

MODEL-FREE ANALYSIS OF FMRI

Turku PET Centre Brain Imaging Course 2025

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Features of model-based analyses

- Require hypotheses
 - What do we now and expect to happen in the brain?
- Estimation of haemodynamic response function
 - What does the brain response look like?
 - Unlikely similar in all brain areas
- Interpretational difficulties with complex models
 - Did we answer to this question with this model?
- A ton of researcher degrees of freedom
 - Replicability of the findings?

Model-free analysis techniques

Blind signal separation

- Independent component analysis (ICA) & principal component analysis (PCA)

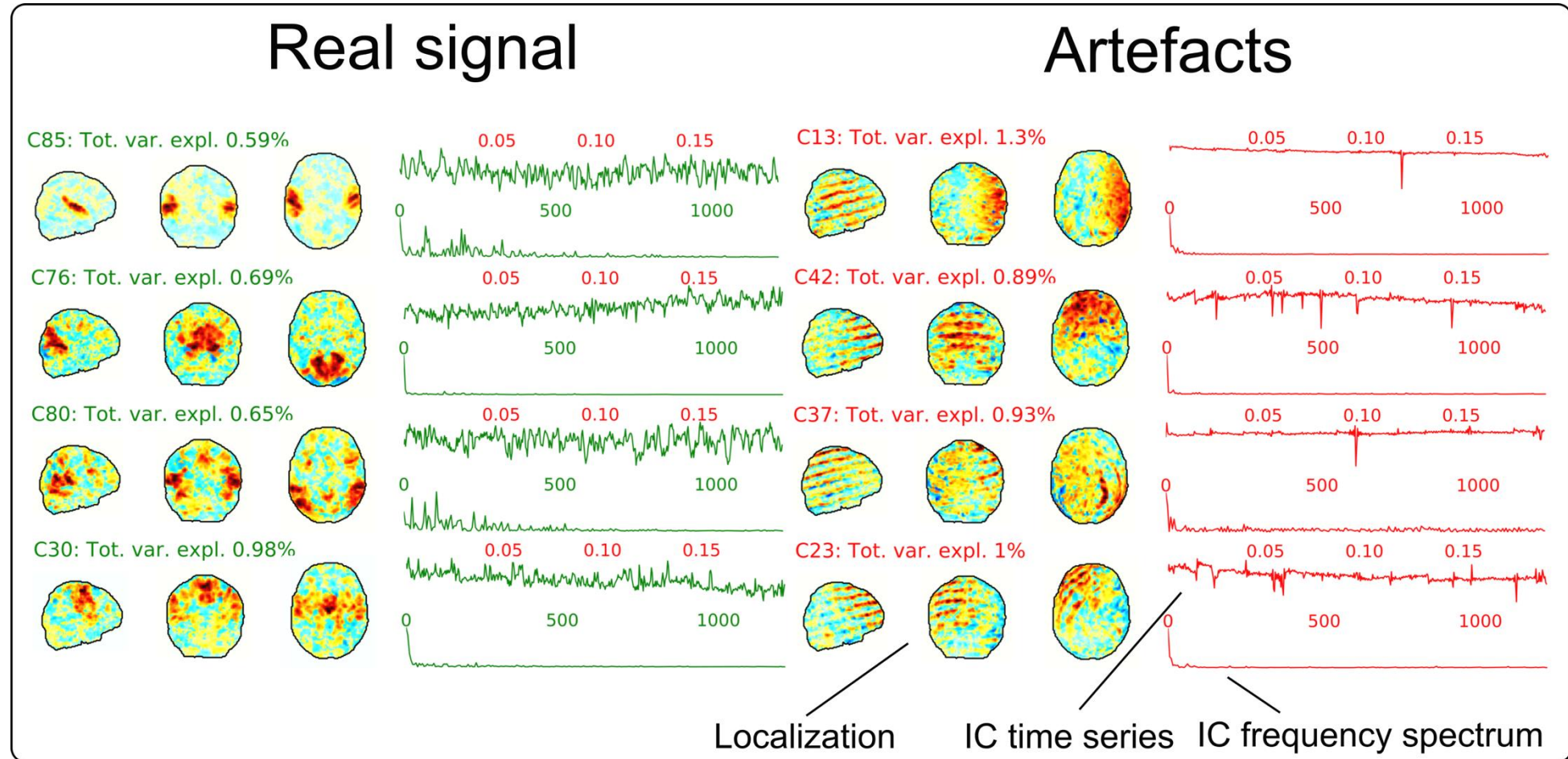
Synchronization analyses

- Intersubject correlation analysis (ISC)
- Time-window ISC analysis
- Intersubject phase synchronisation analysis (ISPS)
- Intersubject functional connectivity analysis (ISFC)

Blind signal separation

- **Motivation:** To extract different or mutual sources of information from a set of variables without prior knowledge
- **Input data**
 - Audio signals from different microphones
 - fMRI signals from different voxels / brain areas
- **Independent component analysis (ICA)**
 - Finds independent sources of information
 - E.g. separates two different speakers from mixed audio signals
- **Principal component analysis (PCA)**
 - Finds uncorrelated components that explain the mutual variance of the source signals
 - Shared component between two speakers, audio intensity?

Independent component analysis (ICA)



Topics

Basic concept of
intersubject synchrony
of brain activation



Methods to measure
intersubject synchrony



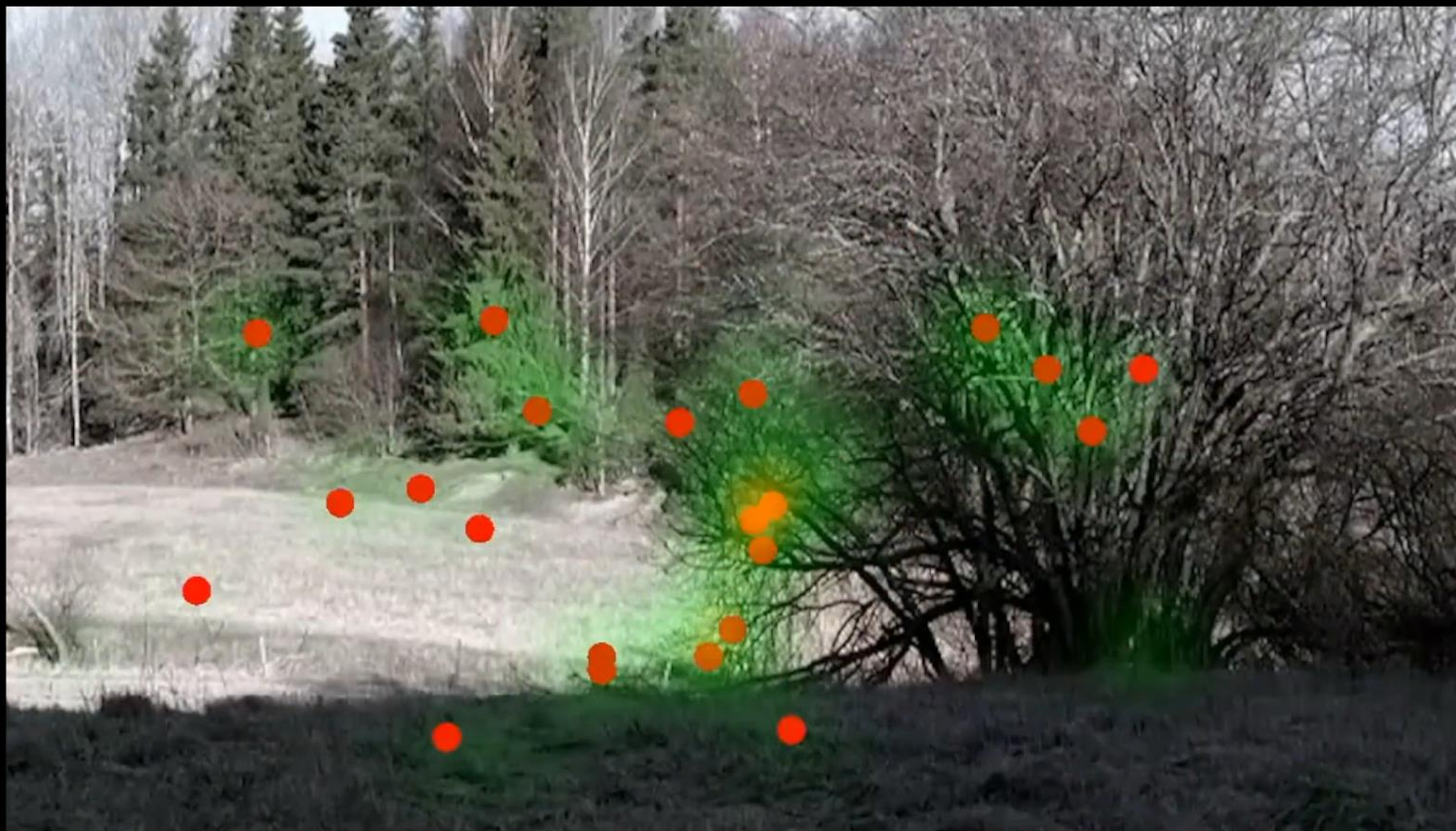
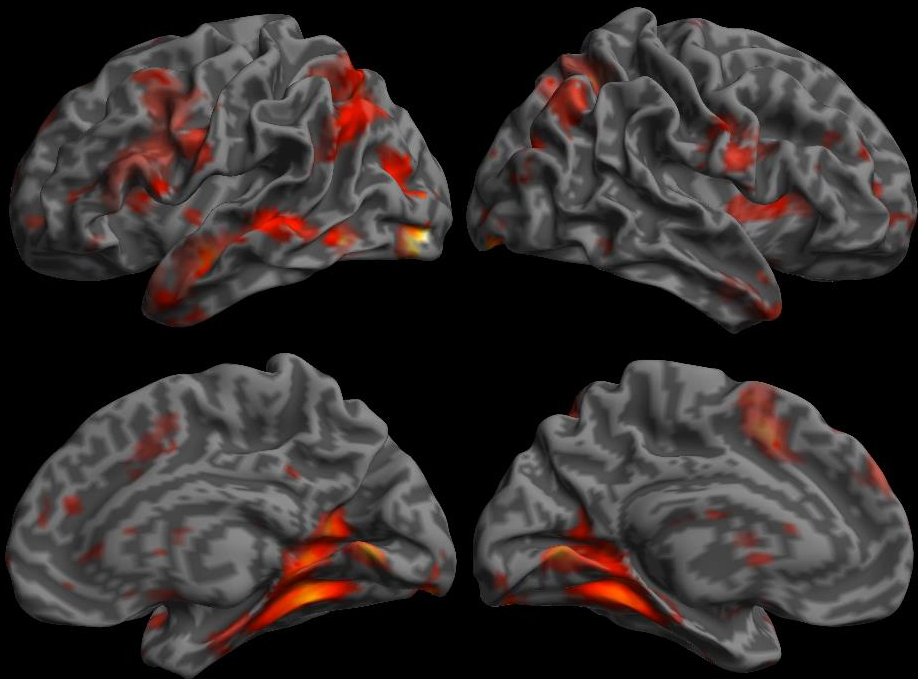
Statistical testing in
synchronization
analyses

