

Dynamic Causal Modeling: Experimental and Clinical Stakes

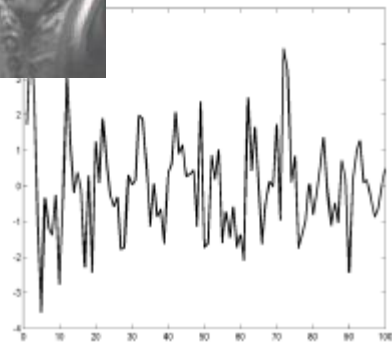
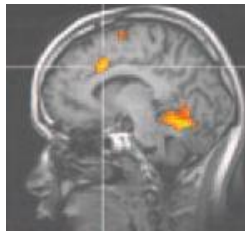


Jérémie Mattout, PhD

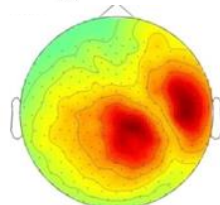
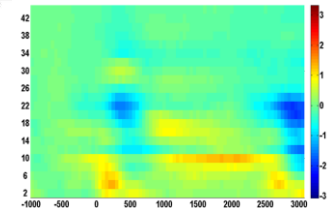
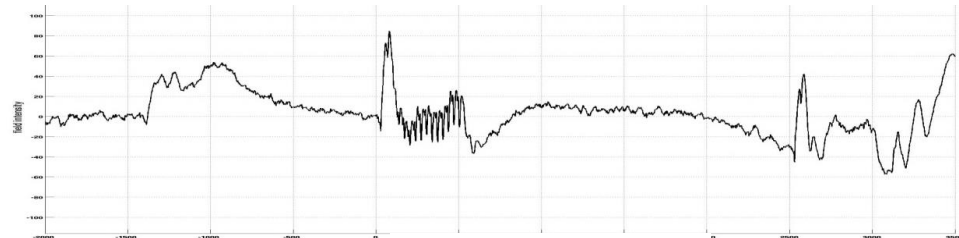
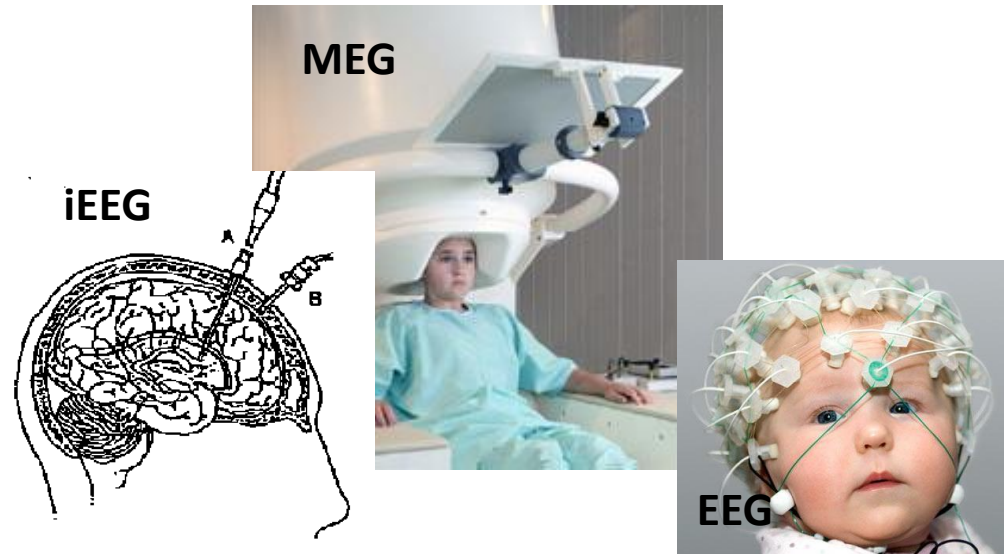
Lyon Neuroscience Research Center, France
Brain Dynamics & Cognition Team (DYCOG)

Measures of brain activity

fMRI



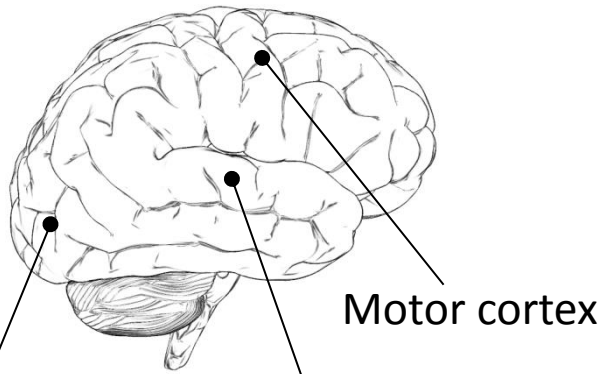
Electrophysiology



A systemic approach

- Apprehends task-related brain activity as the result of complex, non-linear interactions between neuronal populations within a network

