MGH/HST Athinoula A. Martinos Center for Biomedical Imaging

MASSACHUSETTS GENERAL HOSPITAL

Harvard-MIT Health Sciences & Technology

Università di Roma Tor Vergata

Reconstructing multivariate causal structure between functional brain networks through a new Laguerre-decomposition based Granger causality approach

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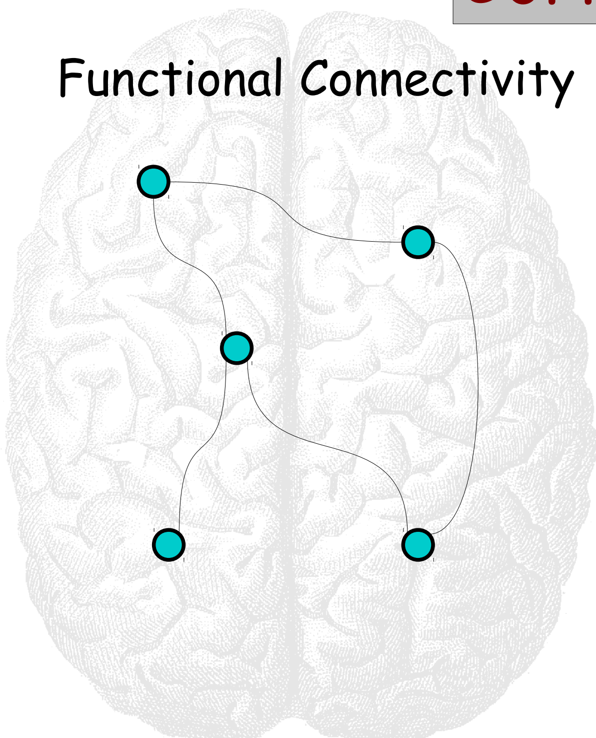
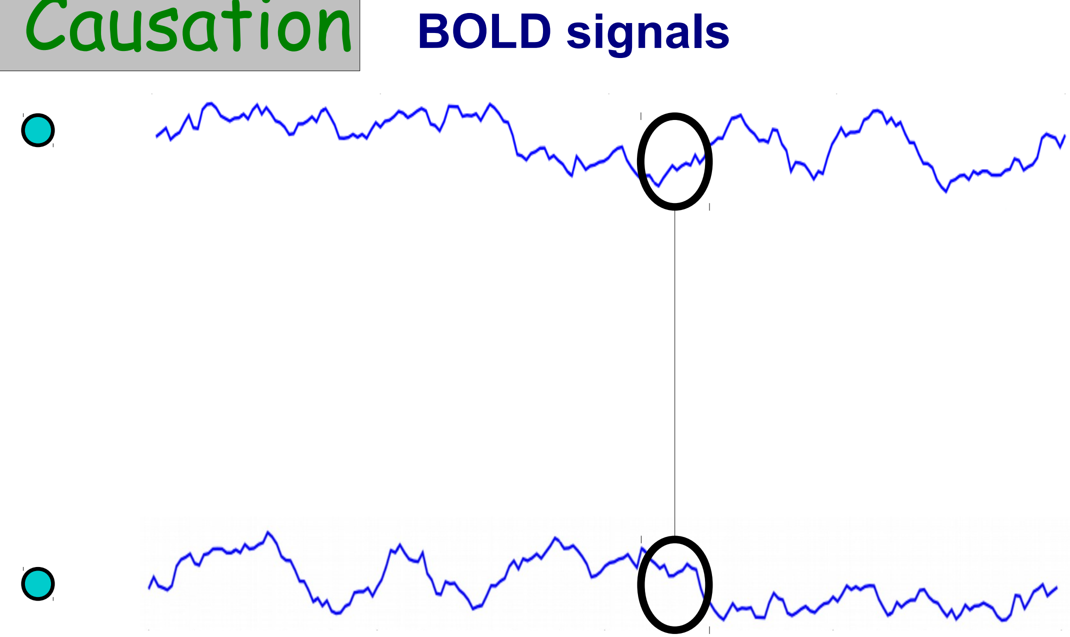
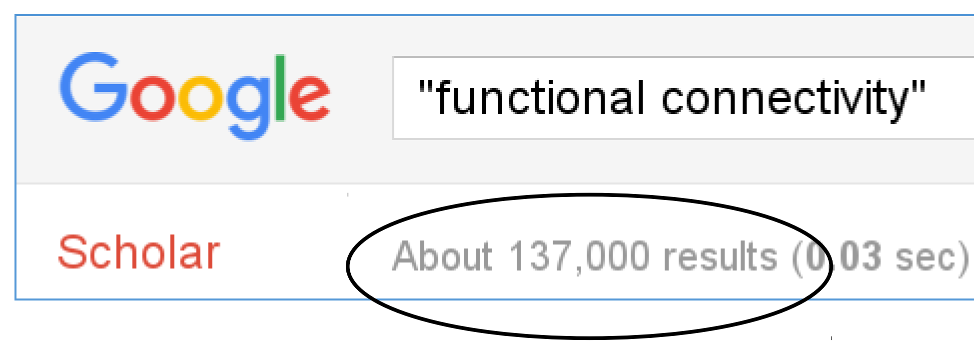
From Correlation to Causation

