



Beth Israel Deaconess
Medical Center



A teaching hospital of
Harvard Medical School

Connectivity Analysis

Correlation, Coherence and Causality

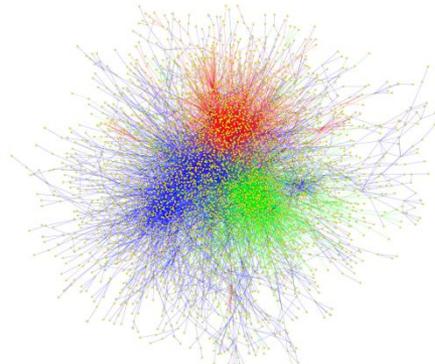
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Connectivity

A central property of any complex system

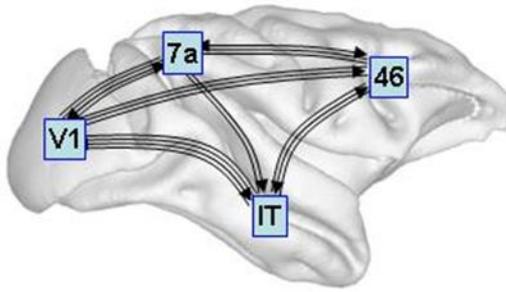


Protein Interactions

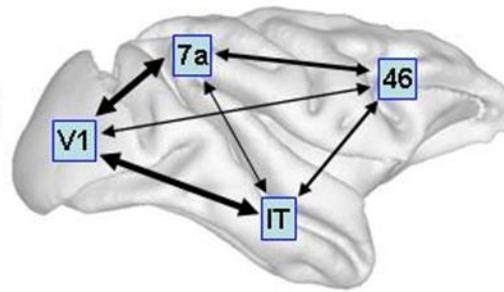


Connectivity in Brain

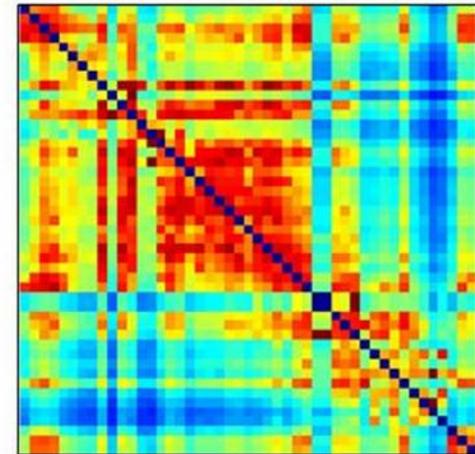
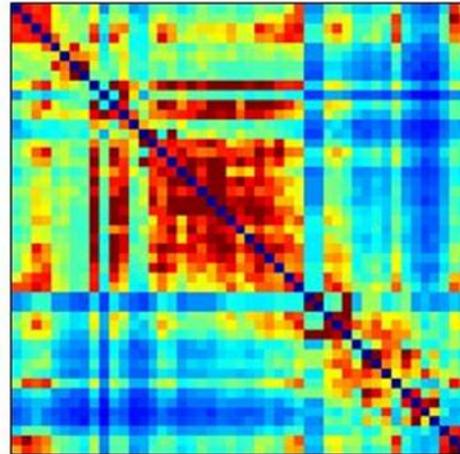
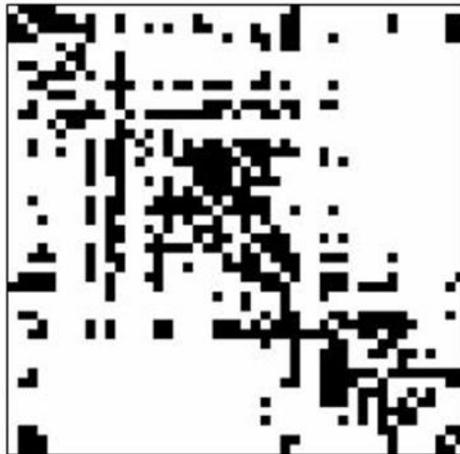
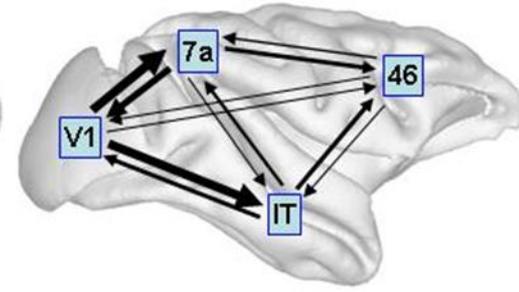
structural connectivity