Functional specialisation

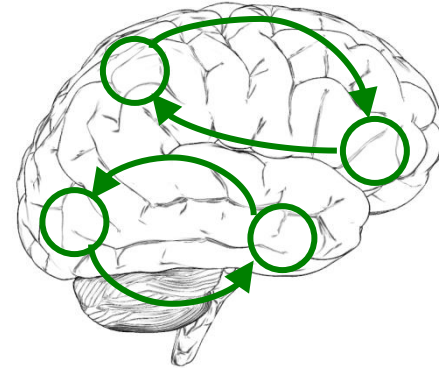


Visual cortex

Auditory cortex

Motor cortex

Functional integration

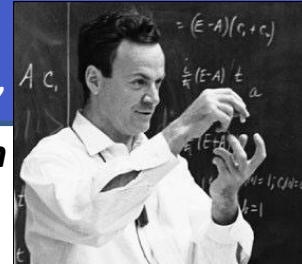


- Unifies and concentrates on the interaction between elements
- Studies the effect of interactions
- Emphasizes global perception
- Modifies groups of variables simultaneously
- Integrates duration of time and irreversibility
- Validates facts through comparison of model predictions with reality

A generative (dynamical) model approach

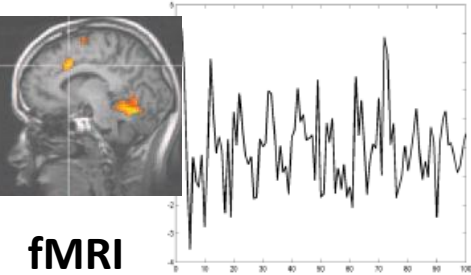
“What I cannot create, I cannot understand”

Richard Feynman

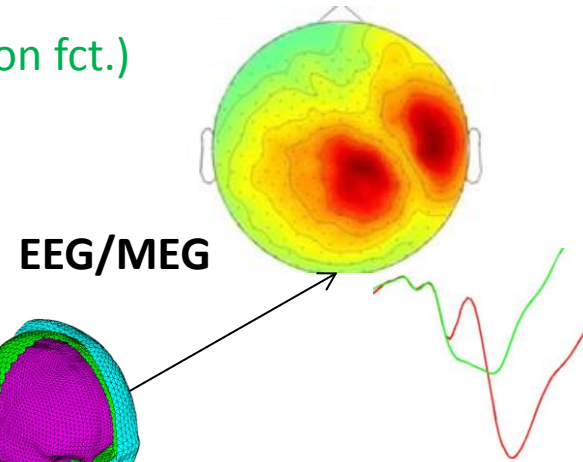


- From underlying neuronal activity to observed data

Hemodynamic



Electromagnetic



mapping from state to data (observation fct.)

$$y = g(x, u, \theta) + \varepsilon$$

temporal
Convolution

spatial
convolution

neural state dynamics (evolution fct.)

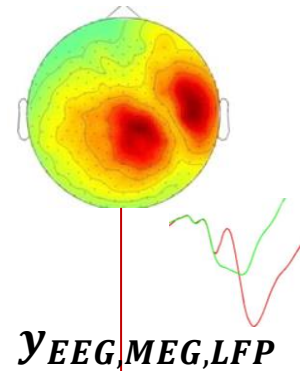
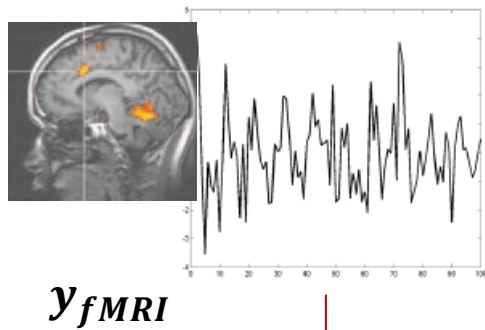
$$\dot{x} = f(x, u, \theta)$$