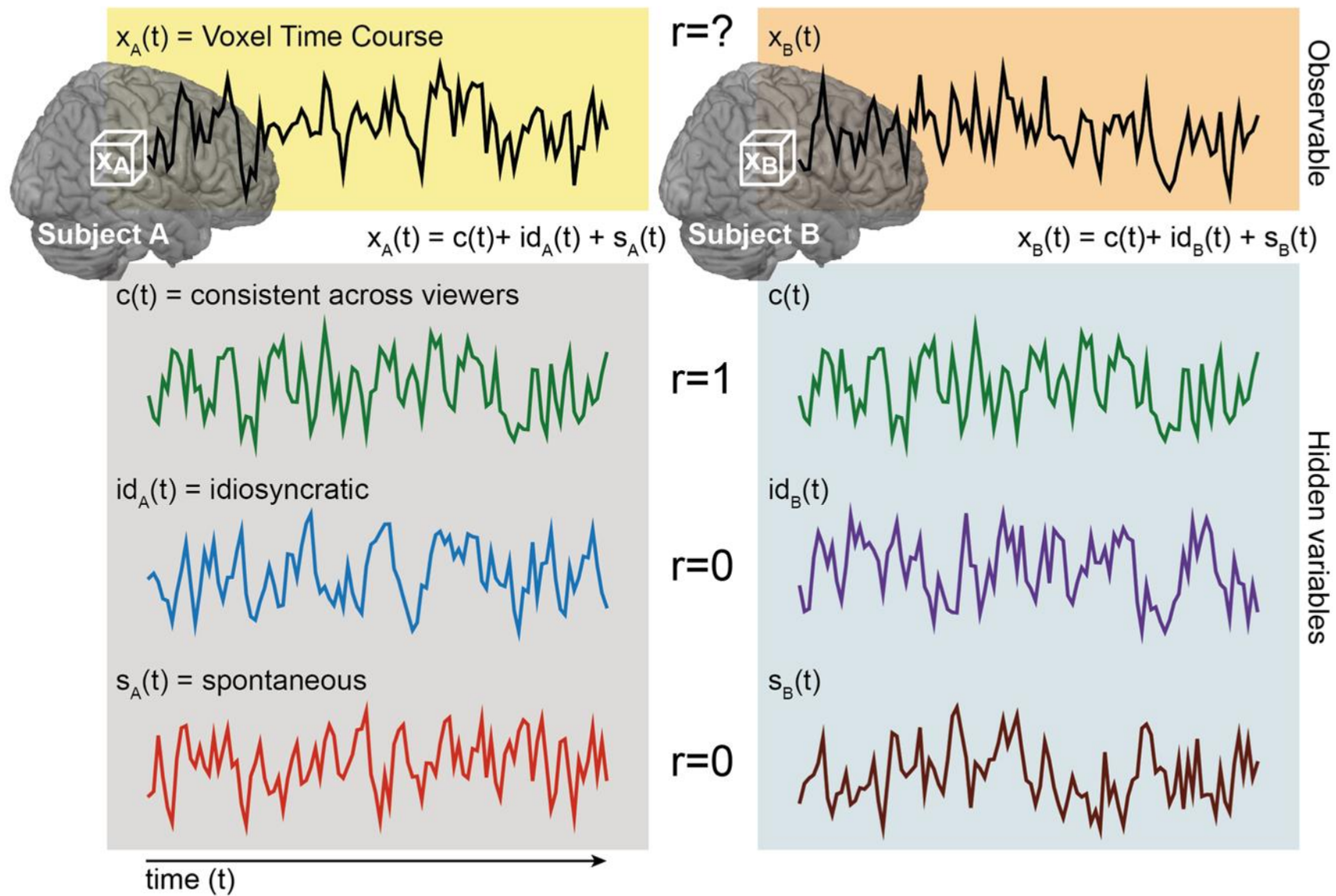


ISC toolbox for ISC
analysis

Films induce consistent brain activation across subjects

(Hasson, Nir, Levy, Fuhrmann, & Malach, 2004)





(Nastase, 2019)

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graph TD; A([Benefits of measuring synchrony]) -.- B([No need for detailed hypothesis/models]); A -.- C([Easy to use complex stimuli]); A -.- D([Capture shared stimulus dependent signal]); A -.- E([Simple designs -> better replicability?]); A -.- F([synchrony vs. hemodynamic (de)activation]);
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Benefits of measuring synchrony

No need for detailed hypothesis/models

Easy to use complex stimuli

Capture shared stimulus dependent signal

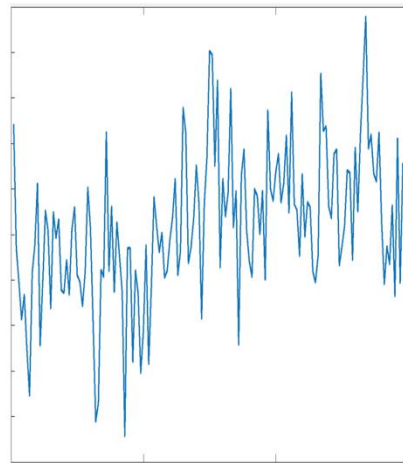
Simple designs
-> better replicability?