functional connectivity

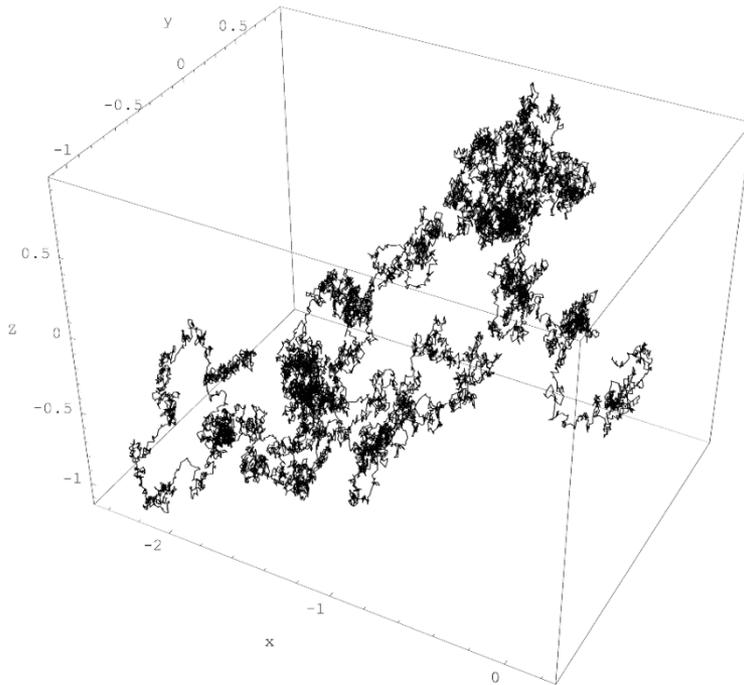


effective connectivity

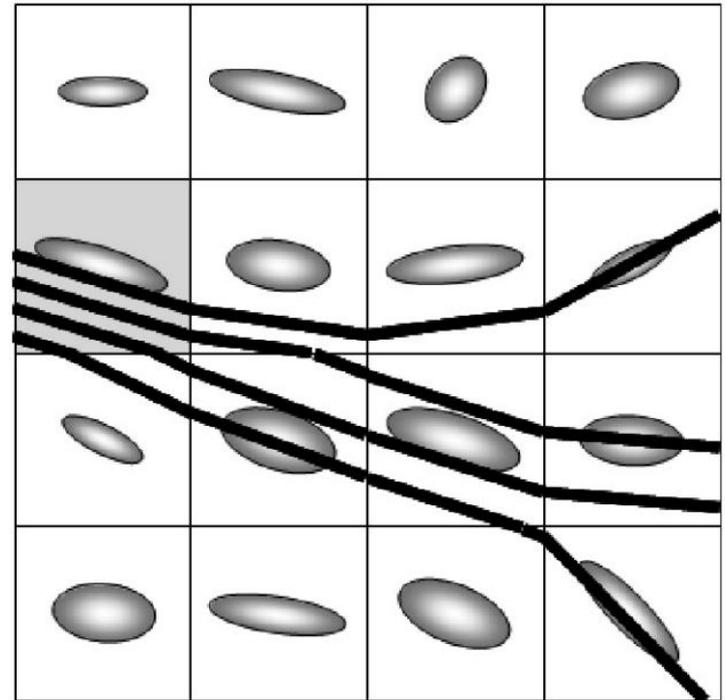


Structural Neuroimaging

Diffusion Tensor Imaging

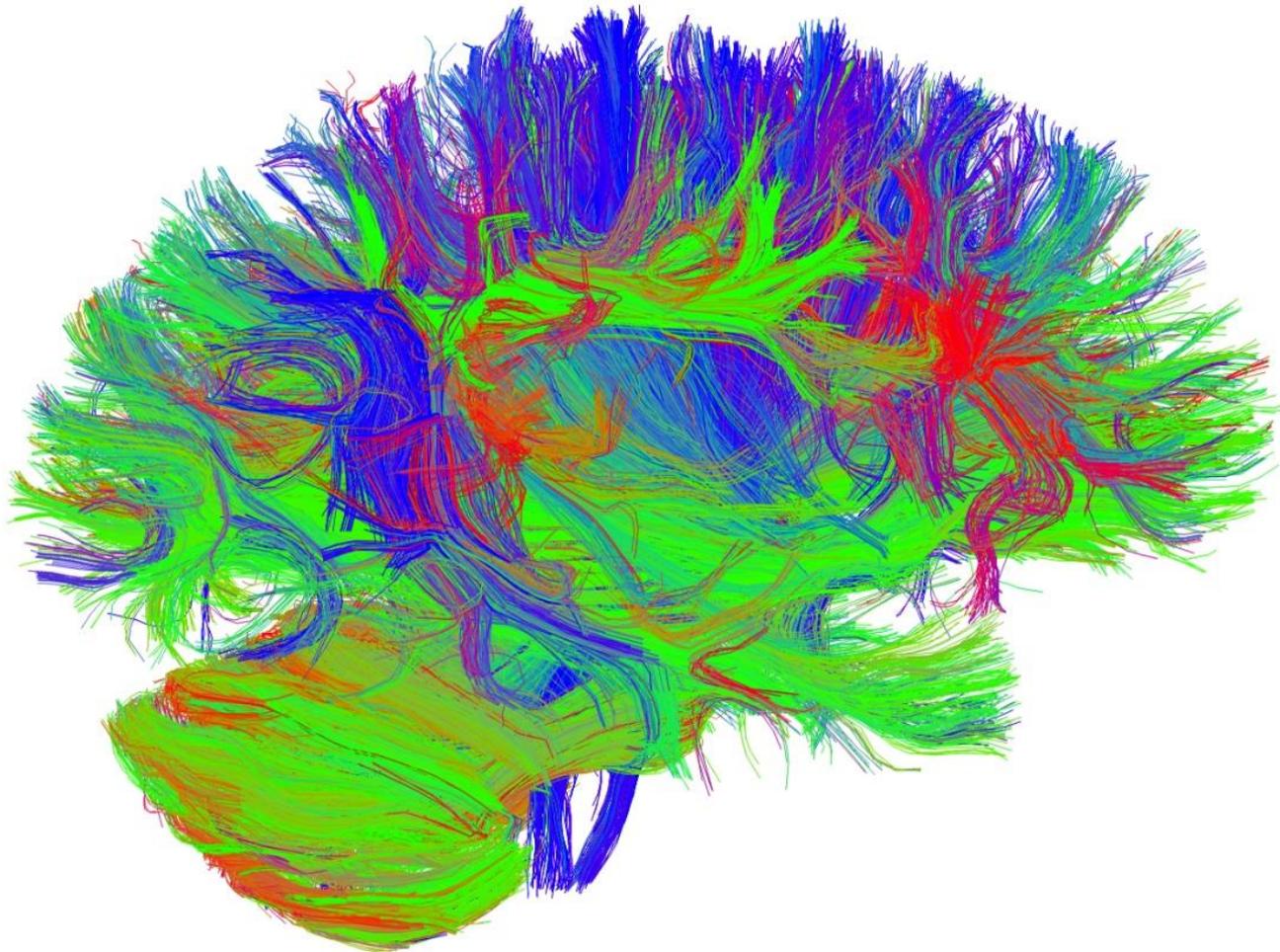


Brownian motion of water molecule

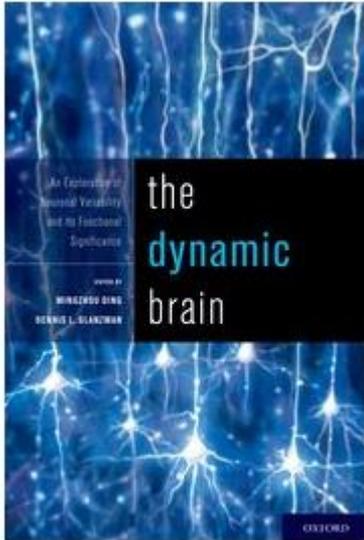


Tracking neuronal fibers

Structural Brain Networks



The Dynamic Brain



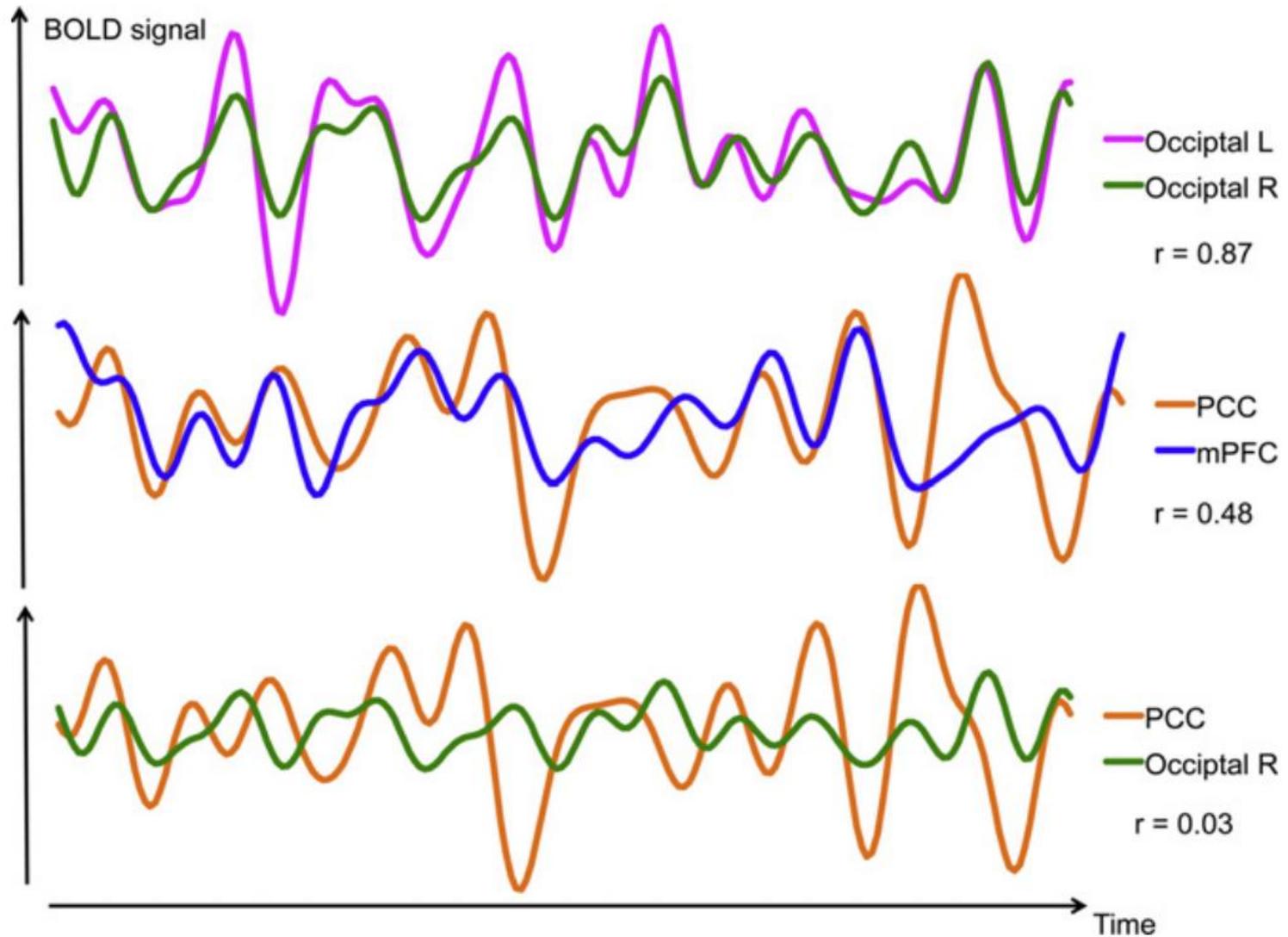
“The **noisy variability** seen in single neuron responses may in fact contain real, meaningful information.”

“To understand how neurons work in concert to bring about coherent behavior and its breakdown in disease, neuroscientists now attempt to evaluate the network activities by computing various **interdependence measures.**”

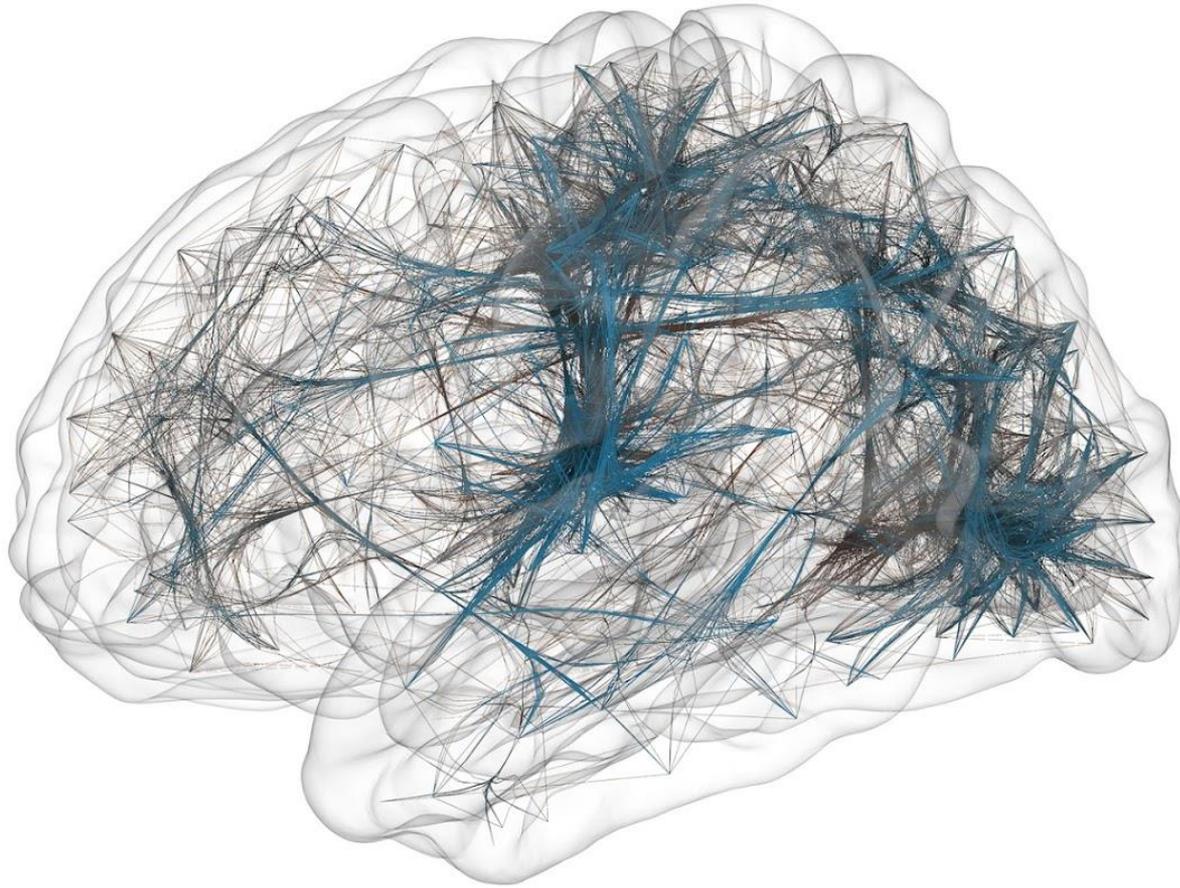
The Dynamic Brain

Edited by Mingzhou Ding, PhD and Dennis
Glimzman, PhD

Functional Connectivity



Functional Brain Networks



Correlations between spatially remote neurophysiological events

Functional Connectivity

- Temporal **correlations** between spatially remote neurophysiological events
- Functional connectivity is an **operational measure**
- Does **not** imply **causal** relationship

Dis-connection in Psychotic Brain

Disruption in connectivity
between different brain
regions



Carl Wernicke
(1848-1905)



