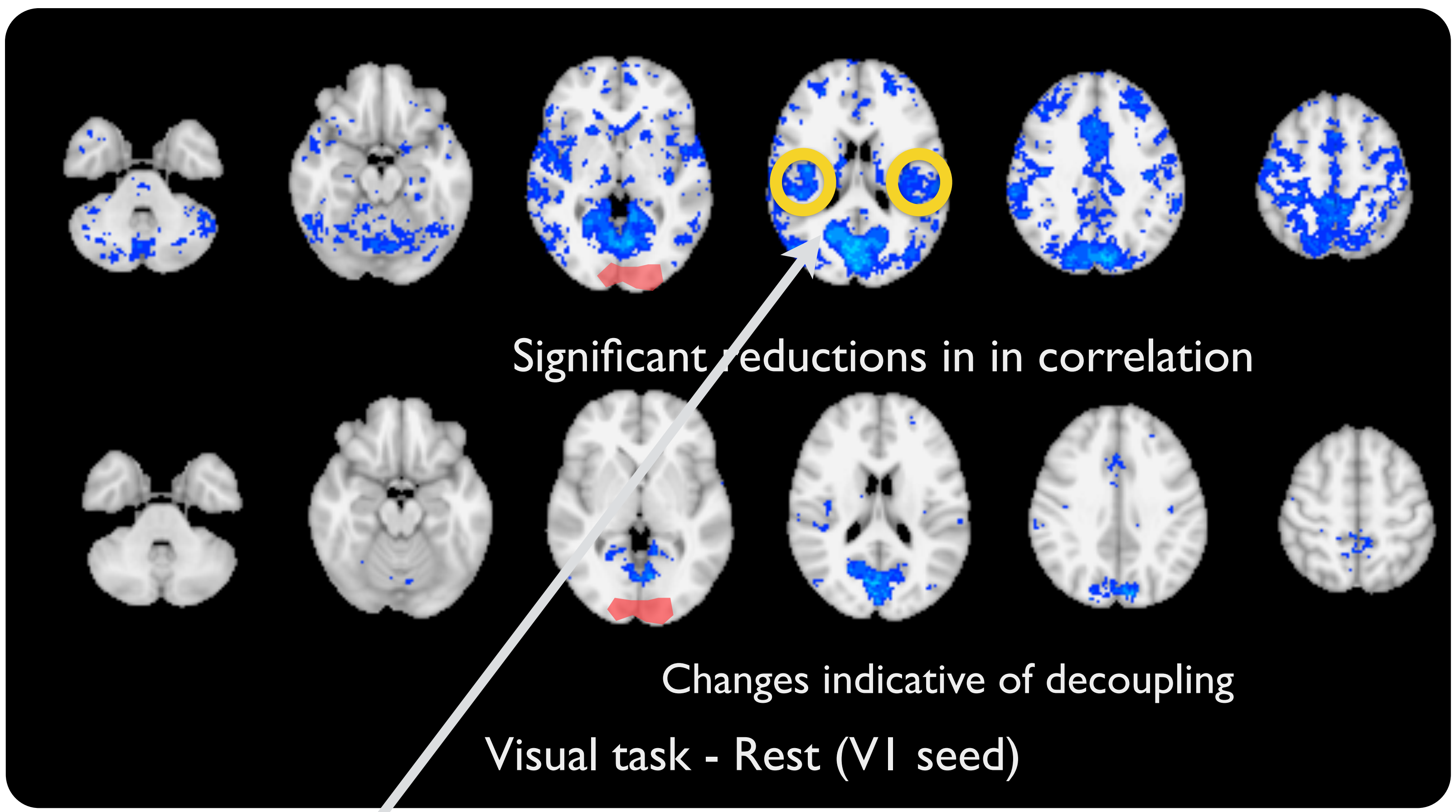


# *Changes between visual condition and rest*



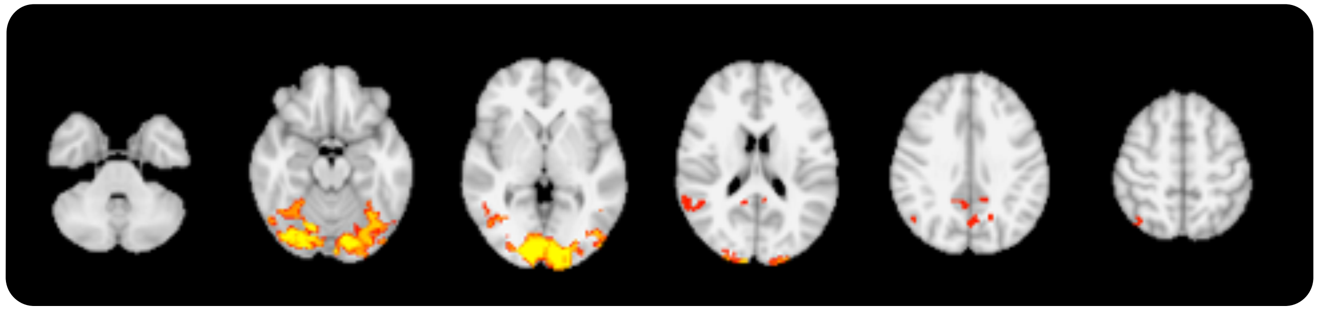
Variance changes from rest for visual condition