synchrony
vs.
hemodynamic (de)activation

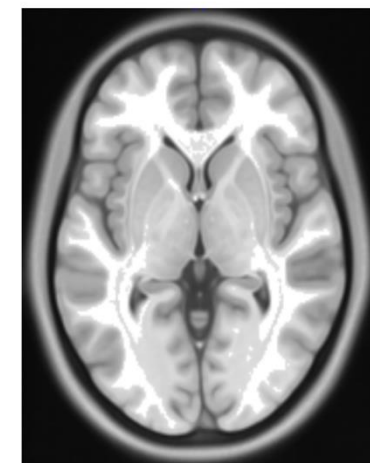
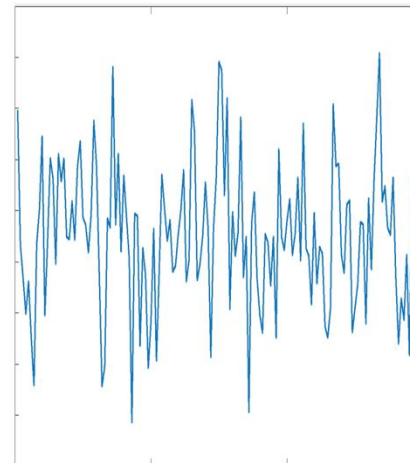
Pre-requirements for synchronization analysis



Shared stimulus



High-pass filtering
(detrending)



Spatial normalization



Smoothing

Shared stimulus

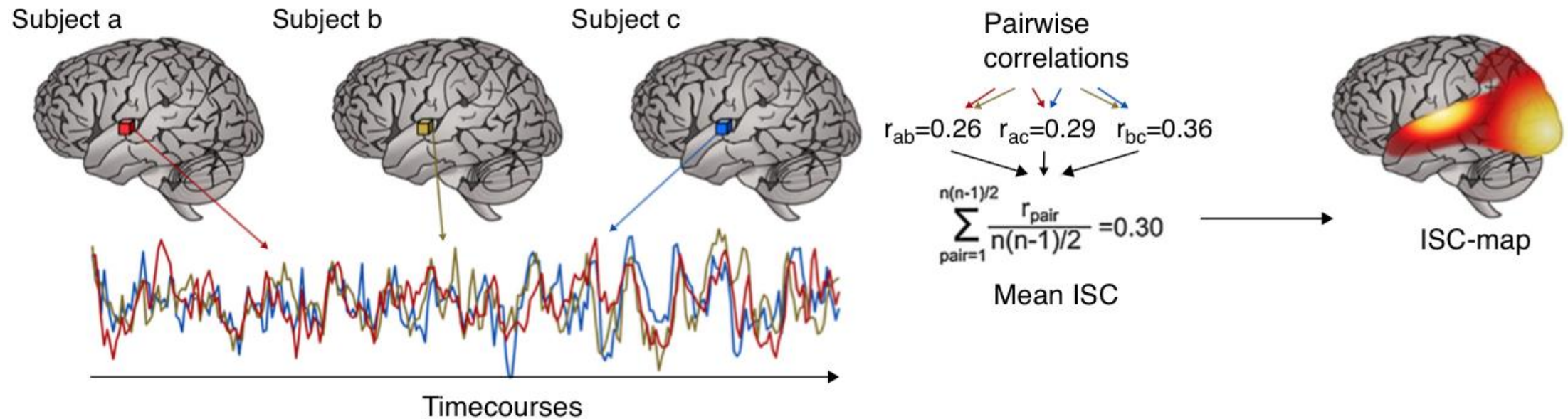
- 1) Exactly the same stimulus, e.g. a movie
- 2) Semantically shared stimulus, e.g. different movies but with synchronous emotional context

Intersubject correlation analyses

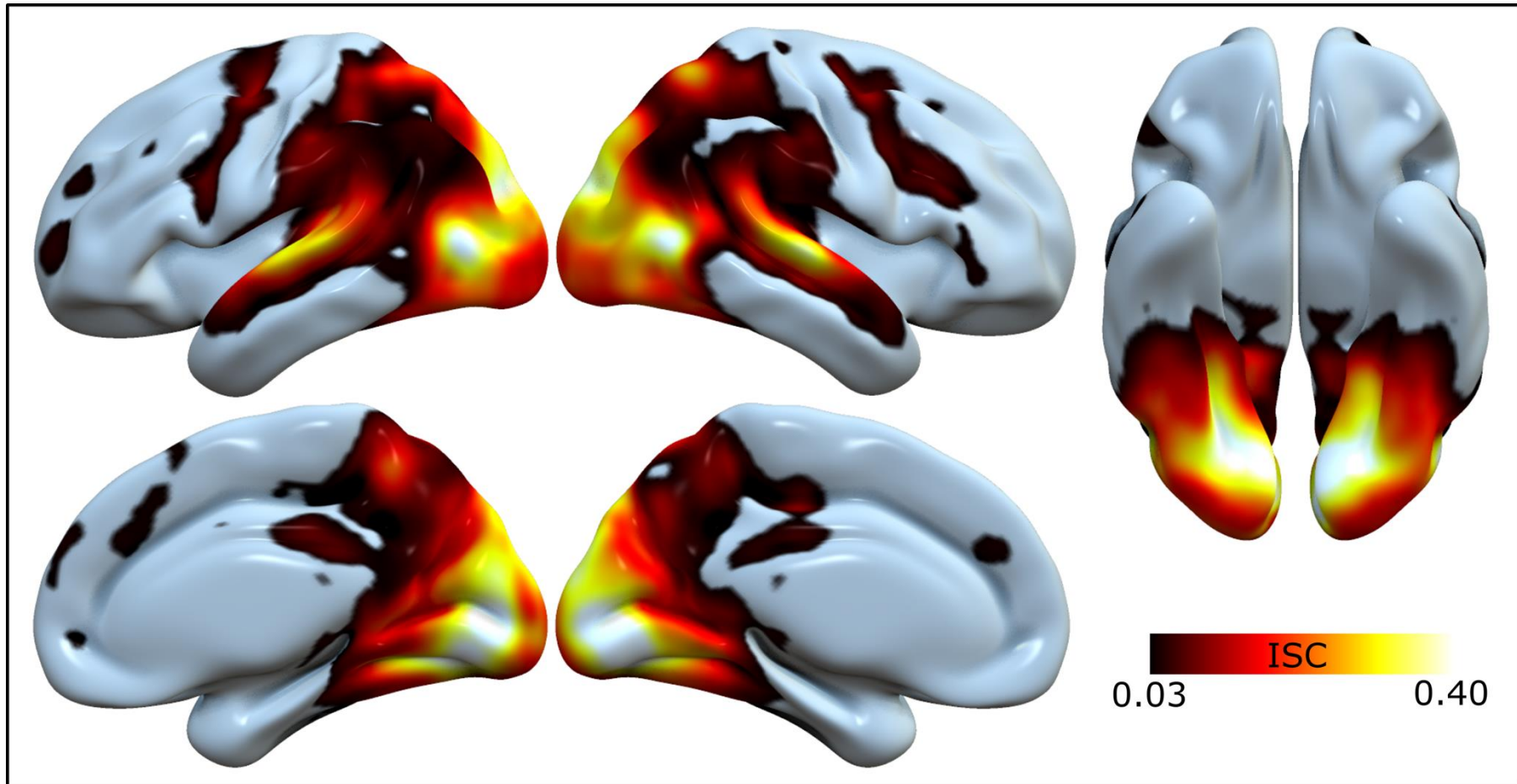
Measure	Time scale of the measured synchrony
ISC	Over the whole experiment (minutes-hours)
Time-window ISC	Specified time-windows (15sec - minutes)
ISPS	Instantaneous (seconds)