Symptoms of psychosis



Schizophrenia
Splitting of mental functions



Eugen Bleuler
(1857-1939)

Inception of Modern Functional Connectivity



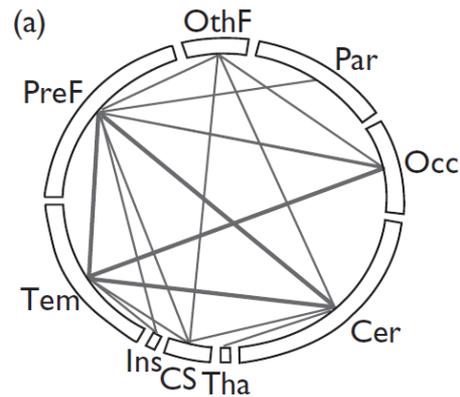
- Inventor of statistical parametric mapping
- Inventor of dynamic causal modeling
- Inception of disconnection hypothesis of schizophrenia

Disconnection Hypothesis

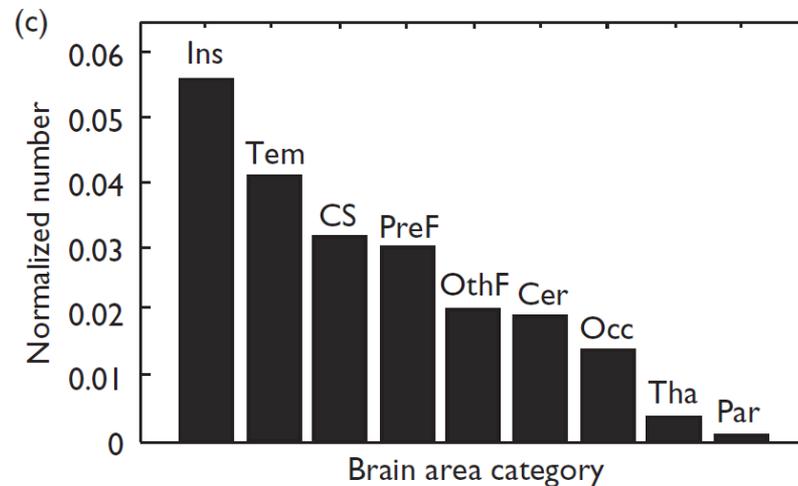
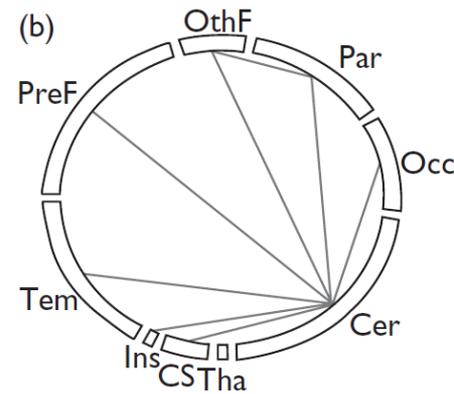
- Observed **functional disconnection** between prefrontal and temporal brain region in schizophrenic patients relative to healthy controls.
- Schizophrenia's core symptoms can be described in terms of **abnormal functional integration between distinct brain regions.**