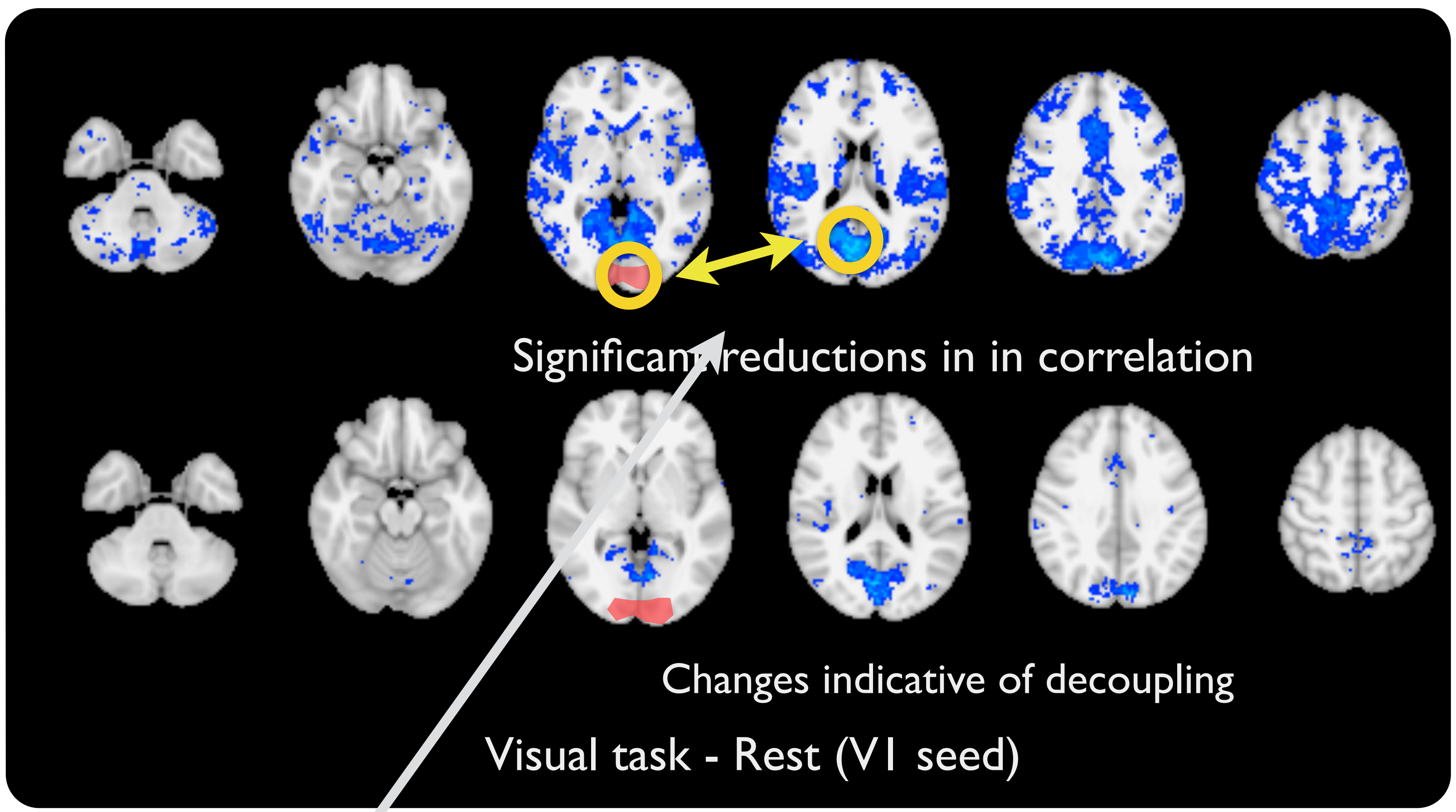

Correlation changes from rest for visual

Reduction in shared signal

# *Changes between visual condition and rest*



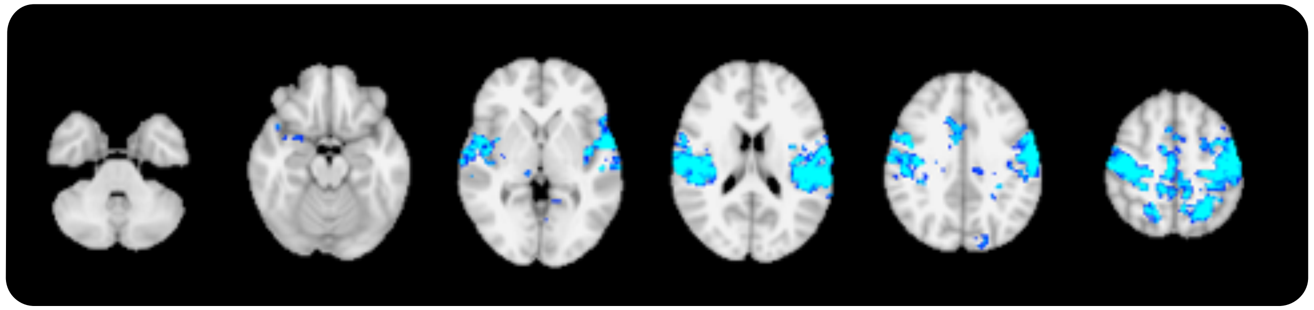