↓
Shorter time scale

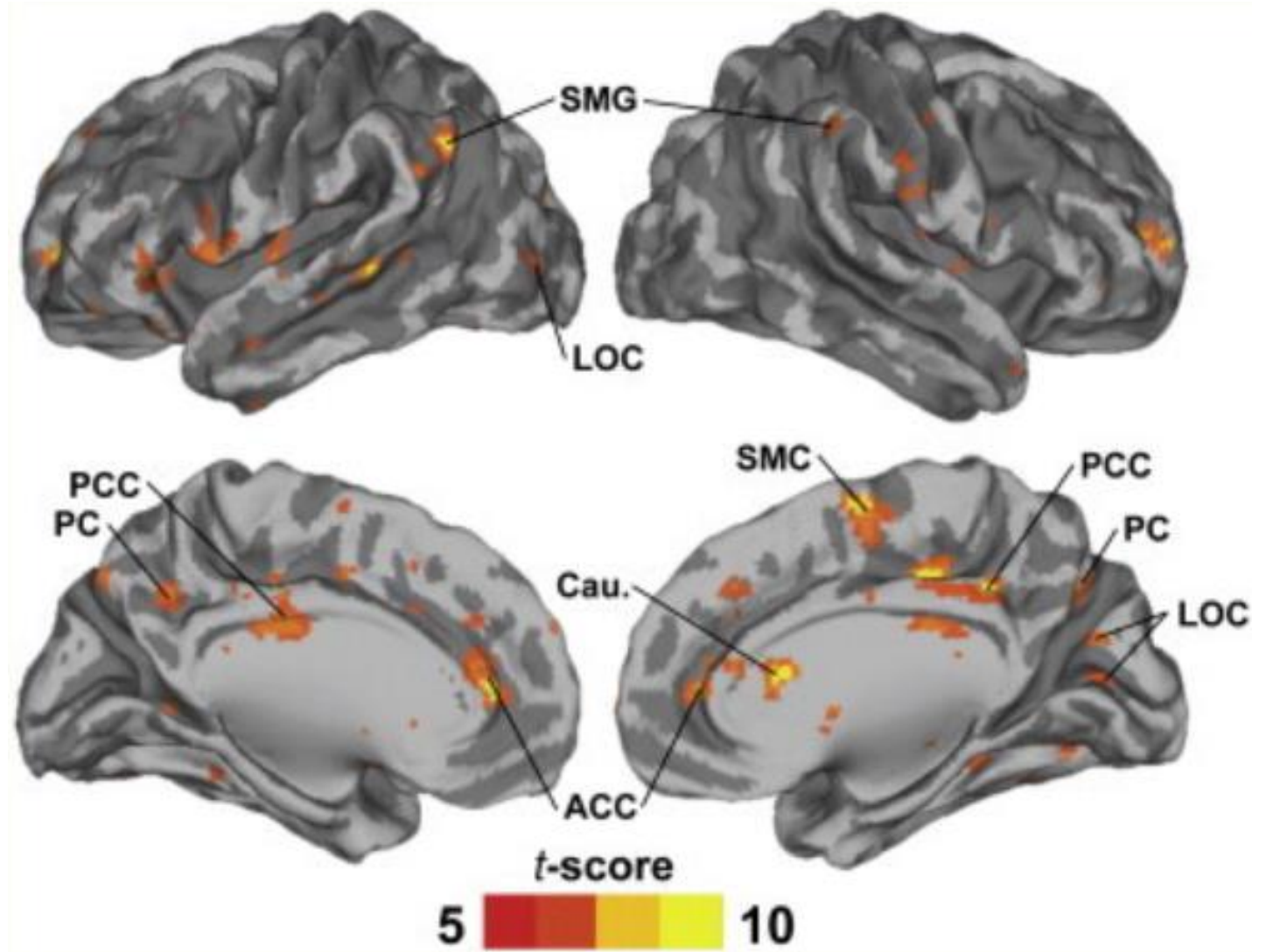
Basic concept of intersubject correlation (ISC)



Typical ISC in movie experiments

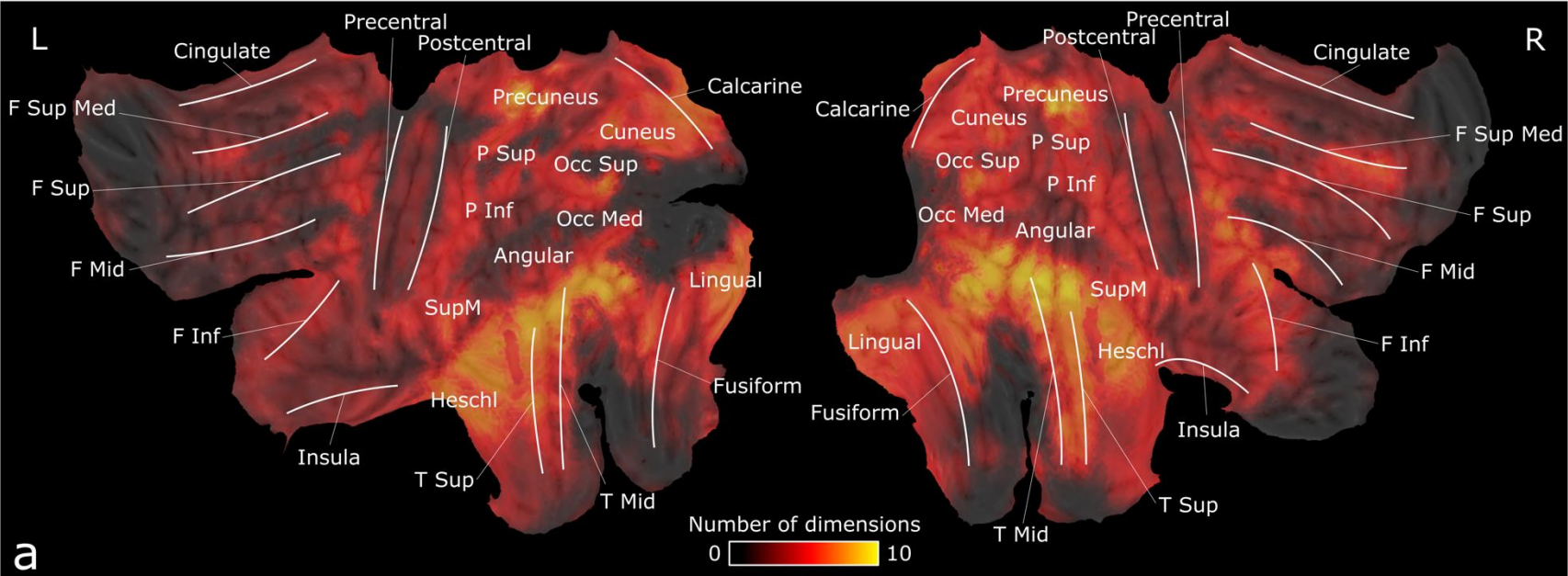


Decreased
ISC in autism
spectrum
disorders

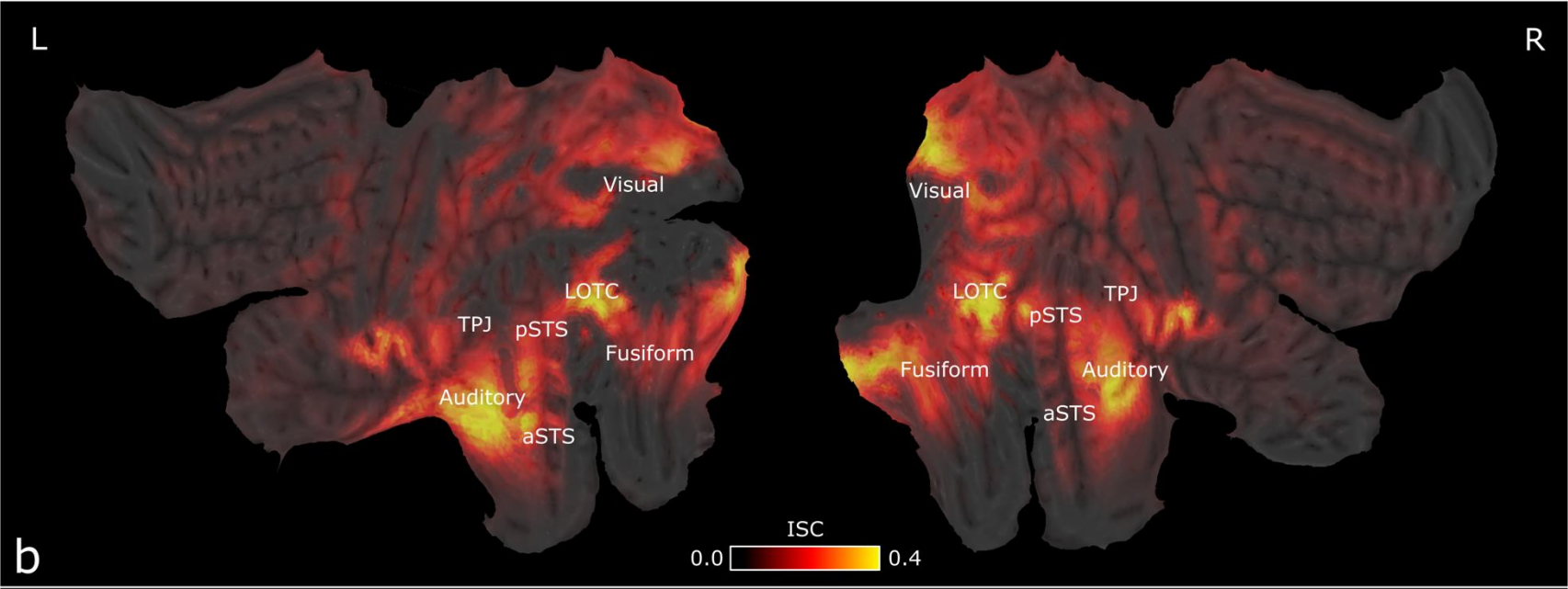


(Salmi, 2013)