Abnormal Functional Connectivity in Schizophrenia

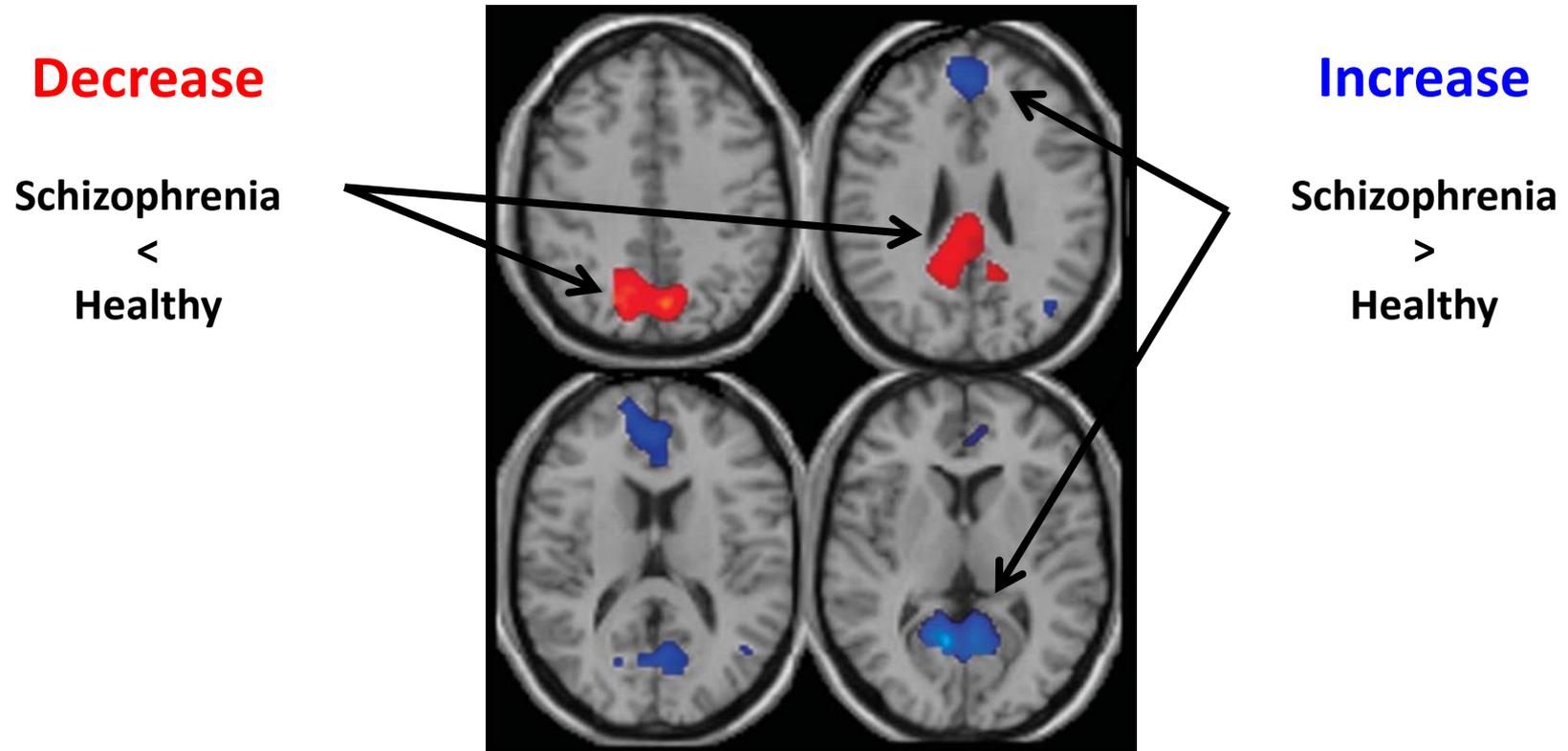
Decreased



Increased

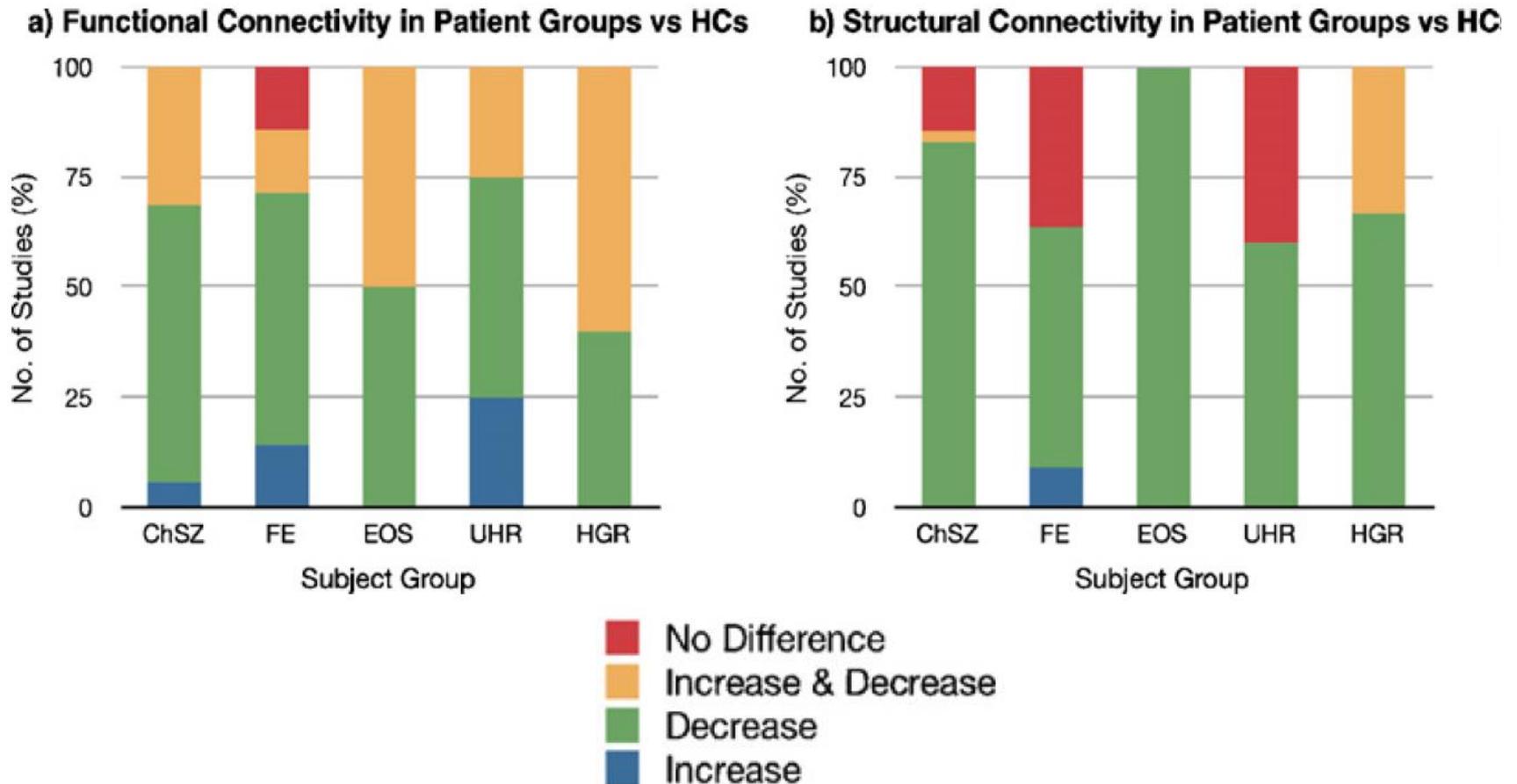


Abnormal Functional Connectivity in Schizophrenia

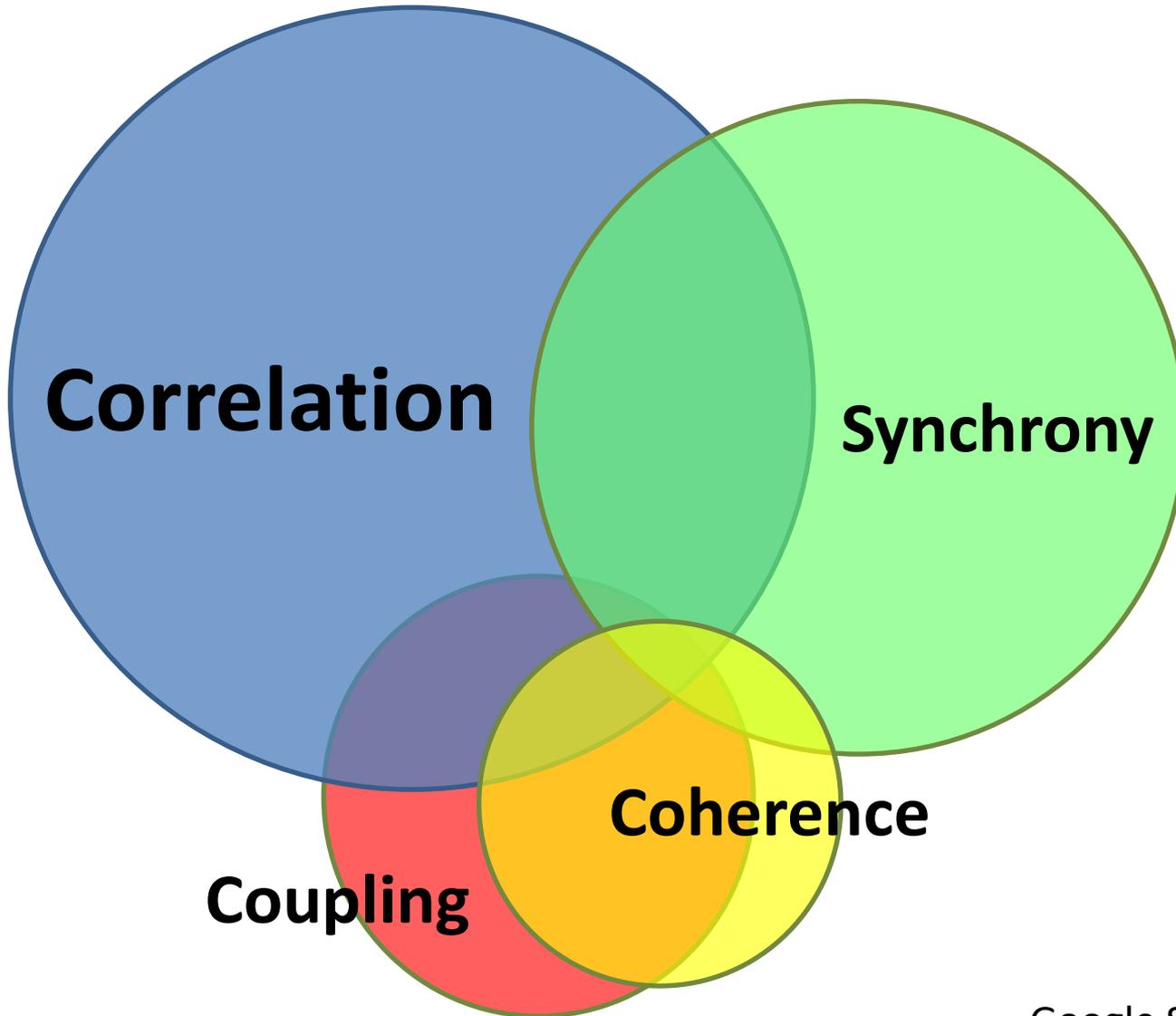


The default mode network may be involved in **overactivity** of brain regions that interfere with normal thoughts and functioning.