Input u

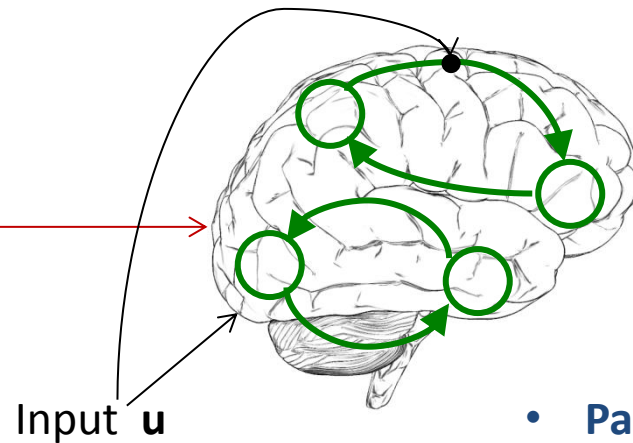
- Simple f
- Complex g

- Complex f
- Simple g

Model fitting



Inverting model $M = \{f,g\}$

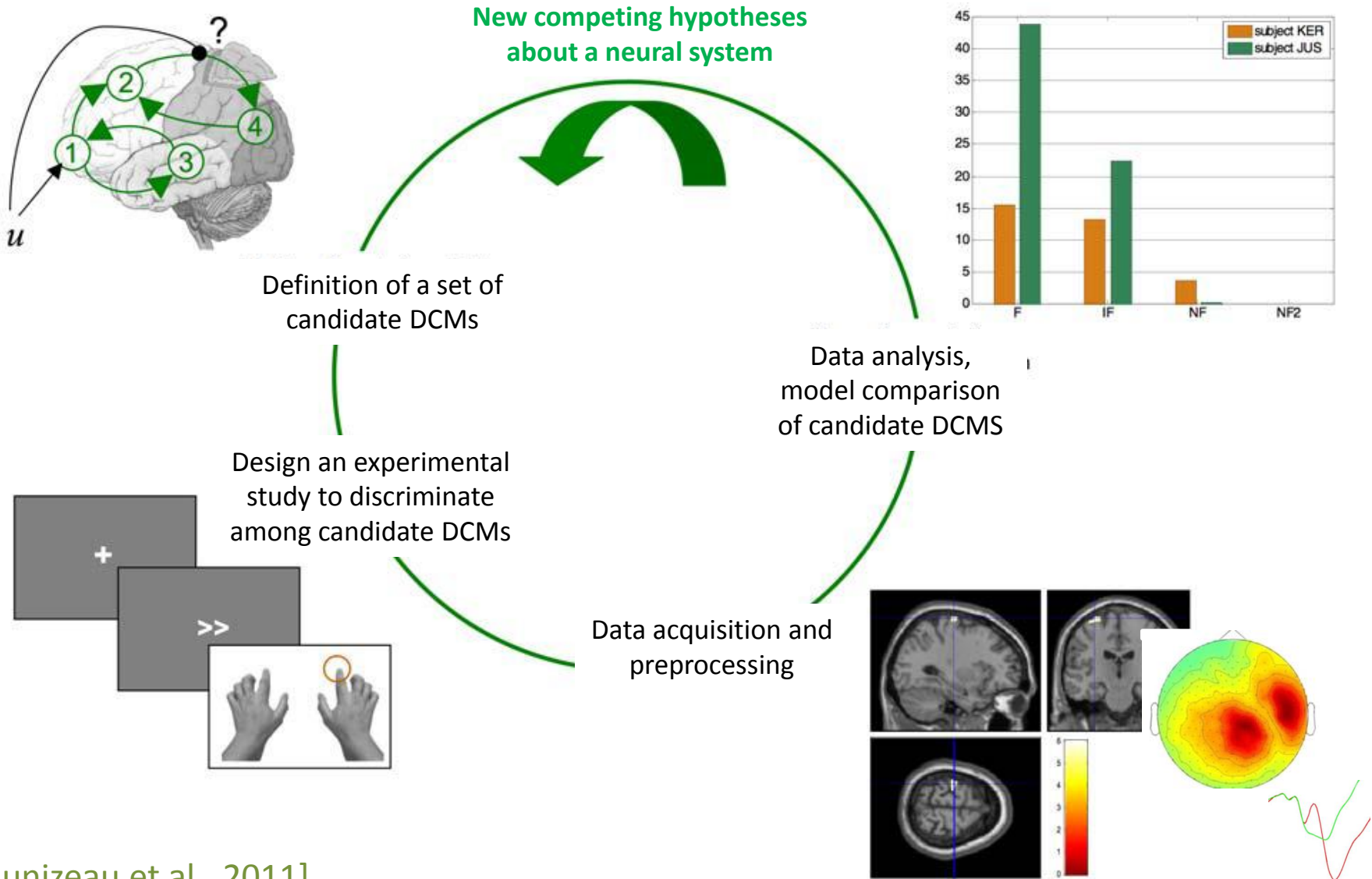


- Parameter estimation
- Probabilistic representation
- Bayesian inference

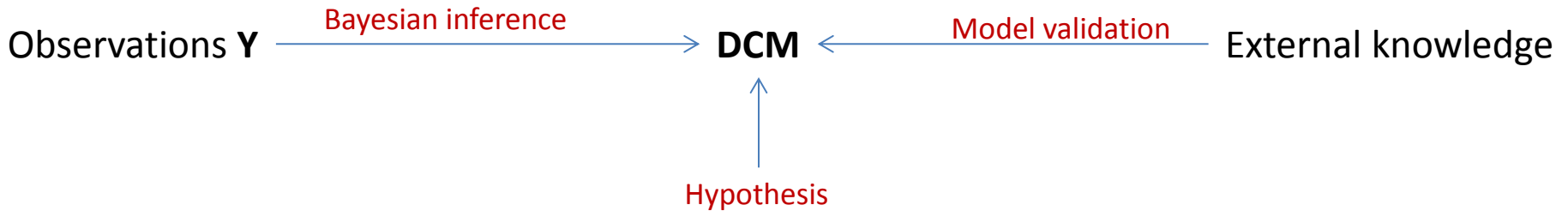
Model comparison

- **Bayesian inference enables formal model comparison/selection**
- **Alternative hypothesis correspond to competing models M1, M2, M3 ...**
- **Models may differ in any of their dimension (e.g. network architecture, modulation of connections, ...)**

The « DCM cycle »



Model validation

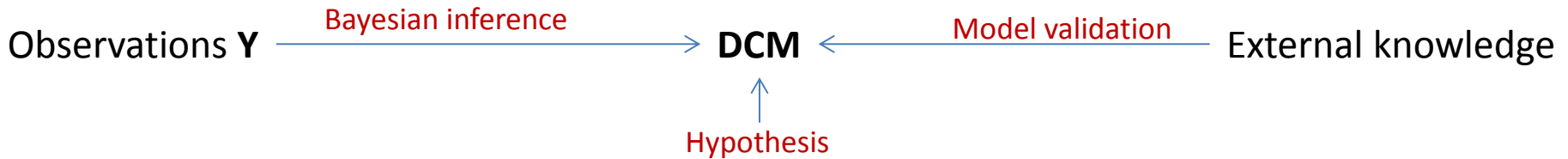


- **Reliability**

- Parameter estimates are highly reliable across sessions [Schuyler et al., 2010]
- Model selection is highly reliable across sessions [Rowe et al., 2010]