Brain areas activated in social information processing



Average ISC of brain activation



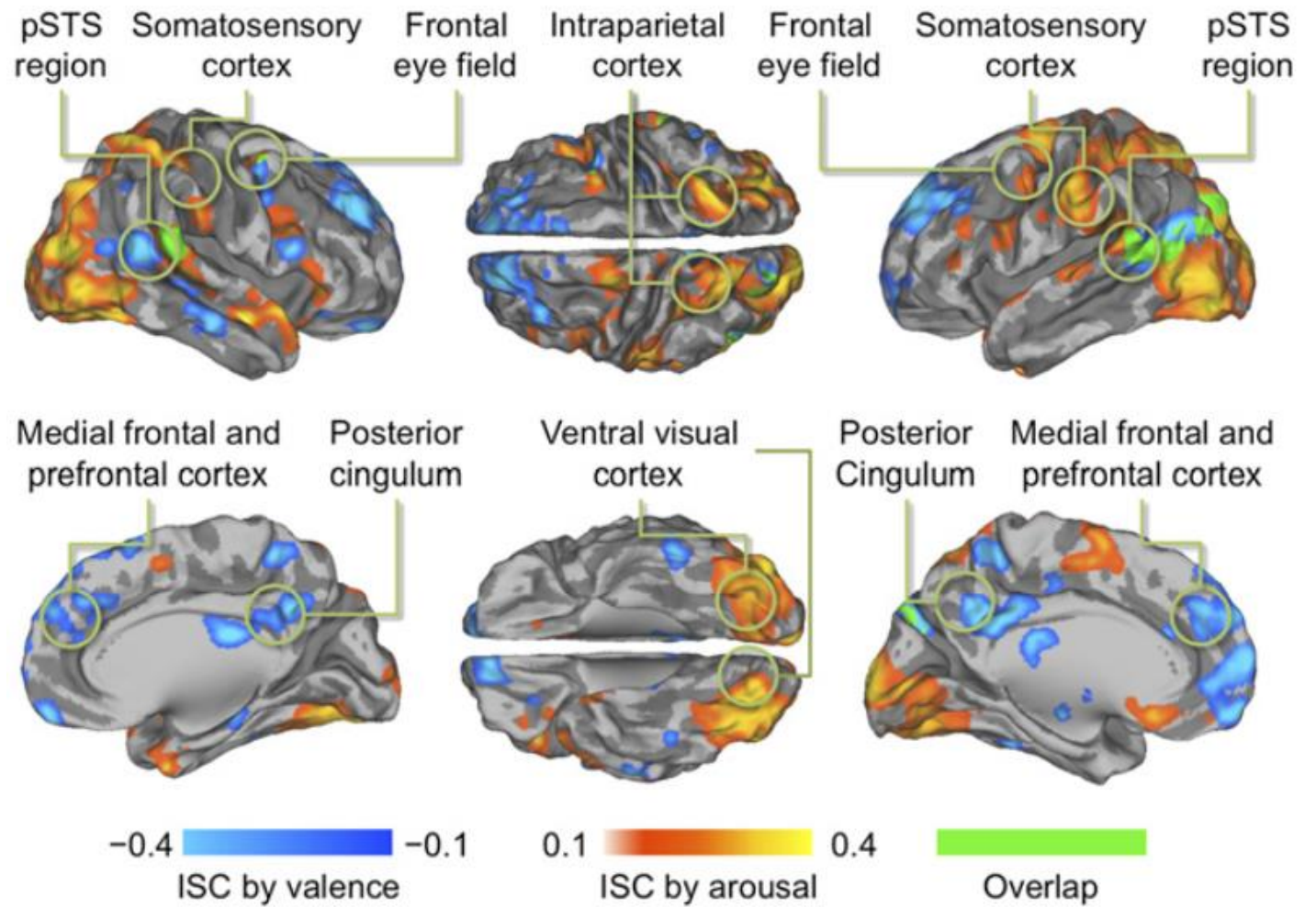
Time windows



Time window ISC

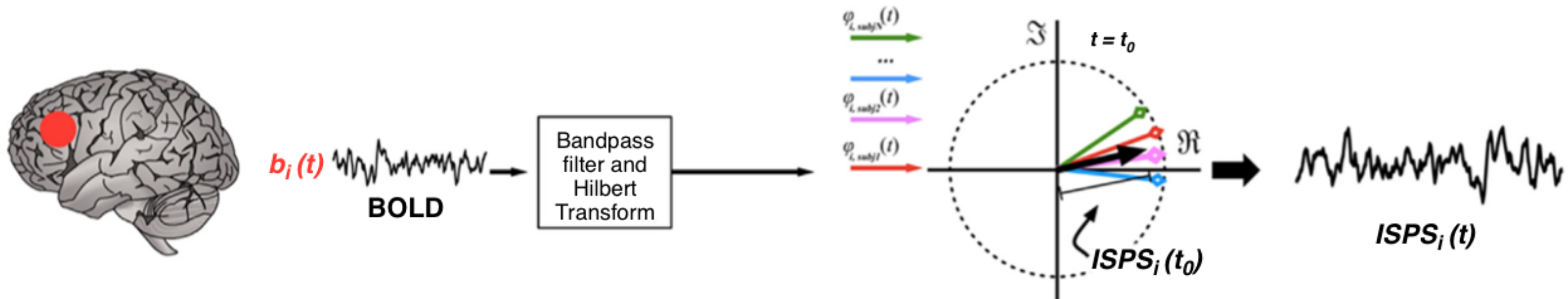
- Dynamic measure of intersubject synchrony
- Sliding window approach
 - Reflects the moving average of ISC
- How to choose the window length?

Valence and arousal predict time-window ISC



(Nummenmaa, 2012)