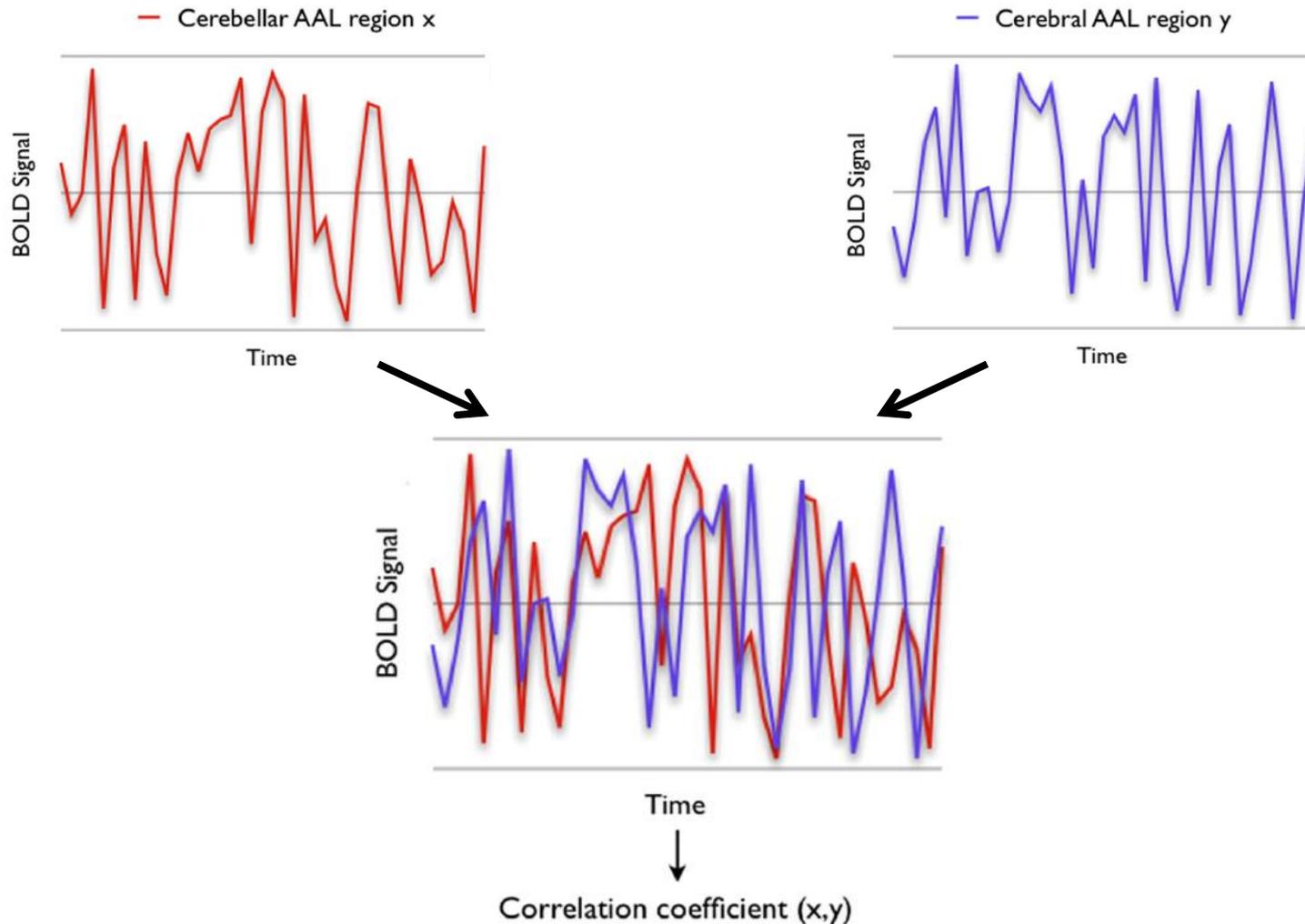
Dysconnectivity in Schizophrenia



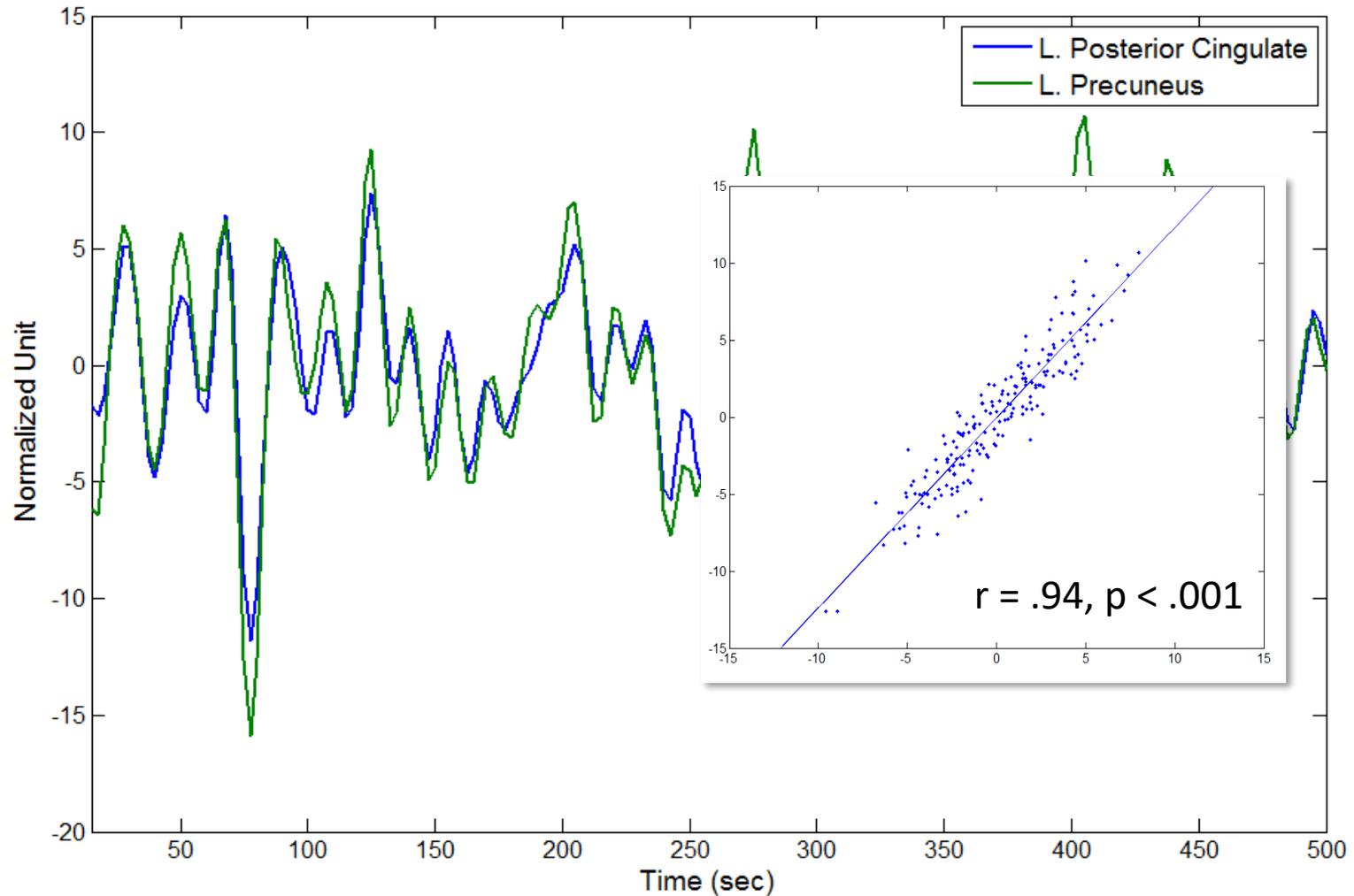
Synonym of Connectivity



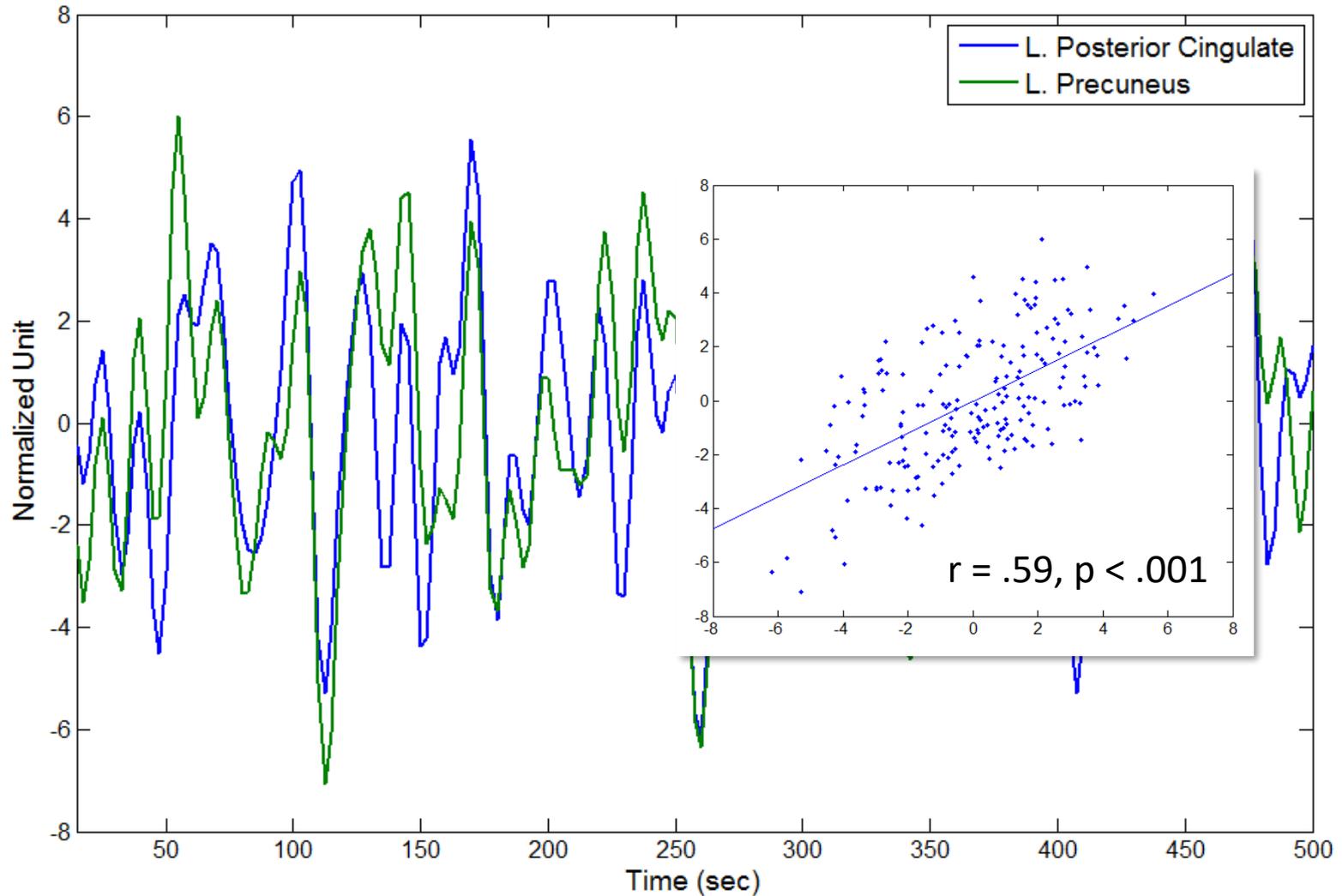
What is Wrong with Correlation?



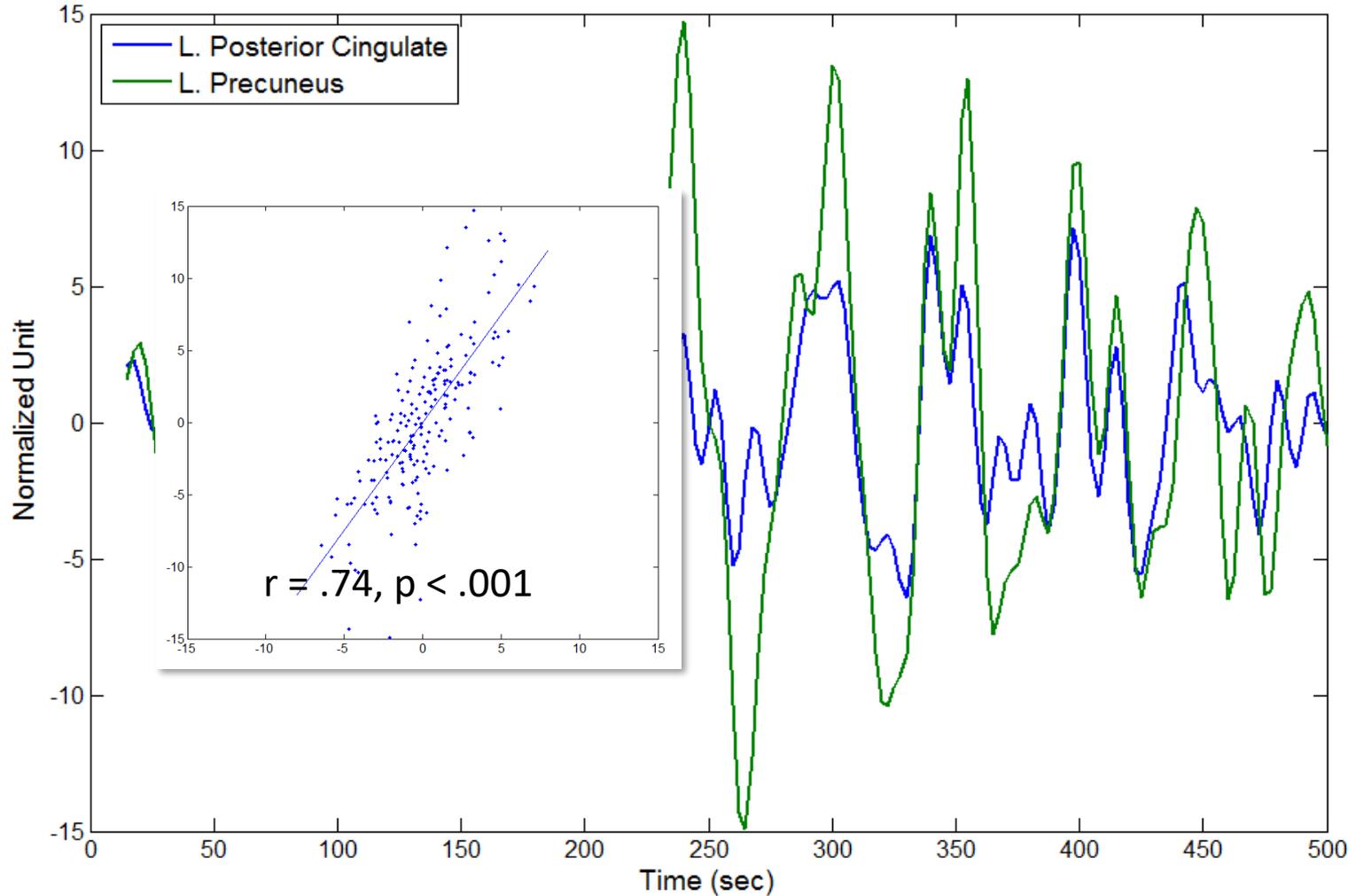
What defines “Correlation”?



What defines “Correlation”?