Variance changes from rest for visual condition



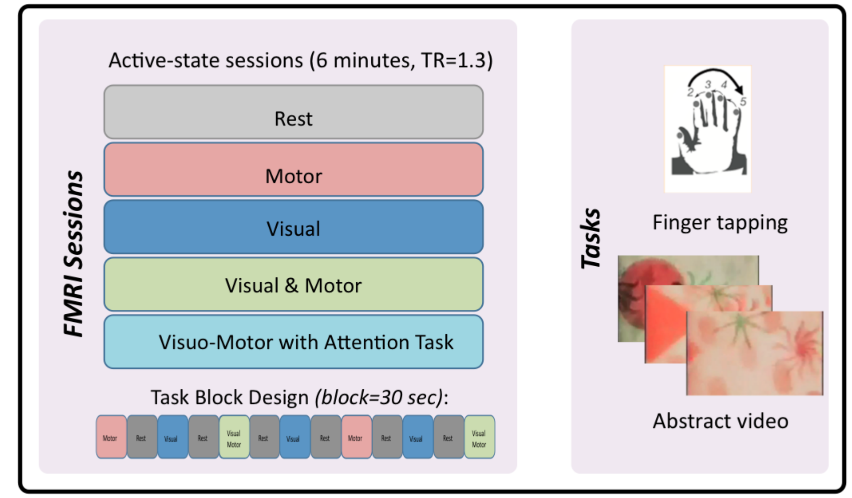

Correlation changes from rest for visual

Decoupling

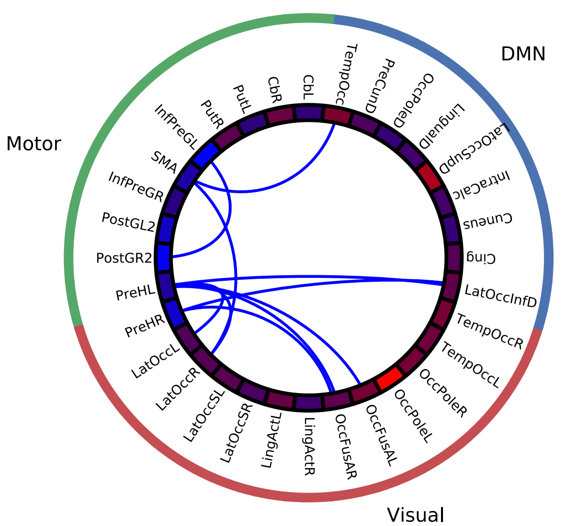
# Changes between motor condition and rest