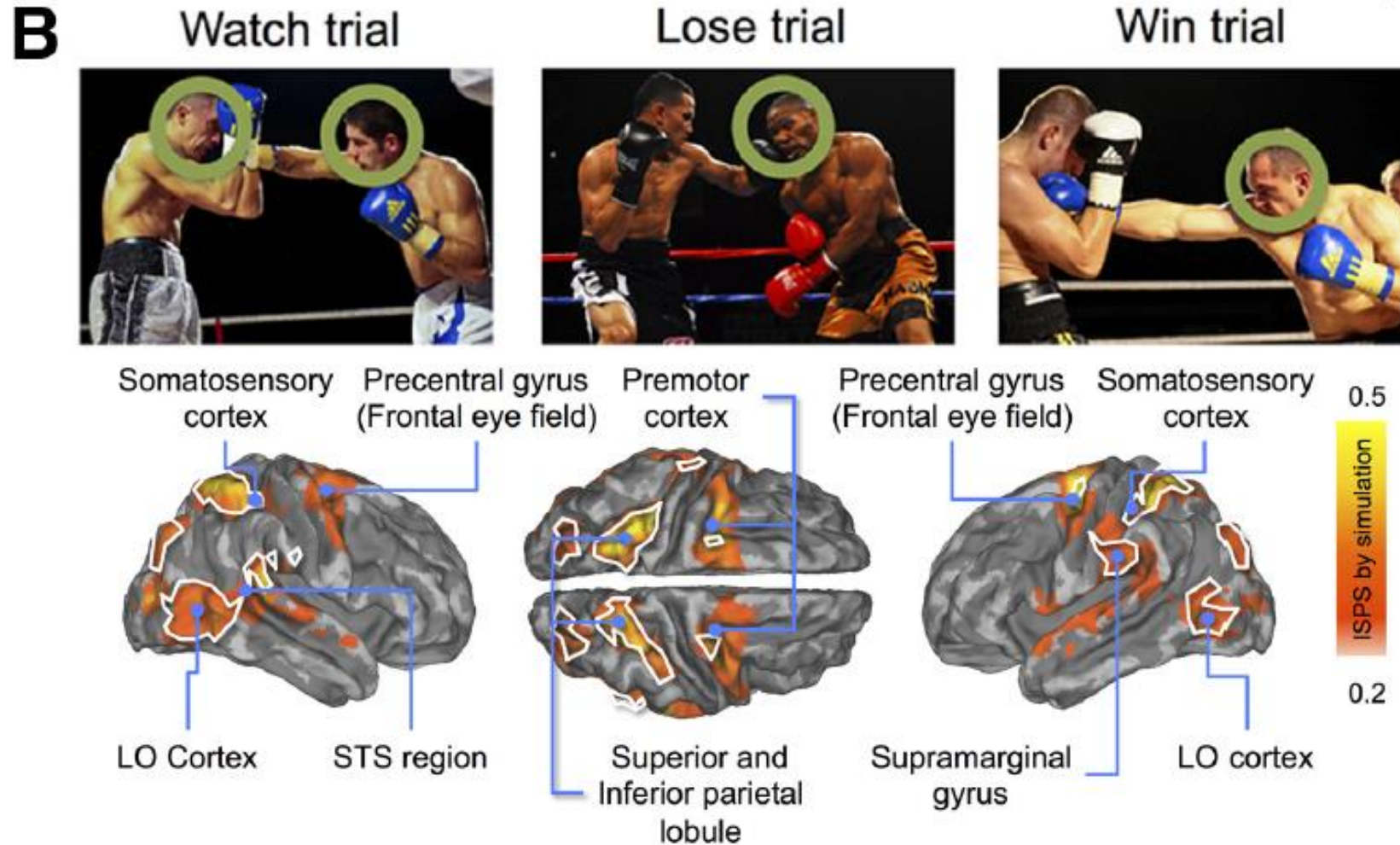
Intersubject phase synchronization (ISPS)



(Nummenmaa, 2018)

(Glerean, 2012)

ISPS in perspective taking vs. passive watching

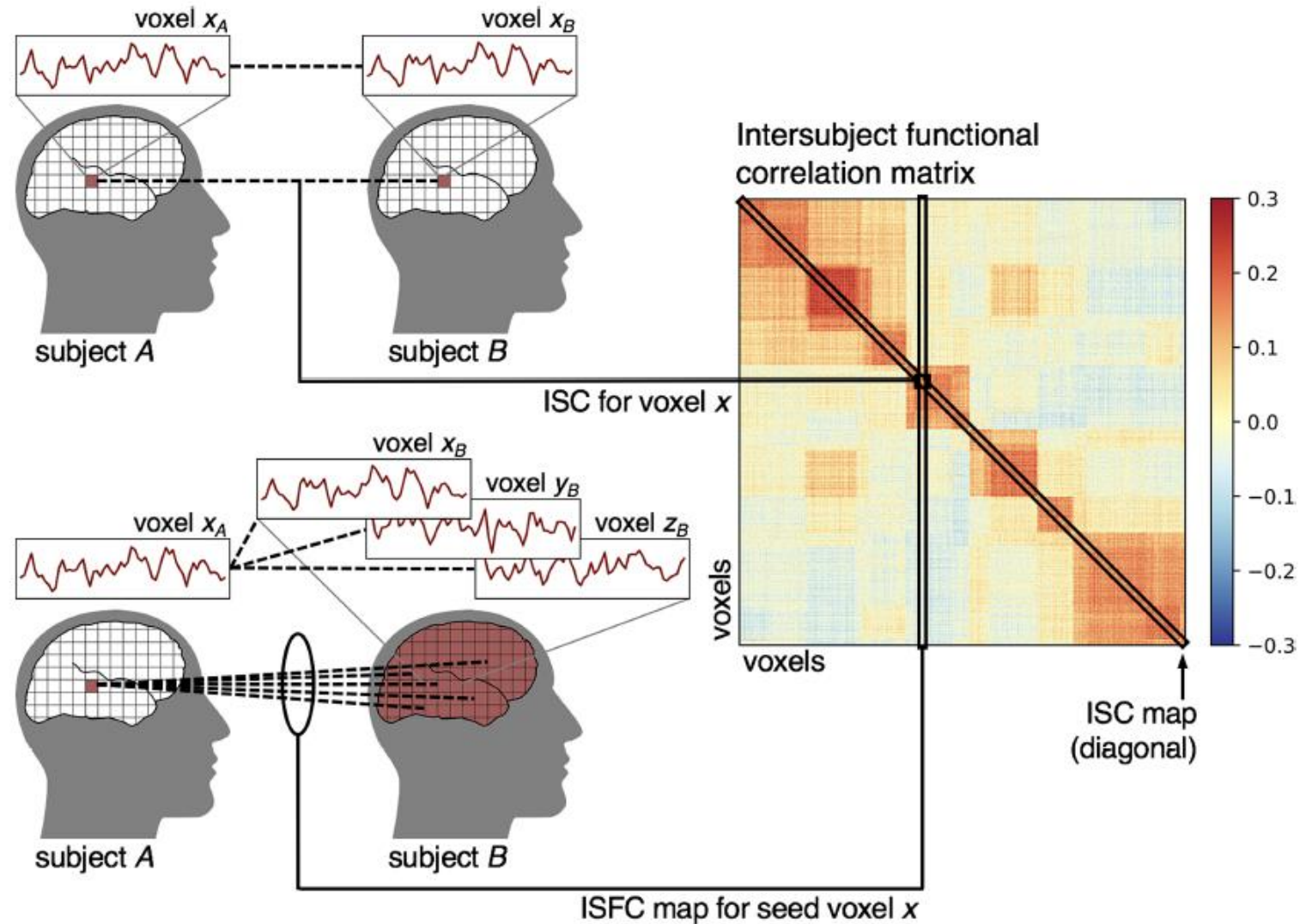


(Nummenmaa, 2014)

Reverse correlation approach

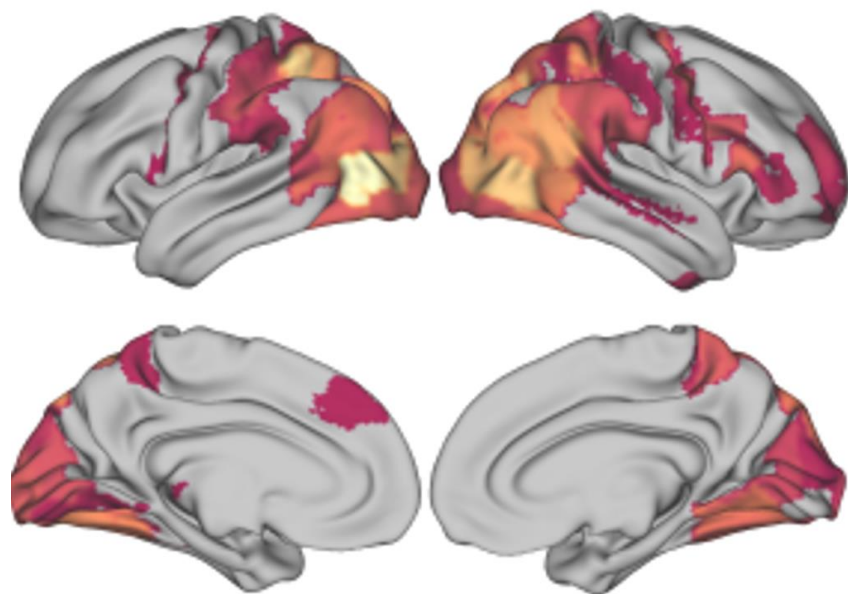
- Traditional analysis:
 - Hypothesis → Model design → GLM → Results
- "Let's turn the analysis upside down"
- Find new hypotheses
 1. Measure dynamic brain synchronization (time-window ISC/ISPS)
 2. Identify time points with high synchrony
 3. Figure out what is happening in the stimulus at the time of high synchrony
 4. Test new hypothesis in future studies.