Correlation ≠ Causation



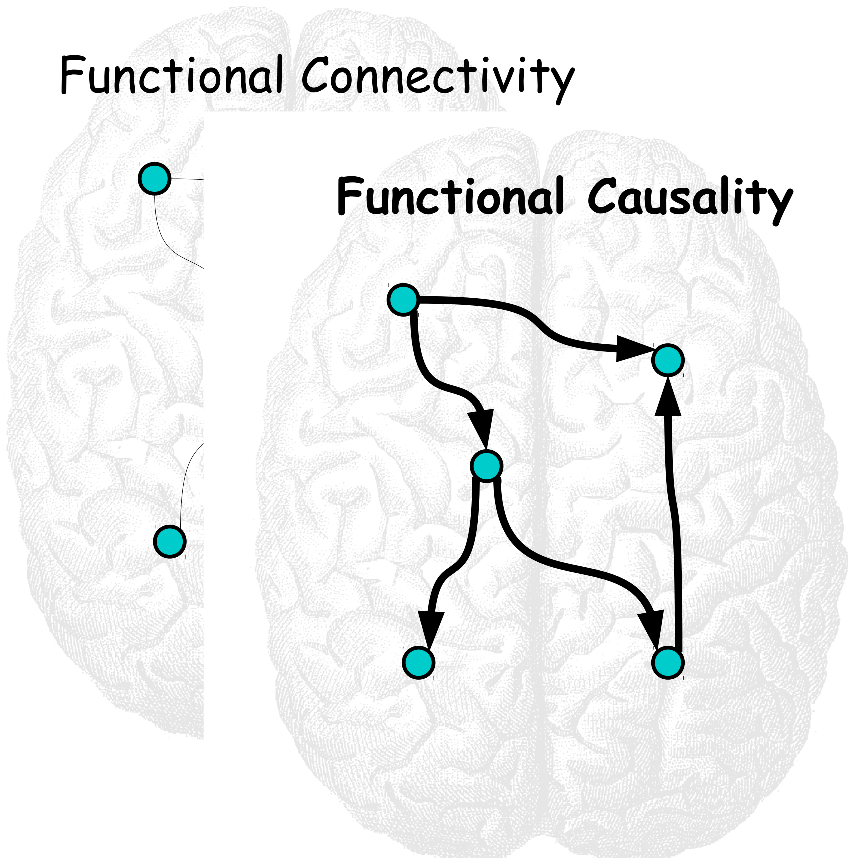


- functional brain connectivity: statistical dependencies among non-spatially-contiguous neuro-physiological events.
- fMRI correlation studies provides important insight

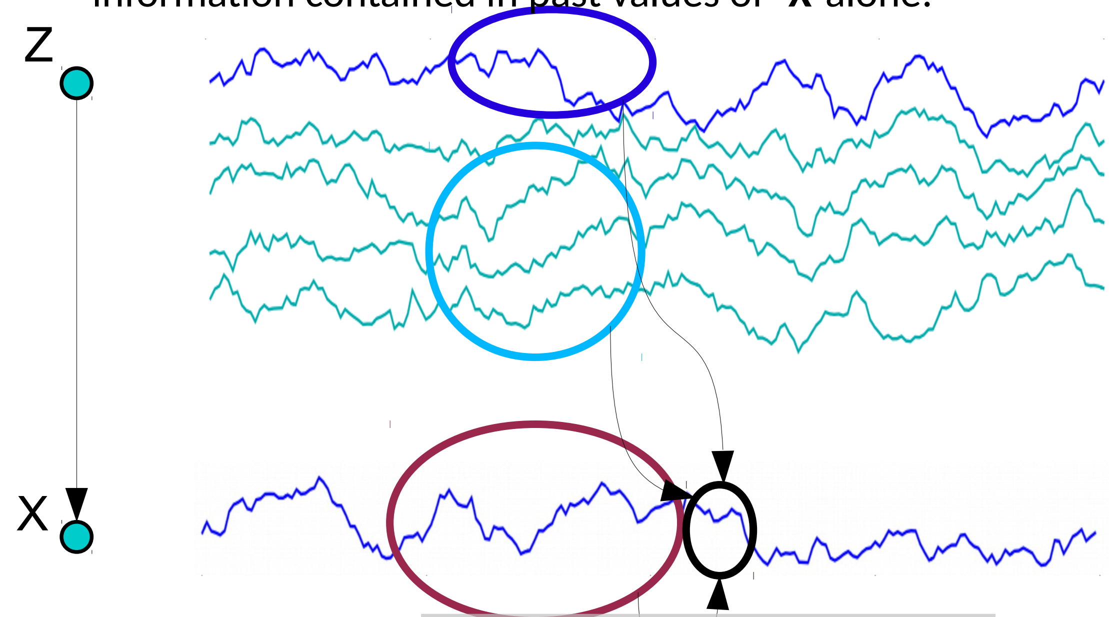


Globally conditioned Granger causality

Conditioned approach



If **Z** "G-causes" **X**, then past values of **Z** should contain information that helps predict **X** above and beyond the information contained in past values of **X** alone:



$$\mathcal{F}_{Z \to X|Y} = \ln \frac{|\varepsilon'|}{|\varepsilon|}$$

- Causality studies provides the **direction** of the interractions

$$X_t = \sum_{k=1}^{p} A'_k X_{t-k} + \sum_{k=1}^{p} B'_k Y_{t-k} + \varepsilon'_t$$

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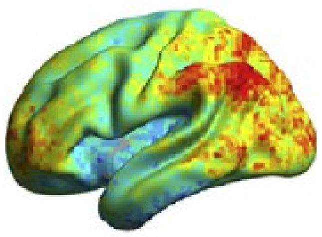
Globally conditioned Granger causality

Limitations in fMRI

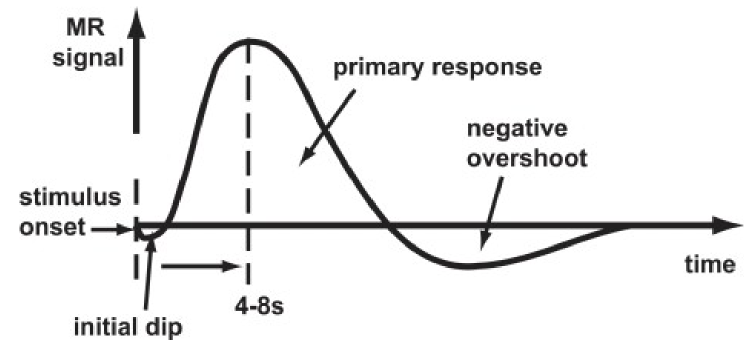
- Inter-regional differences in haemodynamic response function might obfuscate underlying neural dynamics
- Signal not very suitable: need to find a tradeoff between SNR and TR (sampling frequency)
- short signals, and too many parameters