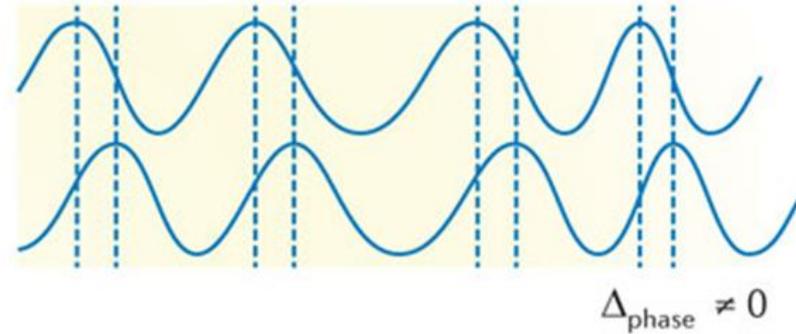
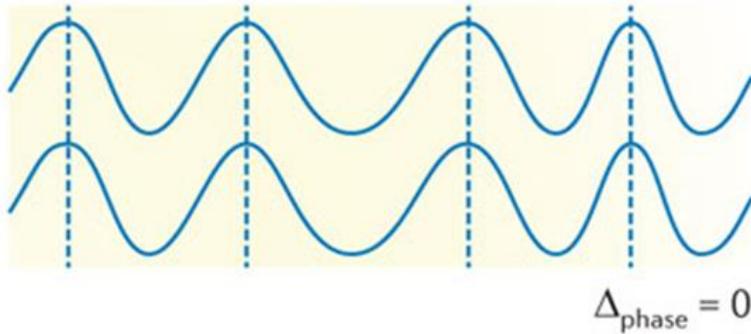


What defines “Correlation”?

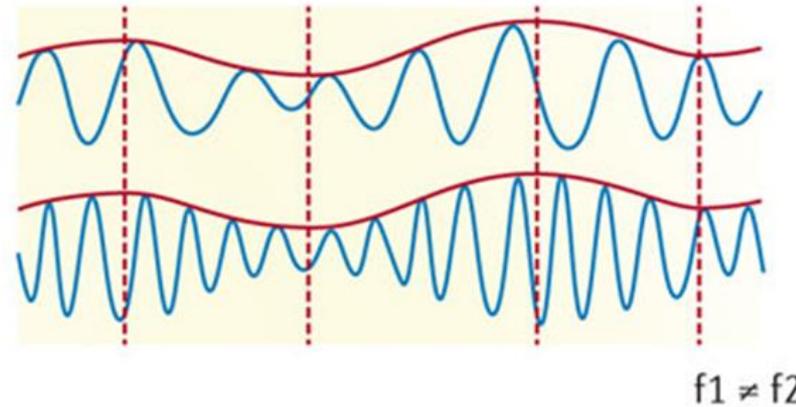
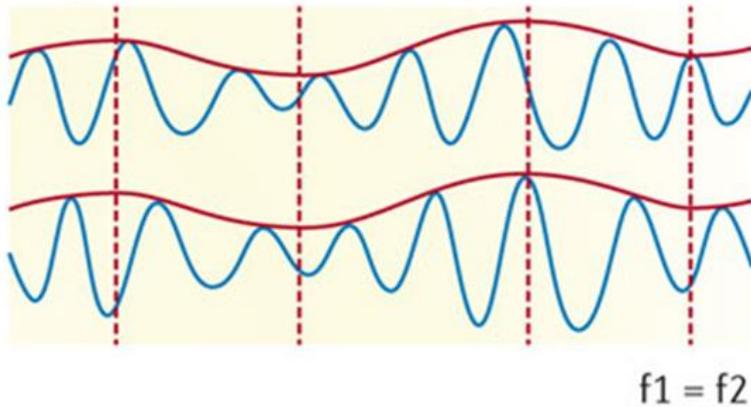


Redefining “Correlation”

a Phase coherence



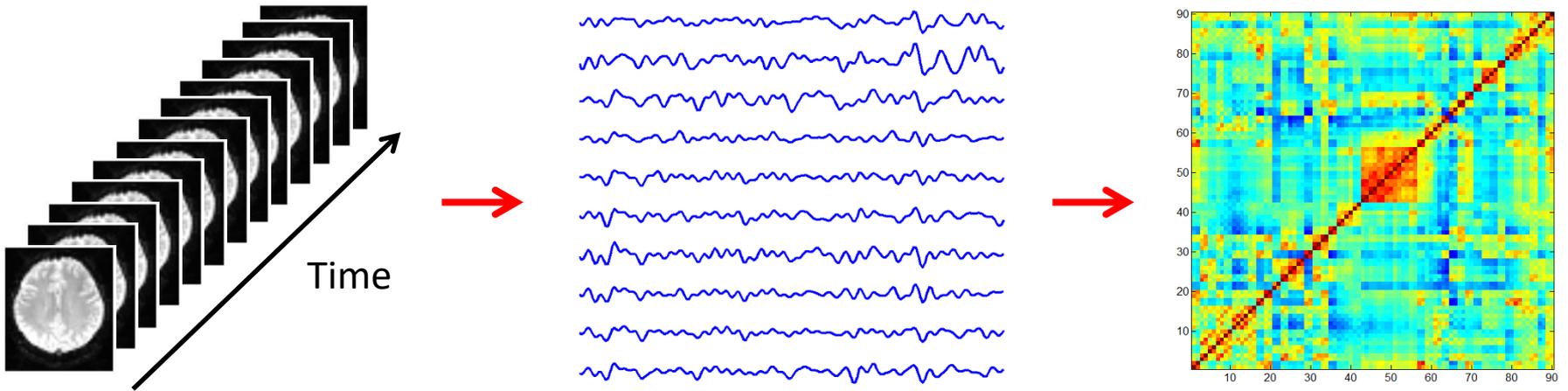
b Amplitude correlation



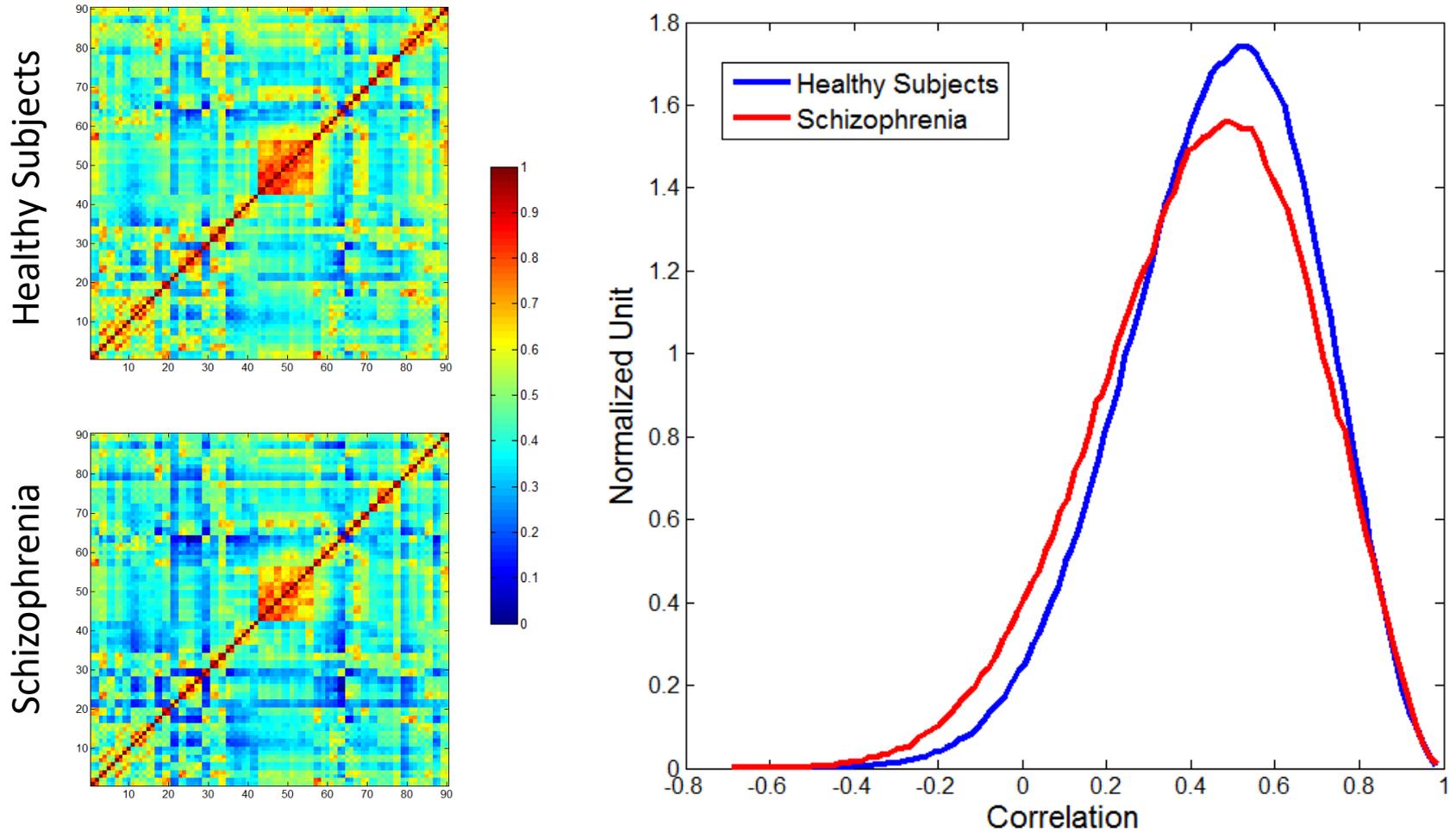
Correlation vs. Coherence

- Pearson's correlation is a measure of “**linear dependence**,” which cannot capture nonlinear, or phase and amplitude modulation of given signals.
- Brain signal is modulated by phase and amplitude in different conditions.
- We need new measures that can quantify phase-phase, amplitude-amplitude, or phase-amplitude relationship.