Intersubject functional connectivity (ISFC)

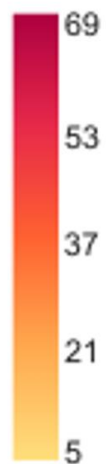
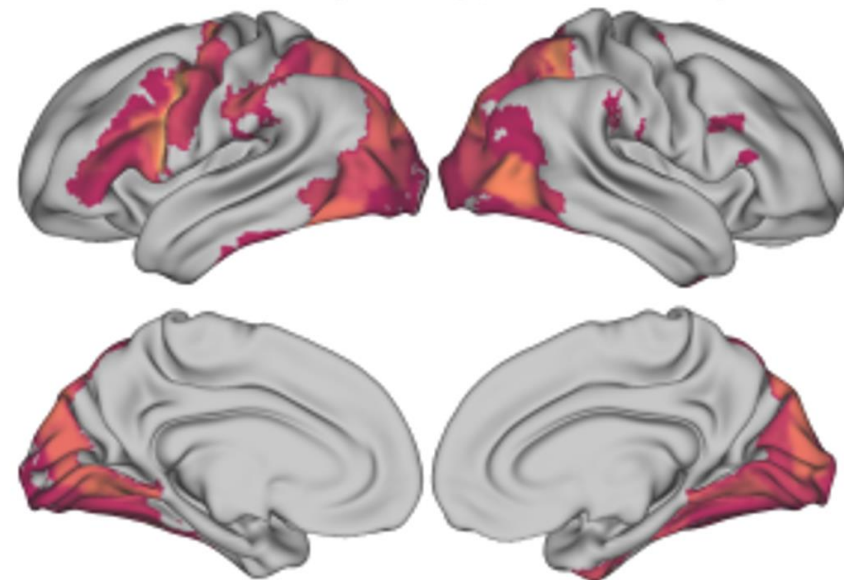


(Nastase, 2019)

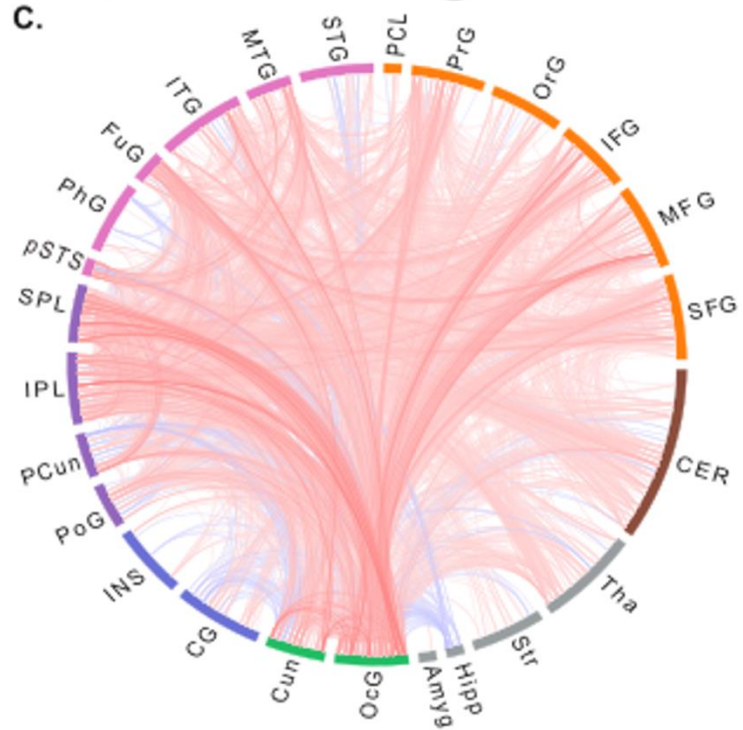
German (Neurotypical > Autism)



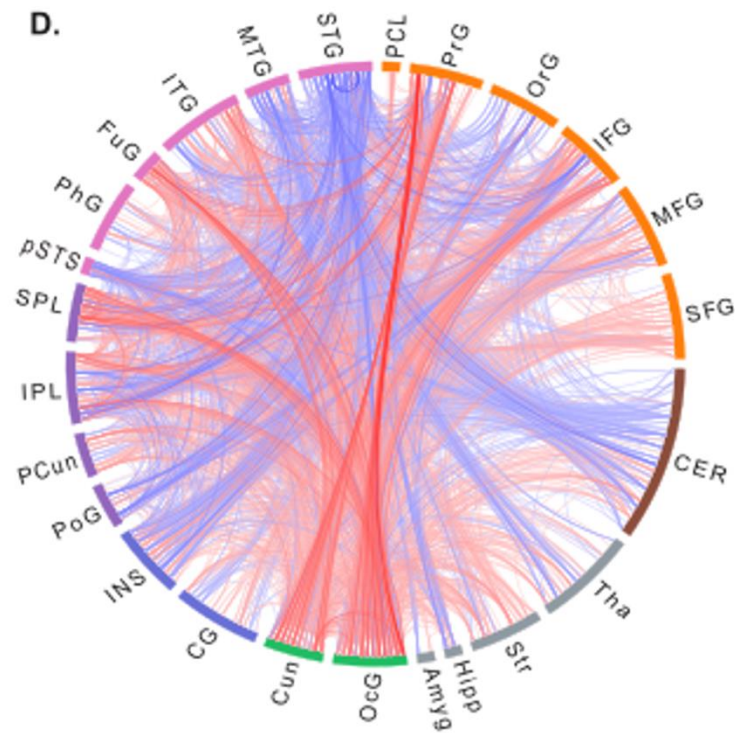
Finnish (Neurotypical > Autism)



C.



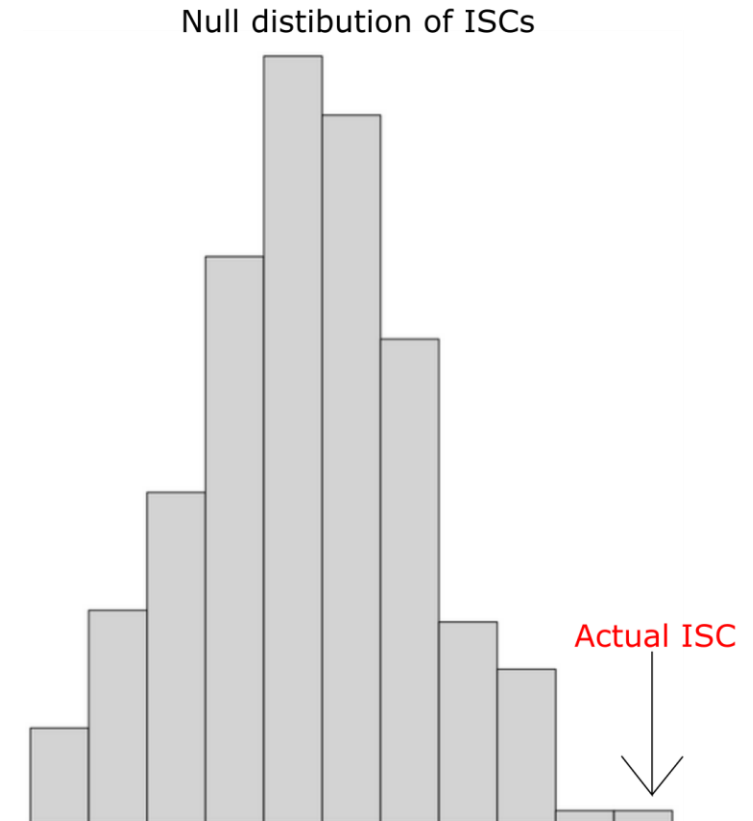
D.