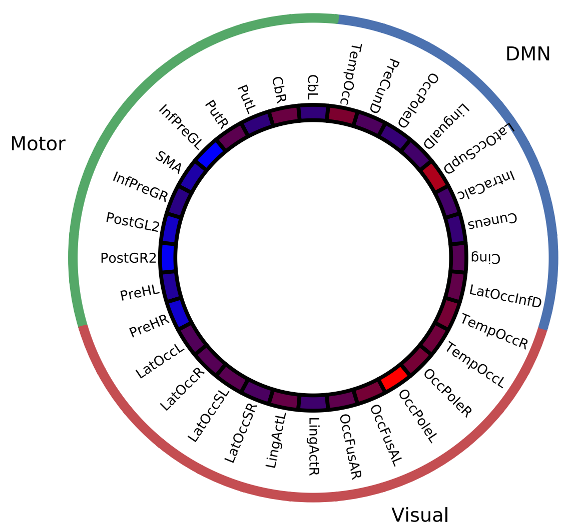
Variance changes from rest for motor condition



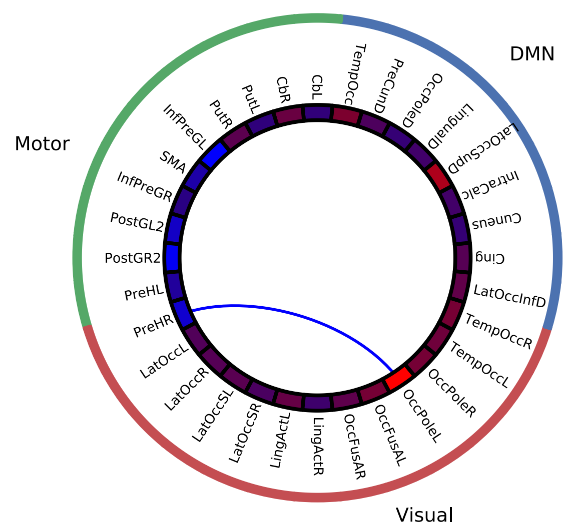

Change in Shared Signal



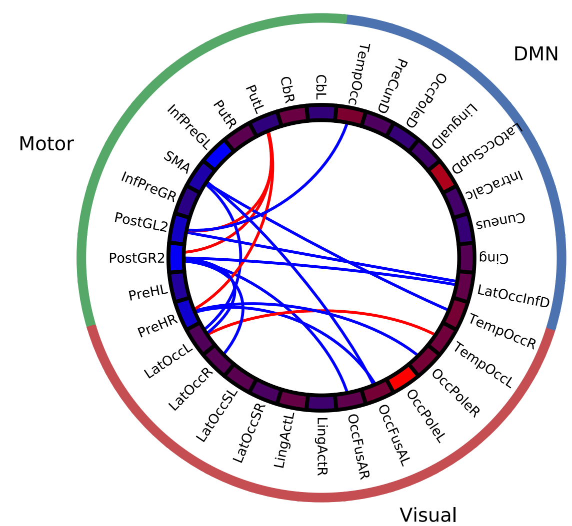

Change in Unshared Signal

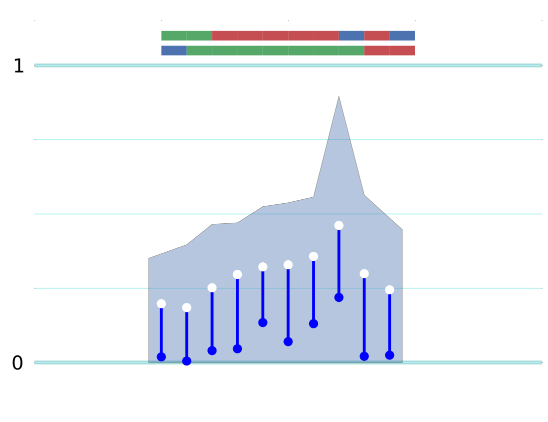


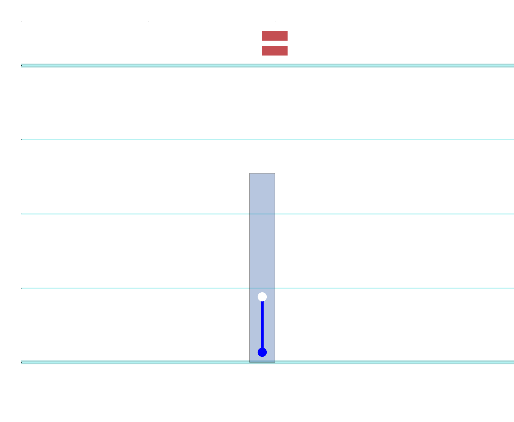

Change in Shared Signal

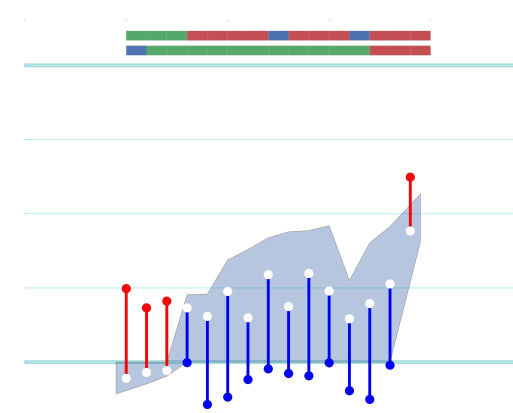



Changes that can't be explained by SNR changes





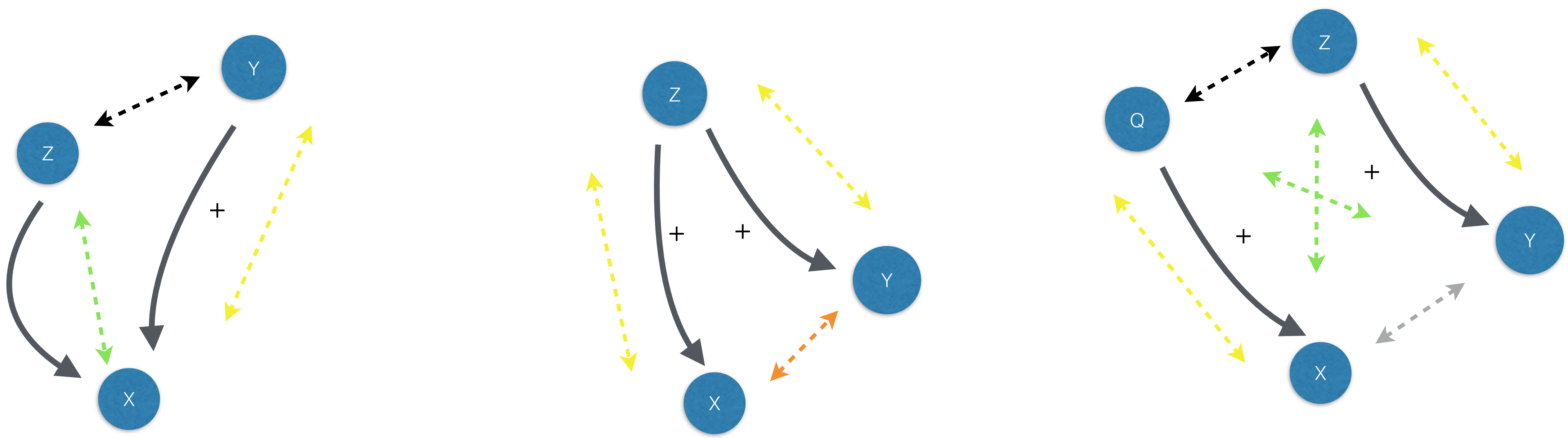
Motor stimulus related connectivity changes

Resting correlations

Visual condition correlations

Range of visual correlations that could be explained by variance changes

# Relation to network modelling (e.g. DCM)




Examples of relationship between directed network models (solid arrows) and pairwise correlation/variance assessment (broken arrows).

**+** - a connection that strengthens across conditions

Joint increase in unshared signal.