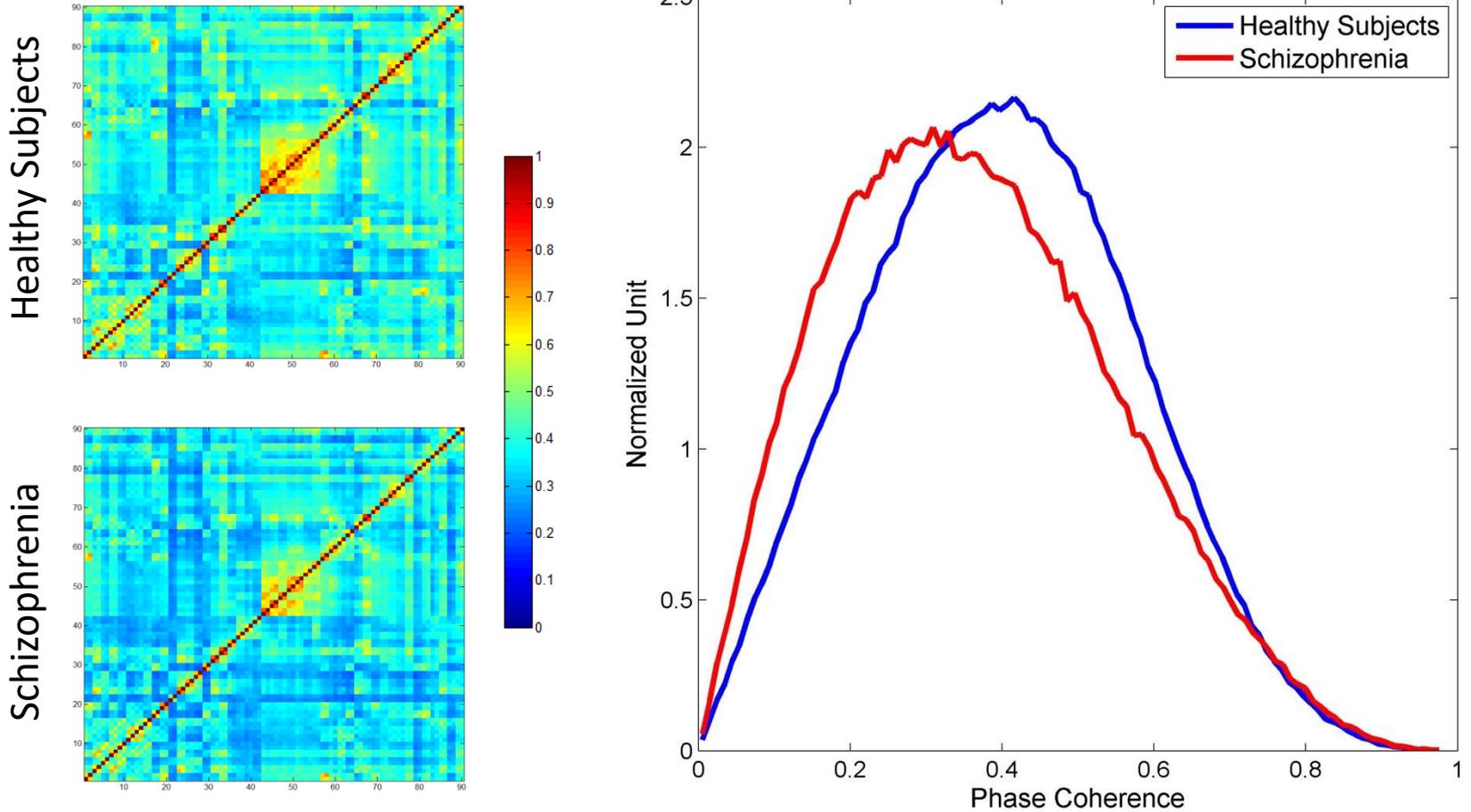
How to Construct a Functional Brain Network?



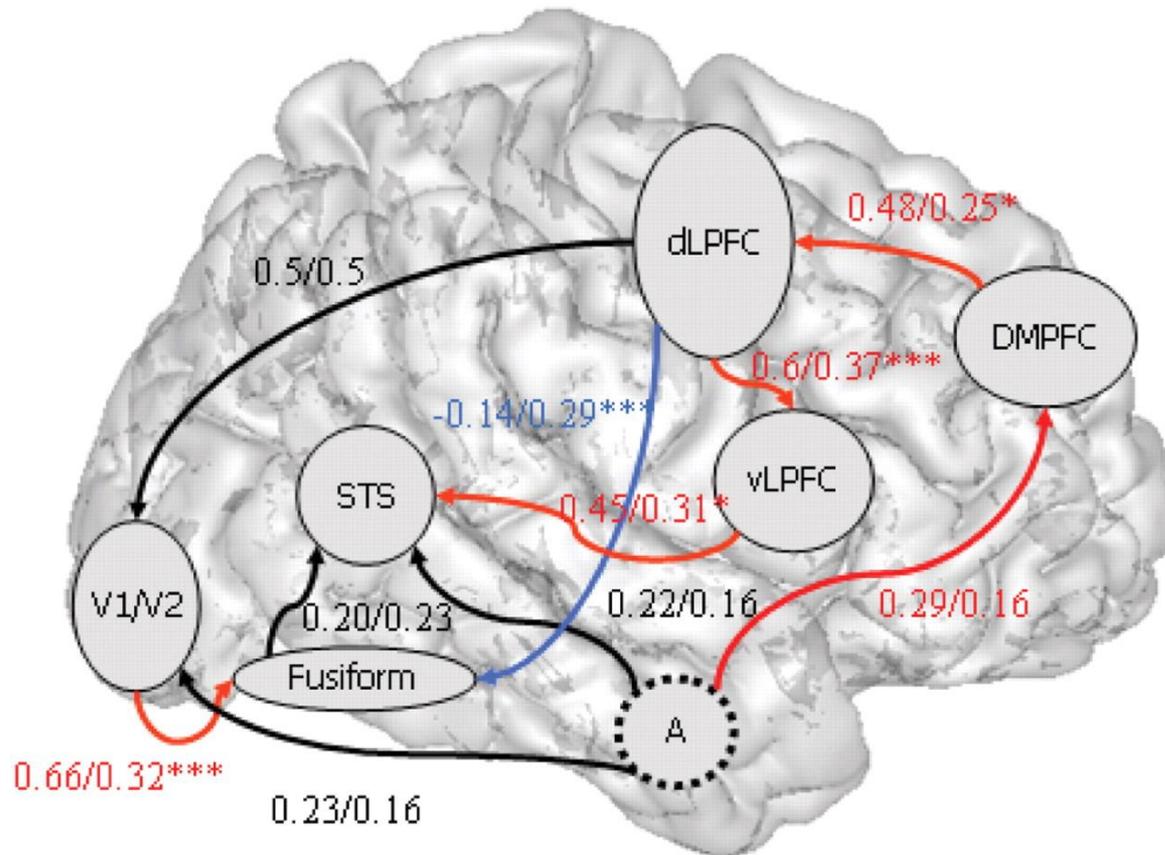
Distribution of Correlation Value



Distribution of Phase Coherence Value



Effective Connectivity



Influence of one neuronal system exerted over another

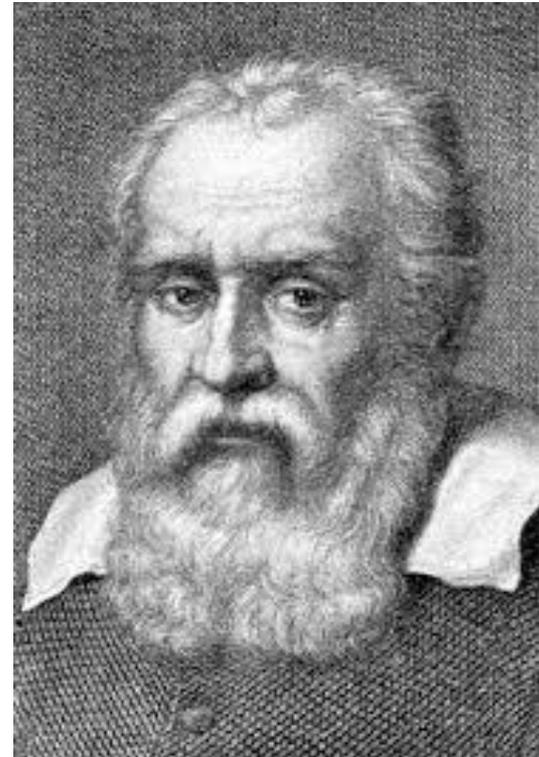
Is Everything a Result of Cause and Effect?

- **KARMA**: intent and actions of an individual influence the future of that individual.
- 范縝(AD510)與竟陵王蕭子良論「因果」
 - 子良問：『君不信因果，何得有富貴貧賤？』
 - 縝答道：『人生如樹花同發，隨風而散，或拂簾幌，墜茵席之上；或關籬牆，落糞溷之中。墜茵席者，殿下是也；落糞溷者，下官是也。貴賤雖復殊途，因果竟在何處？』

Deterministic vs. Stochastic Causality

Cause and Effect

CAUSE is that which put, the effect follows; and removed, the effect is removed.



Galilei G *Dialogo Sopra I due massimi sistemi* 1632

Cause and Effect

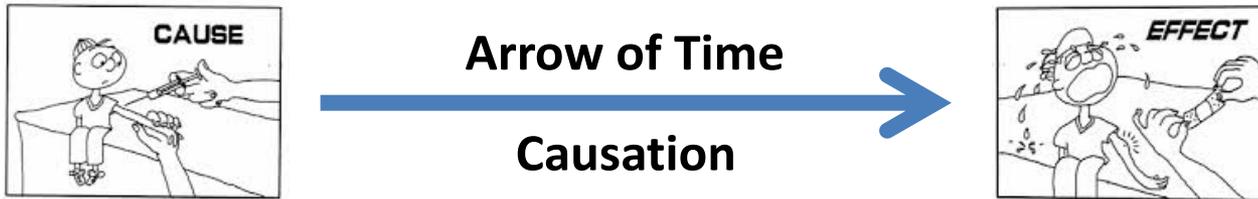
CAUSE is “an object **EFFECT** in time and **contiguous** to another, and where all the objects resembling the former are placed in like relations of precedency and contiguity to those objects that resemble the latter.”