(Lin, under review)

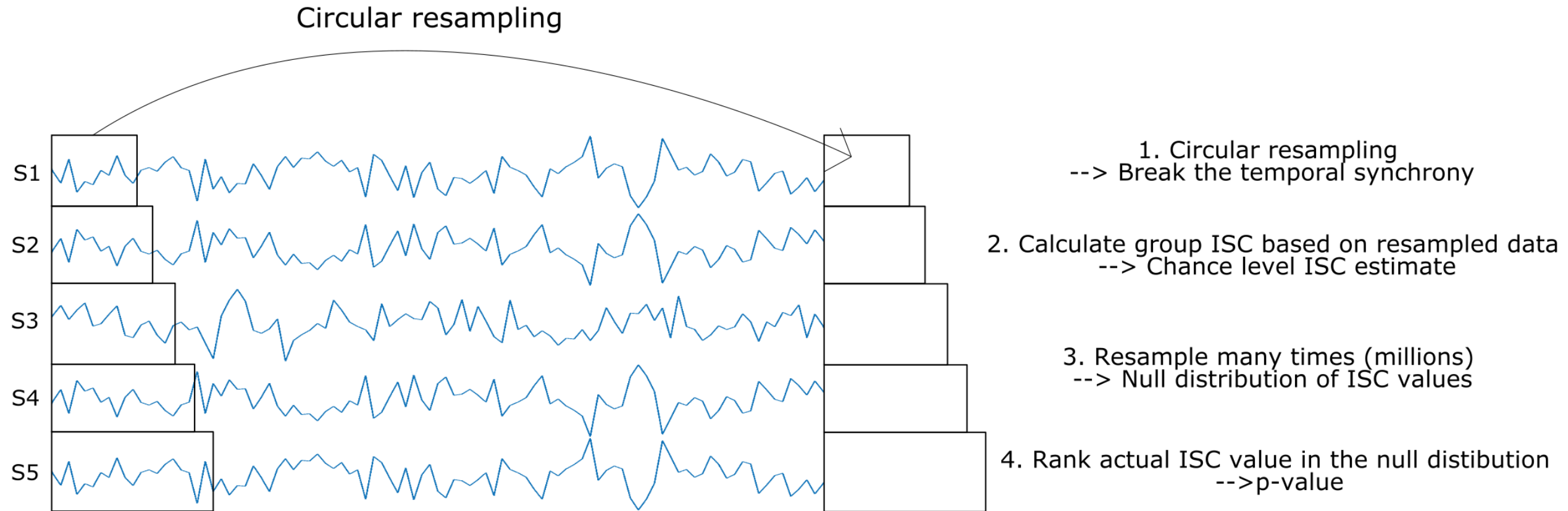
Statistical significance of ISC

- Does ISC differ statistically from zero?
- Pairwise correlation values are not independent from each other
 - Violates the assumption of independent observations in parametric tests
- Non-parametric permutation based testing
 - Circular block-resampling
- Multiple comparisons correction



(Kauppi, 2010)

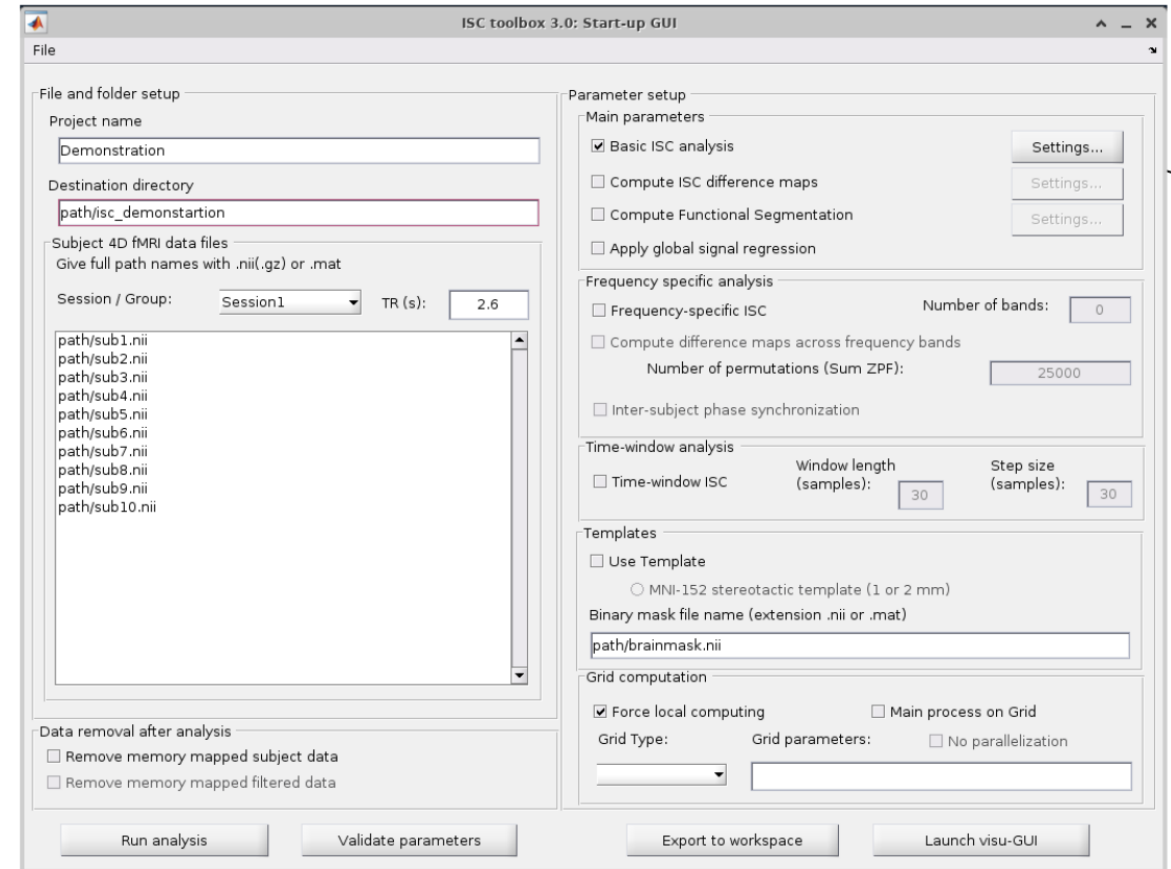
Circular block-resampling method



(Kauppi, 2010)

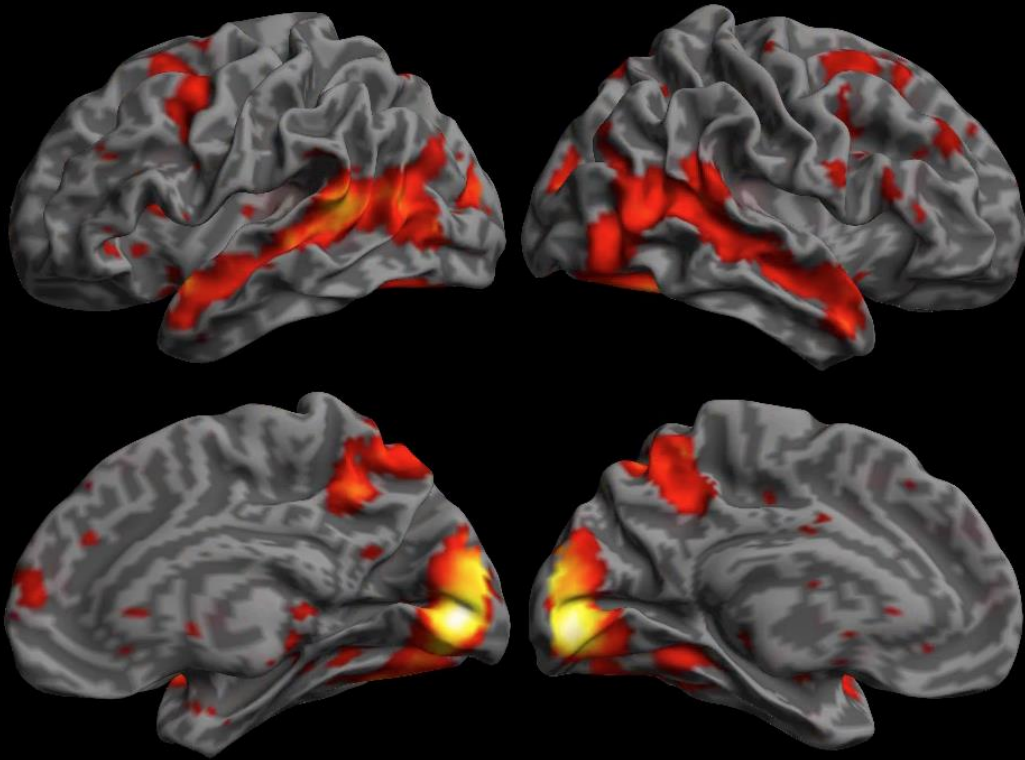
ISC-toolbox

- ISC analysis toolbox for brain fMRI data.
 - <https://www.nitrc.org/projects/isc-toolbox/>
 - Graphical user interference
- Runs on MATLAB
- Features
 - Basic one group analysis
 - Group comparison analysis
 - e.g. patients vs. healthy controls
 - Frequency specific ISC analysis (advanced)
 - Time-window ISC / ISPS
 - Permutations based statistics



(Kauppi, 2014)

Thank you!



References

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