Local variations in HRF parameters

Time to peak



Wu et al, Medical Image Analysis (2013)



- Turns out that GC is **invariant to haemodynamic convolution** *(Deshpande 2010, Shippers 2011, Barnett, 2011, Seth 2013)*
- However, GC is sensitive to sampling frequency and/or eccessively low SNR *(Seth 2013)*
- **Problem in principle becomes "only" problem in practice** (which could be tackled with technology)
- Use of "blind deconvolution approach" for resting state? [*Wu et al, Medical Image Analysis (2013)*]

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We want to “search” into the past but we can't afford a large autoregressive order.

Squeeze more “past” per parameter!

$$x_t = \mathbf{A}\left(\mathscr{L}^{(m)}(x) \oplus \mathscr{L}^{(m)}(z)\right) + \varepsilon_t$$

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$$\mathscr{L}^{(m)}(x) = \sum_{n=1}^{N} \phi_m(n)(x_{N-n} - x_{N-n-1})$$

$$\phi_m(n) = \alpha^{\frac{n-m}{2}} (1-\alpha)^{\frac{1}{2}} \sum_{j=0}^{m} (-1)^j \binom{n}{j} \binom{m}{j} \alpha^{m-j} (1-\alpha)^j$$

Laguerre polynomials

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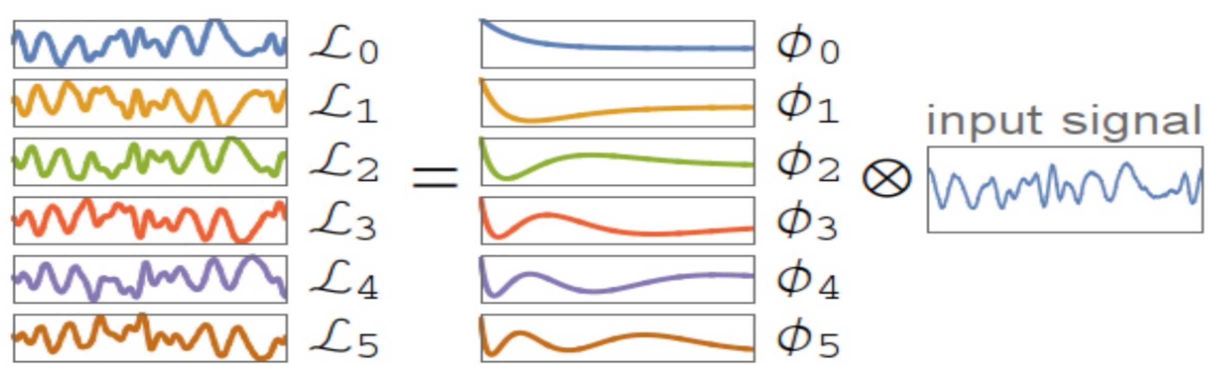
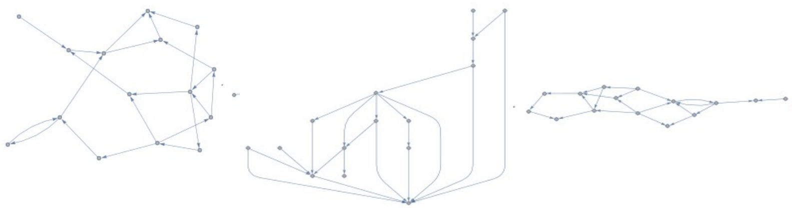


Laguerre-based Granger causality

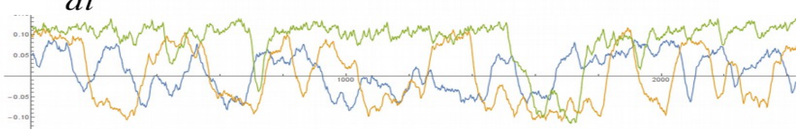
Synthetic simulations

- Several network topologies

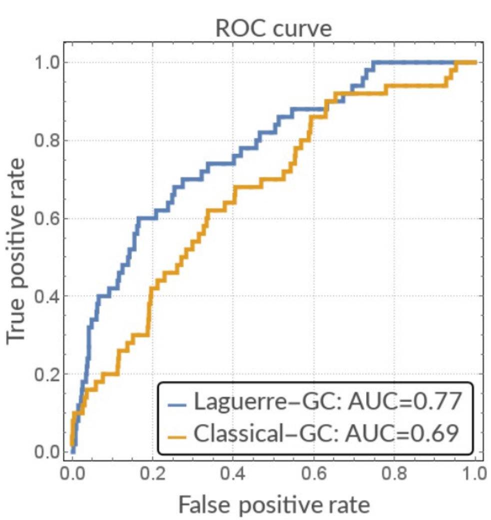


- Duffing oscillators in each node

$$\frac{d}{dt}x_i(t) = y_i + c_{i,j}(\eta_j - x_i) + \xi(t)$$
$$\frac{d}{dt}y_i(t) = -\delta y_i - \beta x_i - \alpha x^3 + \gamma\cos(\omega t + \phi_i)$$
$$\frac{d}{dt}\eta_i(t) = -\eta_i/\tau + b x_i.$$