- Model selection is consistent accross subjects [Garrido et al., 2007]



Model validation



- **Face Validity**

- Does the method measure what it is supposed to measure ?
- Requires knowing the « true » model structure and parameter values -> simulations
[Lee et al., 2006 ; Stephan et al., 2007, 2008]

- **Construct Validity**

- Do we reach similar conclusions with other constructs ?
- > Requires comparison with other inference techniques or methods to assess connectivity
[Penny et al., 2004]

- **Predictive Validity**

- Do DCM predictions fit with independent knowledge of the same phenomenon ?
- > Requires other (reliable) sources of information
[Moran et al., 2008 ; David et al., 2008]

Reproducibility

Reproducibility

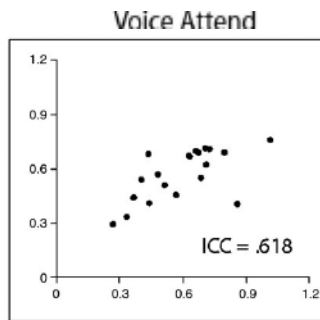
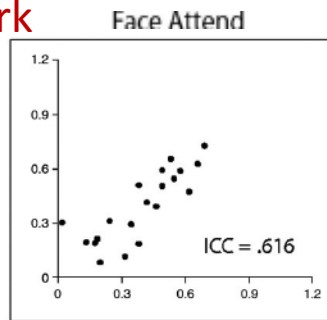
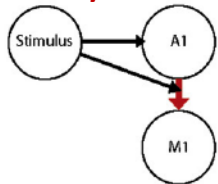
parameter estimates across sessions