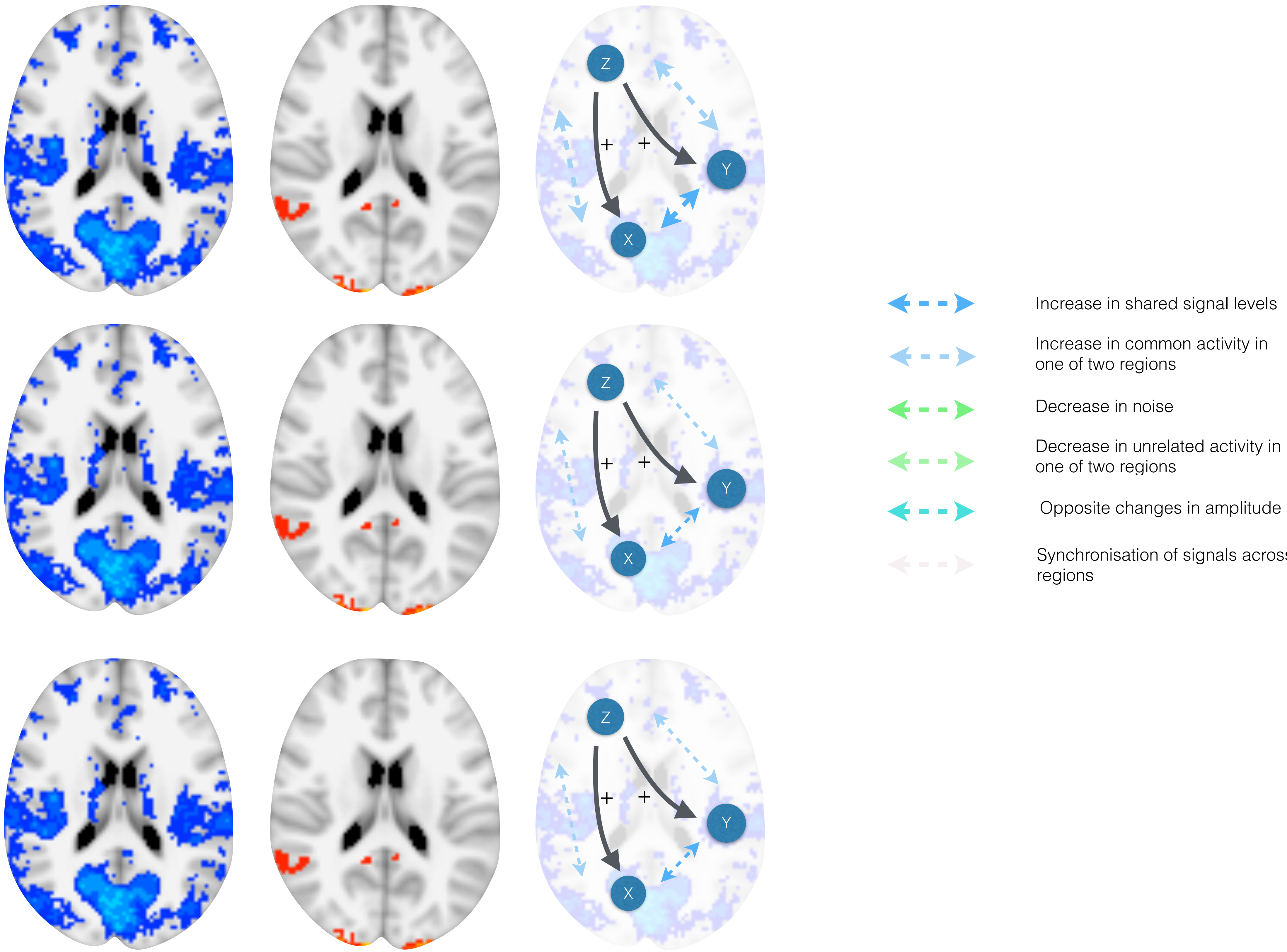
Joint increase in shared signal.

Increase in shared signal in one region.

Increase in unshared signal in one region.

No change

# *Relation to network modelling (e.g. DCM)*



# Summary

We have identified a simple model that links correlation and variance to provides insight into the types of dynamics underlying connectivity changes

In a test dataset we could find almost every proposed feature of dynamics

Most changes in correlation are accompanied by some change in variance

DCM models typically predict variance changes, so are validated by these results

Software is in development

# Future directions

Application to population studies (HCP,DHCP) - cross subject variance

Smooth integration with functional connectivity and DCM analyses

More signal components: relationship to ICA?