- Characterization of sensitivity and specificity



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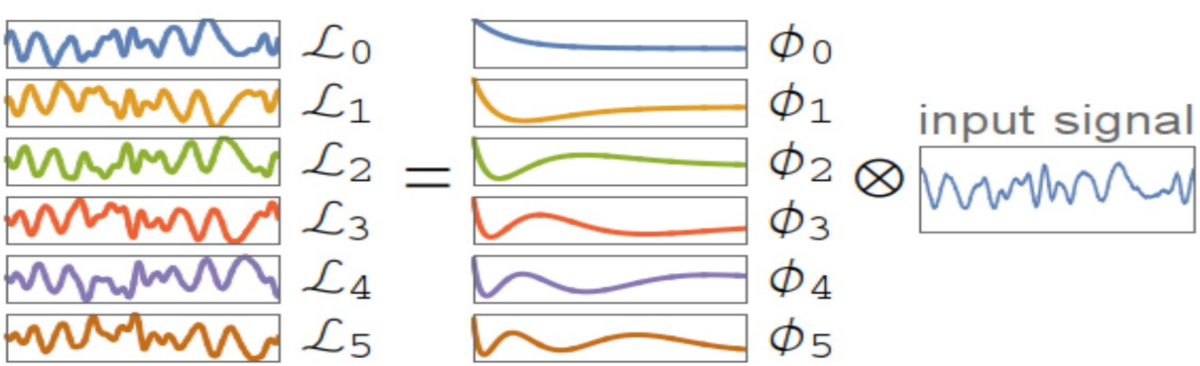

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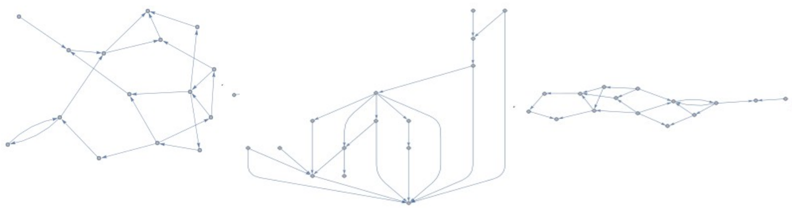

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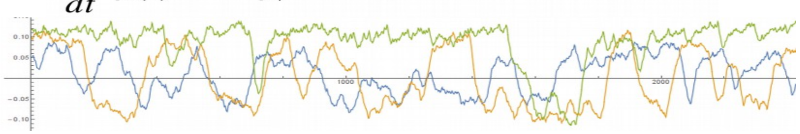
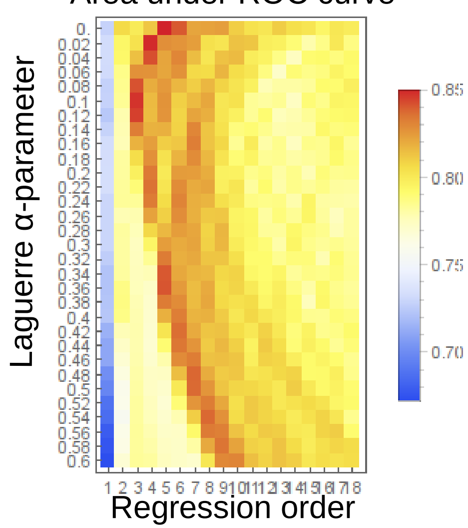