Dynamic Causal Modeling applied to fMRI data shows high reliability

Brianna Schuyler^{a,b}, John M. Ollinger^a, Terrence R. Oakes^{a,d}, Tom Johnstone^{a,e}, Richard J. Davidson^{a,c,*}

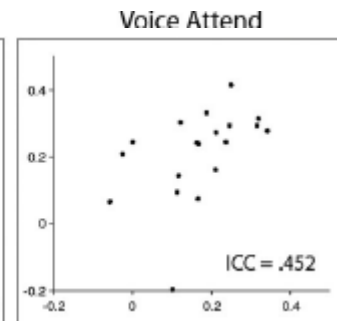
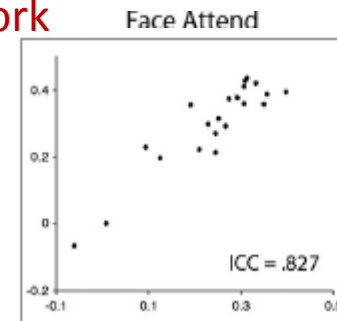
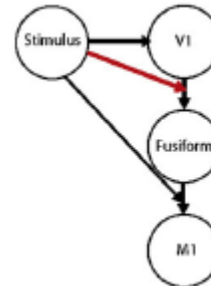
NeuroImage 49 (2010) 603–611

Auditory network



- 2 groups (N = 21 each)
- Scan 1 vs. Scan 2

Visual network



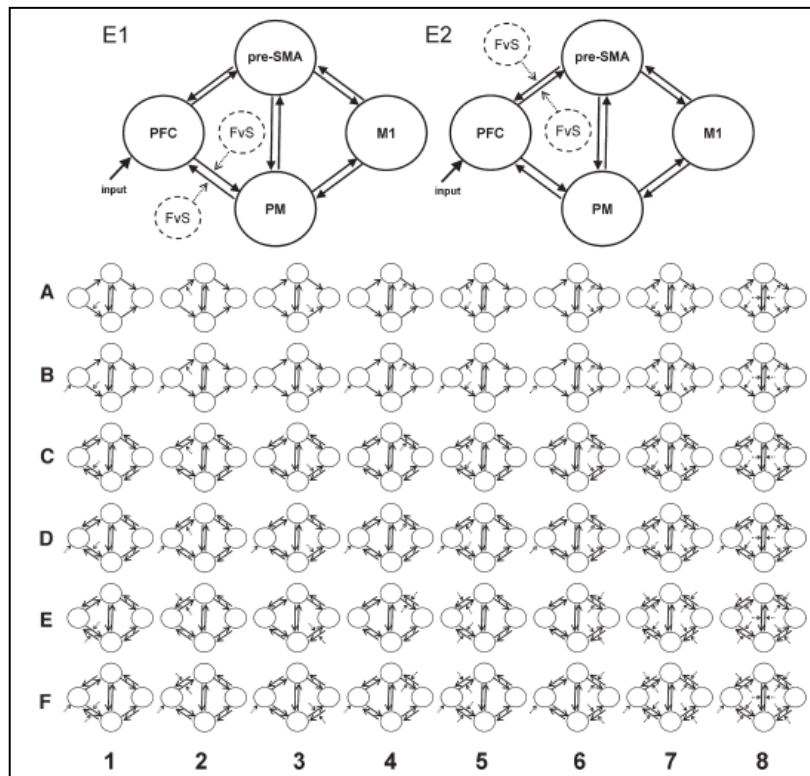
Reproducibility

model comparison across sessions and subjects

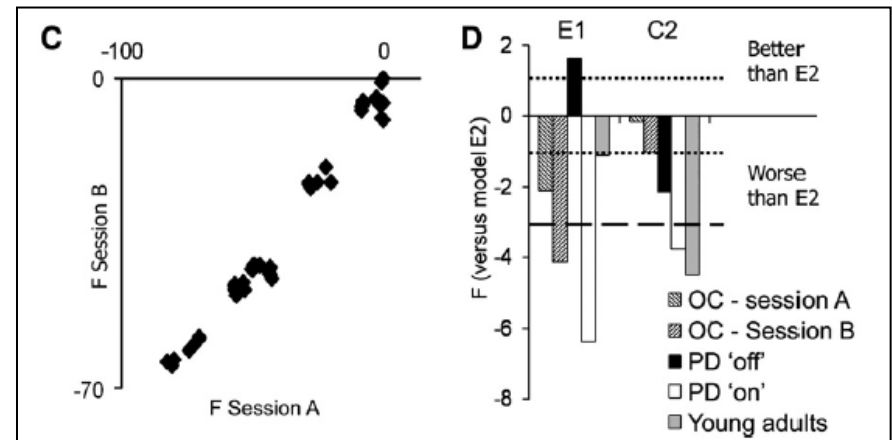
Dynamic causal modelling of effective connectivity from fMRI: Are results reproducible and sensitive to Parkinson's disease and its treatment?