David Hume *A Treatise of Human Nature* 1738

Modern Definition of Causality

- **Temporal Precedence**



- **Covariation of the Cause and Effect**

if X then Y

if not X then not Y

- **No Plausible Alternative Explanations**

Measure Temporal Precedence of Cause and Effect

Granger Causality

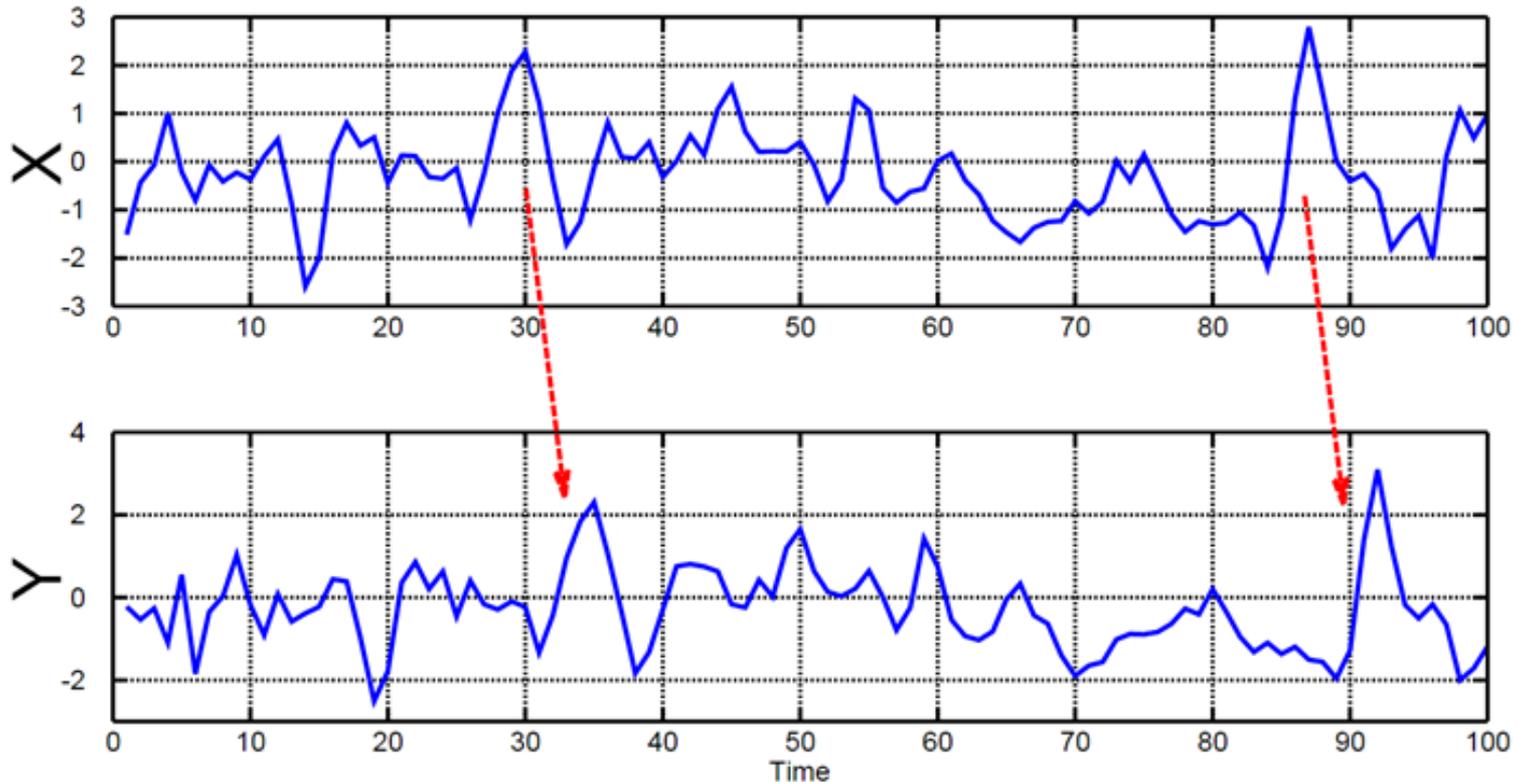
- Variable X is said to cause Y if the predictability of Y improves by incorporating past X values rather than using past Y values alone.



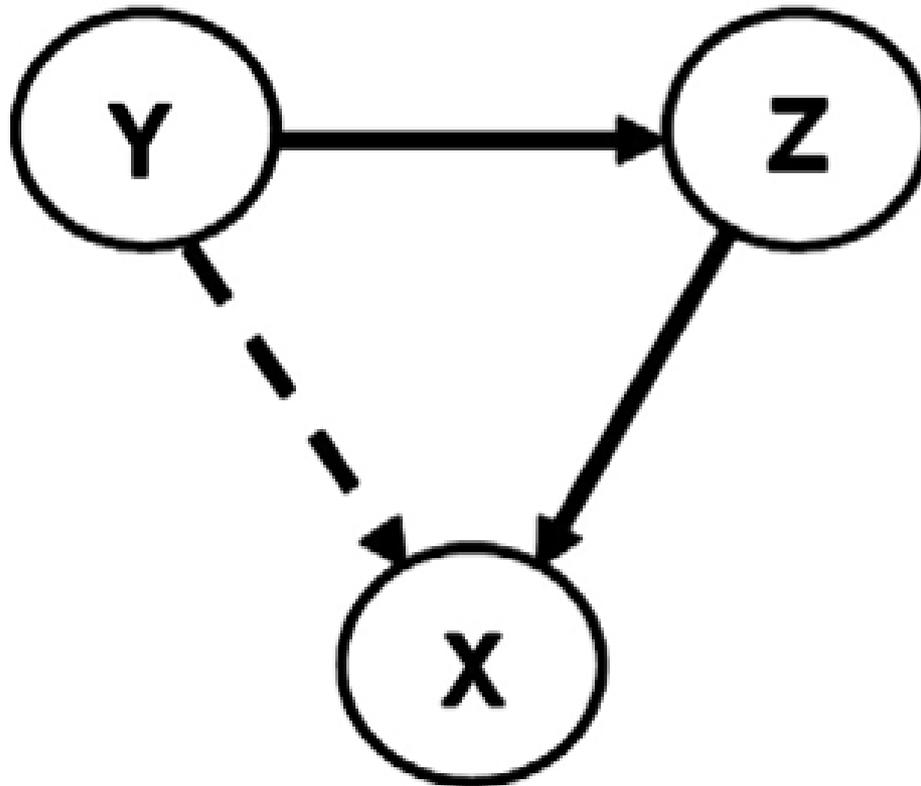
Clive Granger 1934-2009

Granger Causality

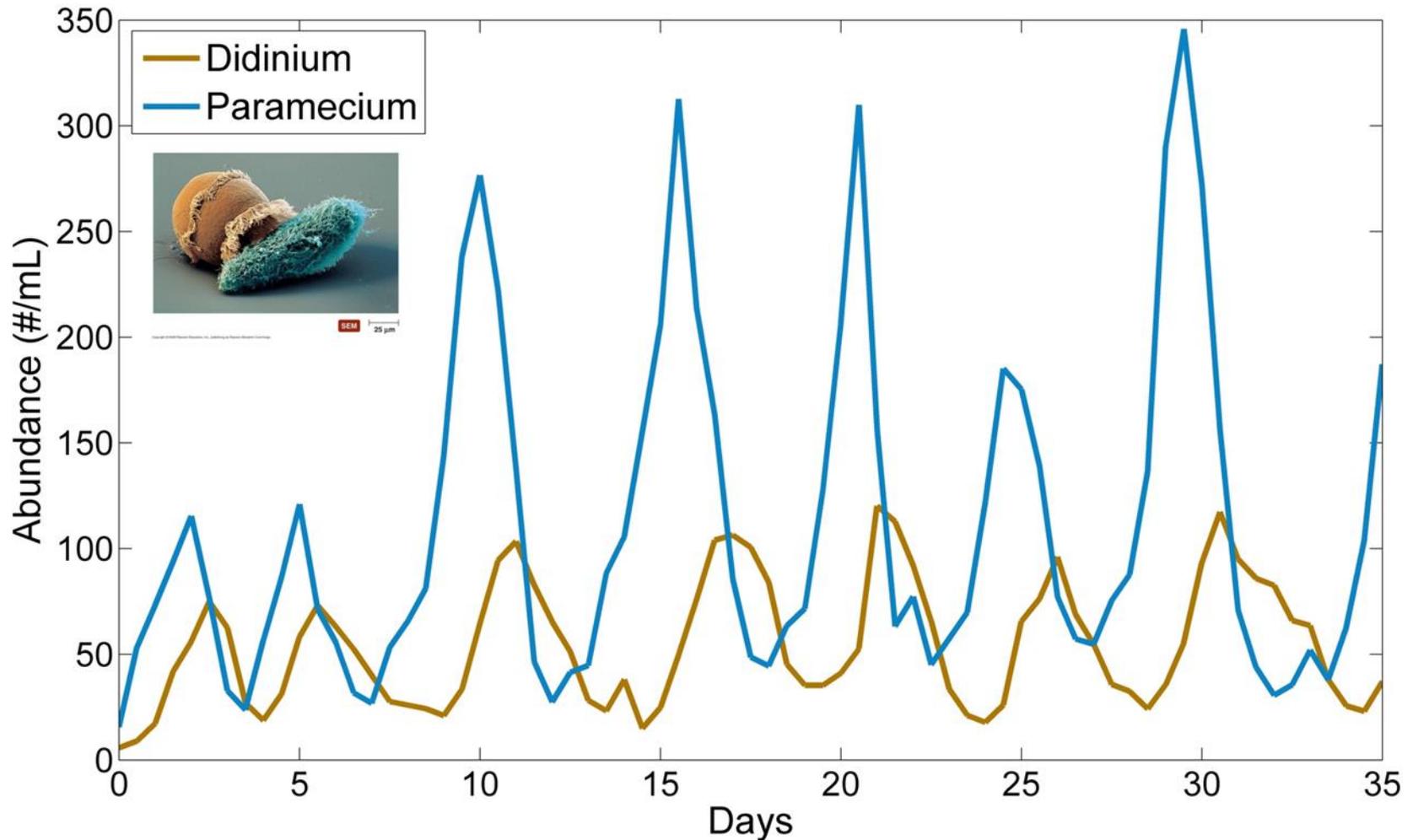
- **Separability:** cause and effect are separable.



Pitfalls of Granger Causality



Mutual Causation: Predator and Prey



Data from Sugihara G et al. **Science** (2013)

Summary

- Correlation is a global measure of dependency between signals that is determined by both phase and amplitude.
- Granger causality is a measure of the cause and effect in time series which is mainly driven by time precedence principle.
- Measures of correlation and causality from brain signal data can help understand the brain connectomes.