- Characterization of sensitivity and specificity

Area under ROC curve



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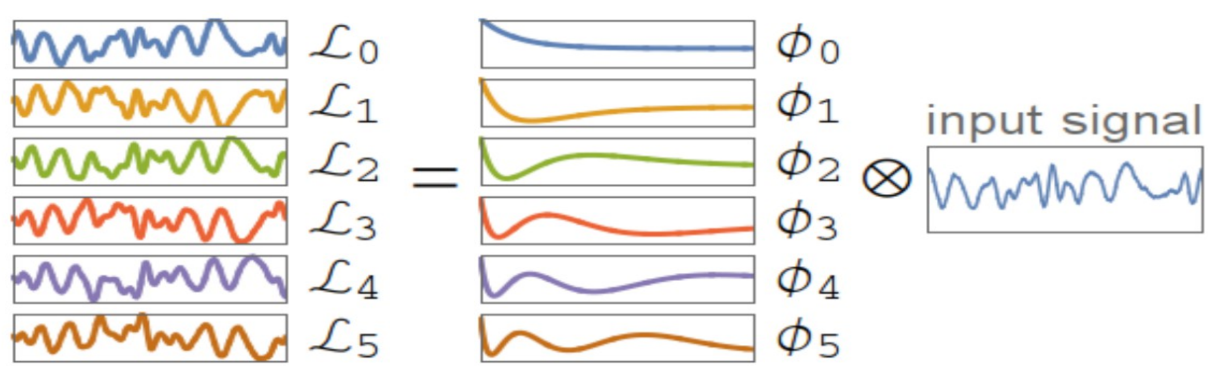
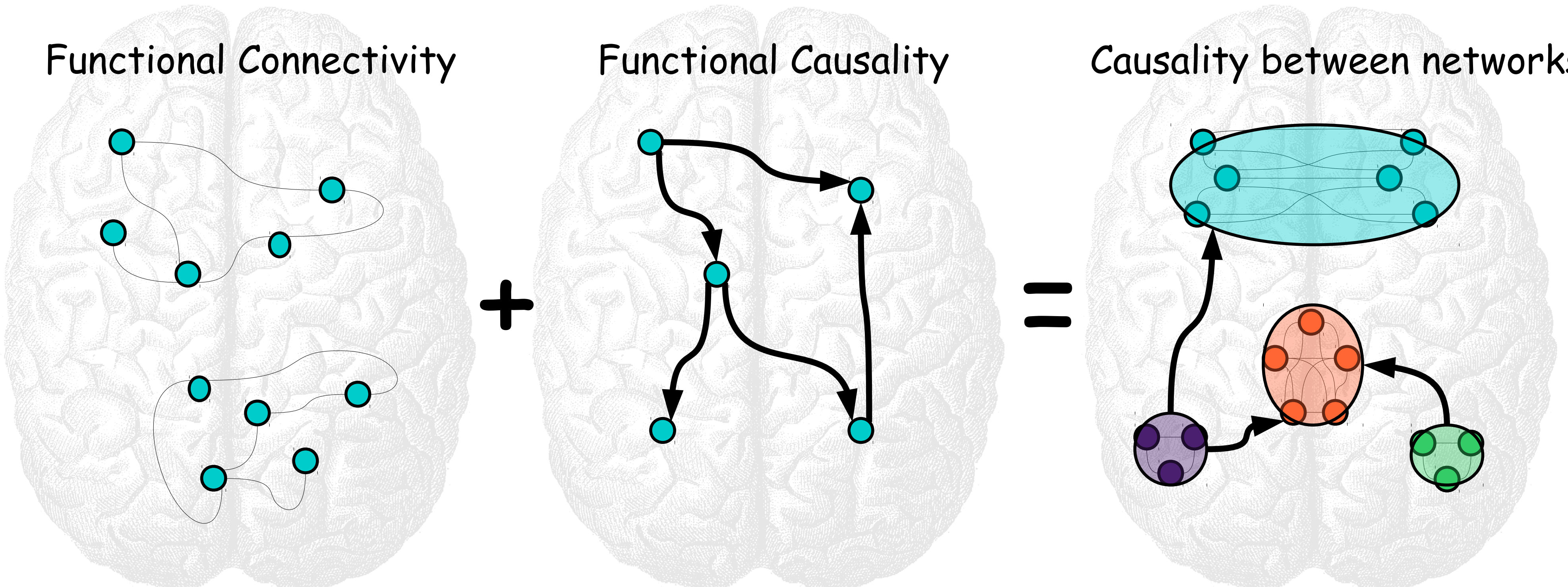
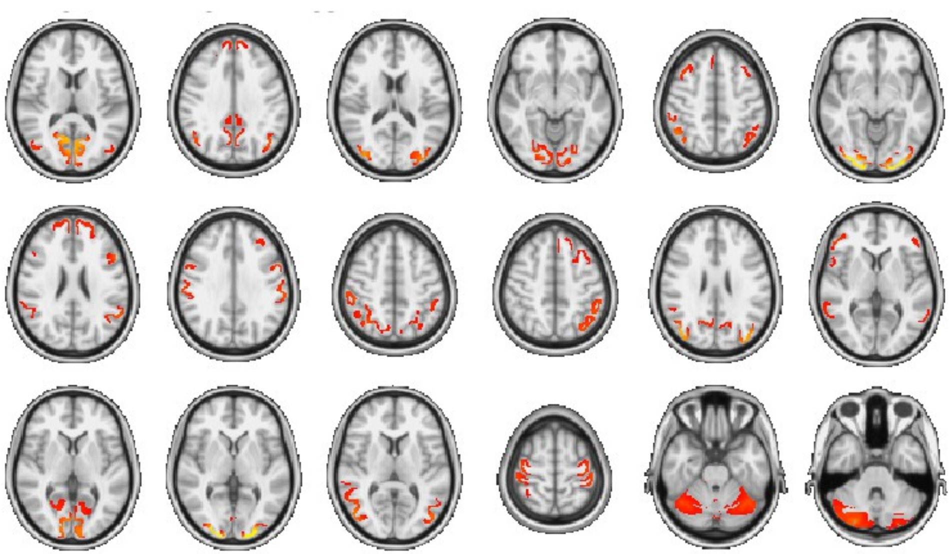


Between-network Laguerre-based Granger causality



Networks definitions by ICA components:



Dataset:

3T fMRI

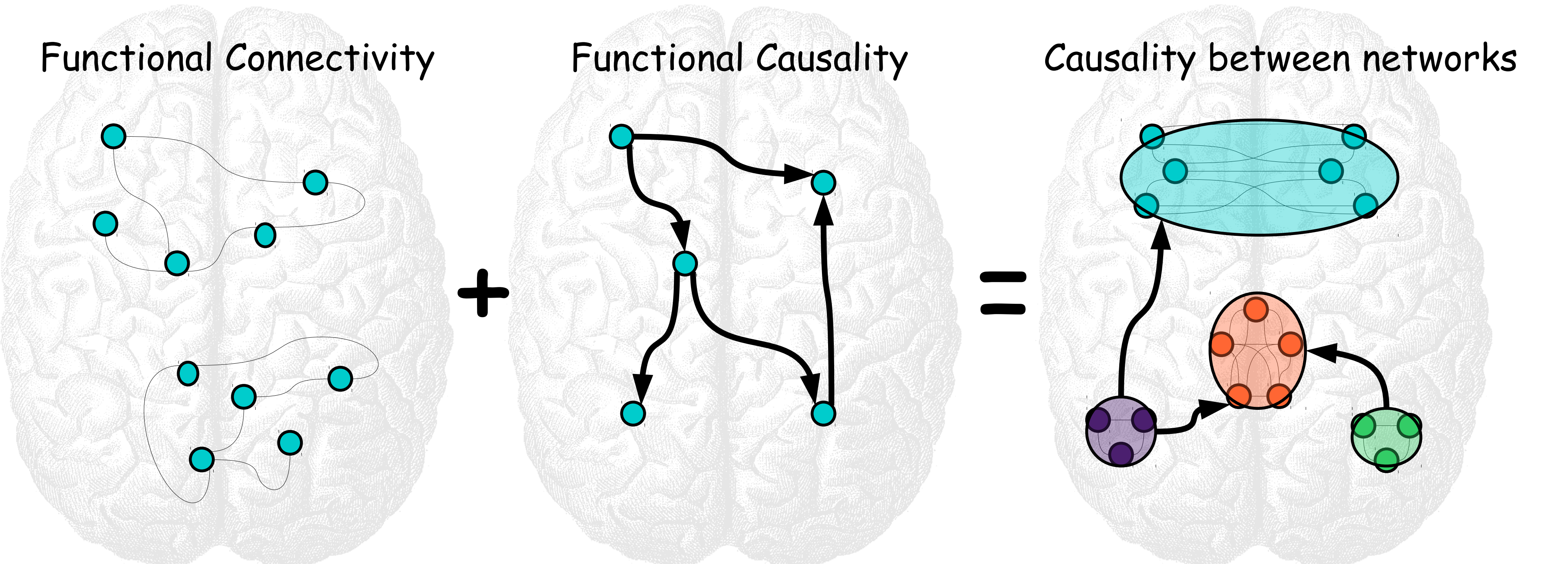
HUMAN Connectome PROJECT

800+ subjects (age 28 ± 3) scanned

Single-shot 2D EPI readout

TR =0.72 s, whole brain coverage

Between-network Laguerre-based Granger causality



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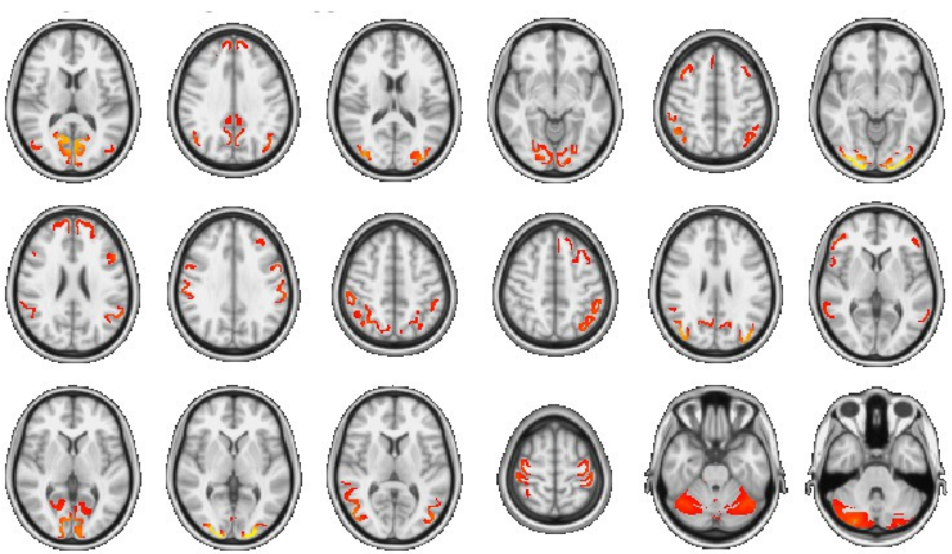
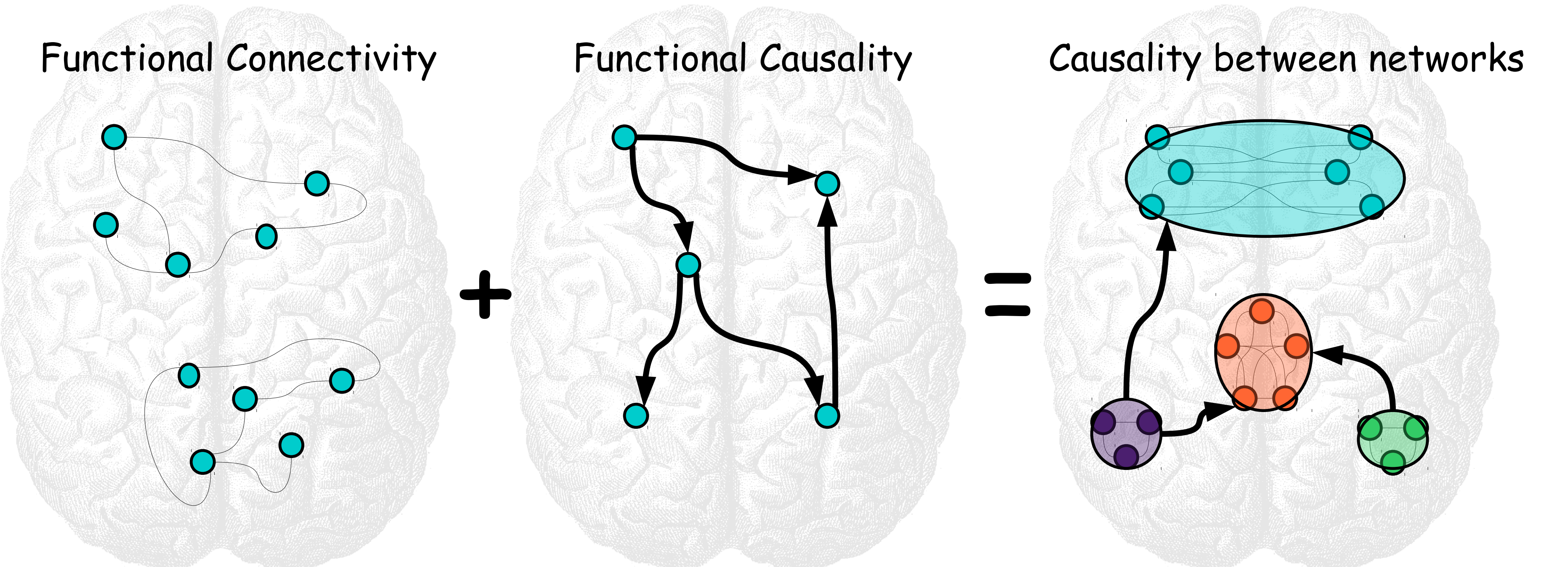


- Subject-level ICA+FIX (physiological noise removal)
- Group-level: Group-PCA (Melodic's incremental)
- Subject-level: Group-ICA (at 15,25,50 components)

Each ICA component signal is an average of a 3D-volume

+ deconvolution for HRF influence removal

Between-network Laguerre-based Granger causality



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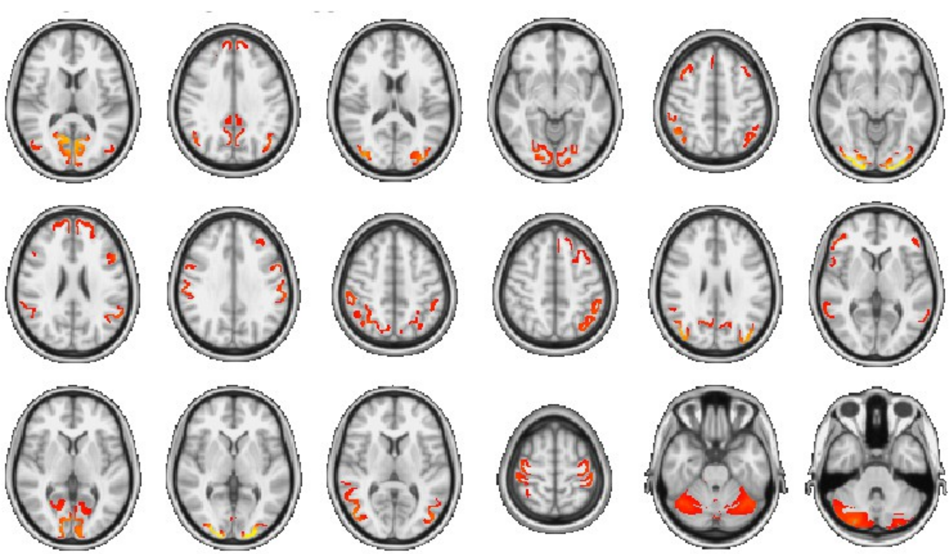
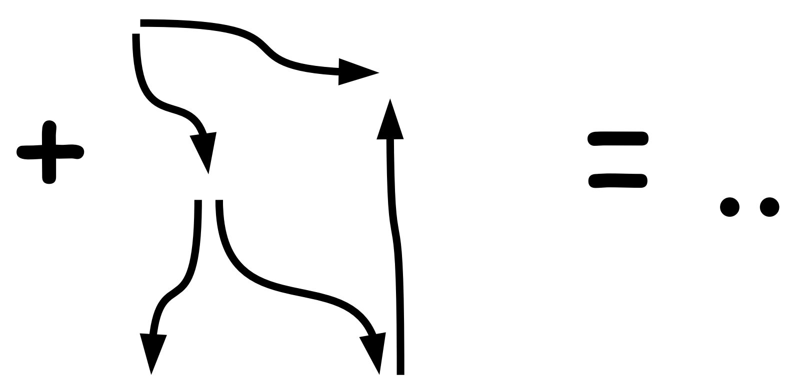
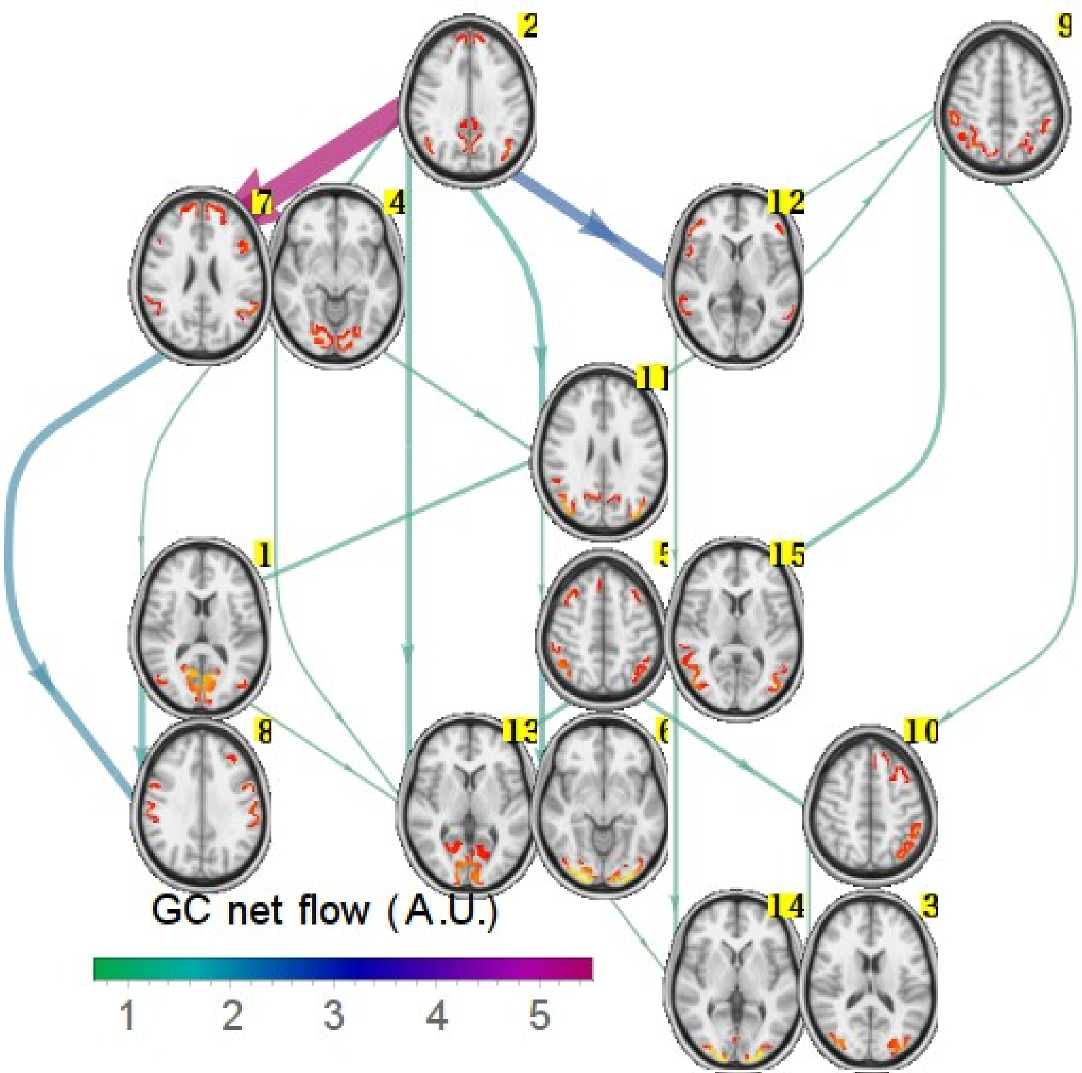


Directed structure



Between-network Laguerre-based Granger causality

Group-wise information net flow



- 450+ subjects analysed
- Results extremely stable; qualitative same results for:
  - small changes of autoregressive order
  - small changes of α-parameter
  - with or without HRF deconvoltion
- Almost hierarchical topology

Neurophysiological interpretation

	ICA neurological meaning
1	Secondary Visual network (extrastriate visual network)
2	Default Mode Network (DMN)
3	Primary Visual network (striate visual network)
4	Visuo-premotor network
5	Fronto-Parieto-Cerebellar network left side
6	Fronto-Parieto-Cerebellar network right side
7	Salience network (SN)
8	Basal Ganglia visual striate network including dmPFC (mainly)
9	Cerebellar network
10	Hippocampal, medial temporal lobe memory spatial orientation network
11	Sensory-motor network
12	Fronto-temporal-parietal “language” network
13	*no unique neurophysiological interpretation*
14	Fronto-polar-higher executive function network
15	*no unique neurophysiological interpretation*

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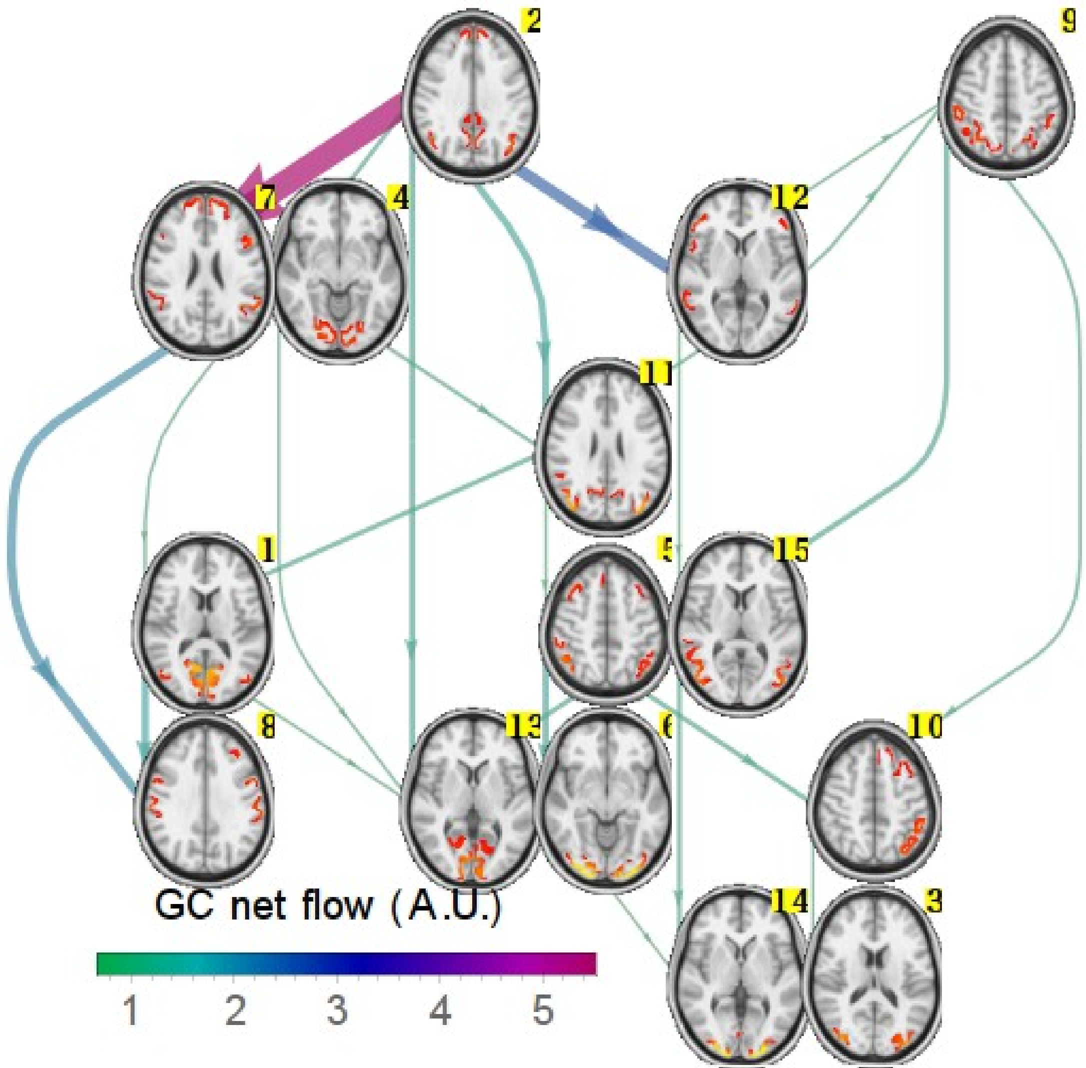

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Neurophysiological interpretation

- The default-mode-network (DMN) modulate the salience-network (SN) **We demonstrate for the first time that this interaction may be driven by top-down signal from the DMN to SN**
- DMN "top-down" influence on fronto-temporal circuits localized across regions strongly implicated in language production, comprehension and semantic memory. DMN top-down inputs to the extended fronto-temporal language network as the basis of the linguistic self-referential processes (thought to enhance the consciousness experience).

Conclusions

- Laguerre-based GC delivers better performance as compared to classical, linear MVAR-based Granger causality methods.
- Laguerre-based GC applied detect in vivo functional interactions and causal dynamics across multiple neural networks

Future work

- Investigation of information flow between in vivo functional networks during specific-task (cognitive, memory, sensory, motor, etc...).

Thank you!