J.B. Rowe ^{a,b,c,*}, L.E. Hughes ^{a,b}, R.A. Barker ^{a,d}, A.M. Owen ^b

NeuroImage 52 (2010) 1015–1026



- 4 groups (patients & controls)
- 48 models of action selection



Face validity

- Does the method measure what it is supposed to measure ?

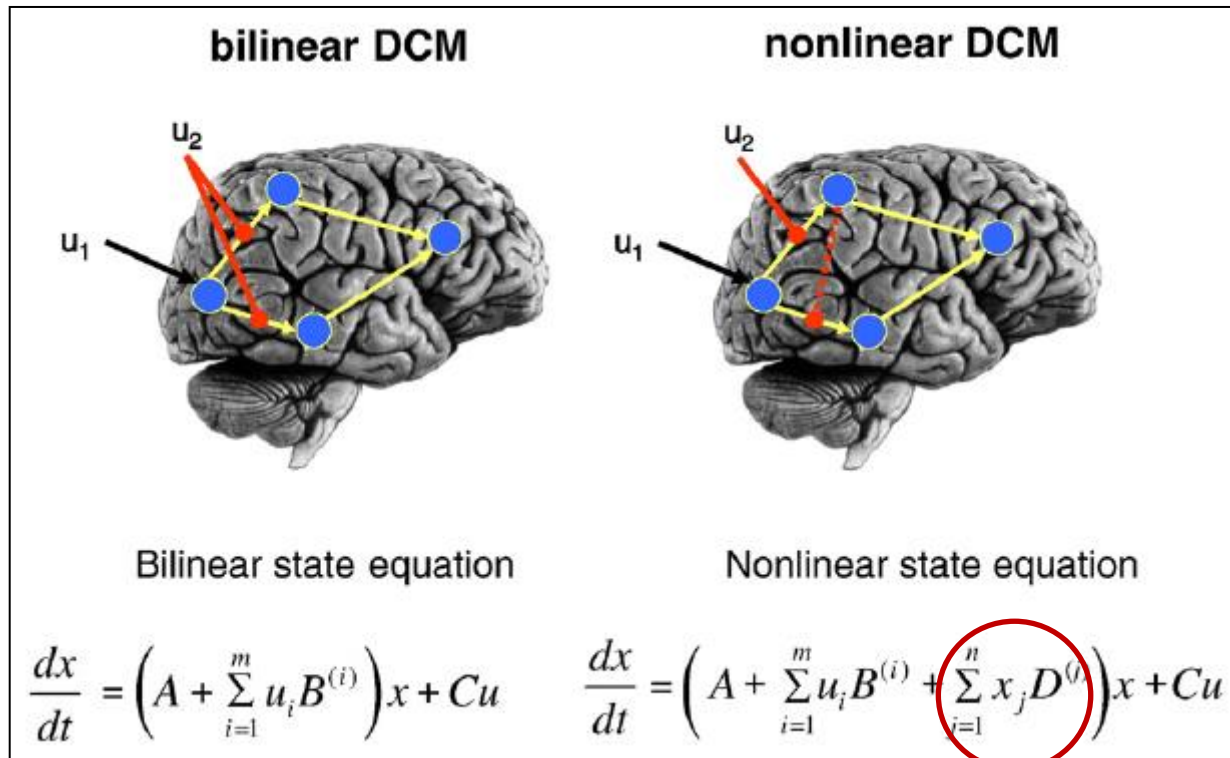
Face validity

simulations

Nonlinear dynamic causal models for fMRI

Klaas Enno Stephan^{a,b,*}, Lars Kasper^c, Lee M. Harrison^a, Jean Daunizeau^a, Hanneke E.M. den Ouden^a, Michael Breakspear^c, Karl J. Friston^a

NeuroImage 42 (2008) 649–662

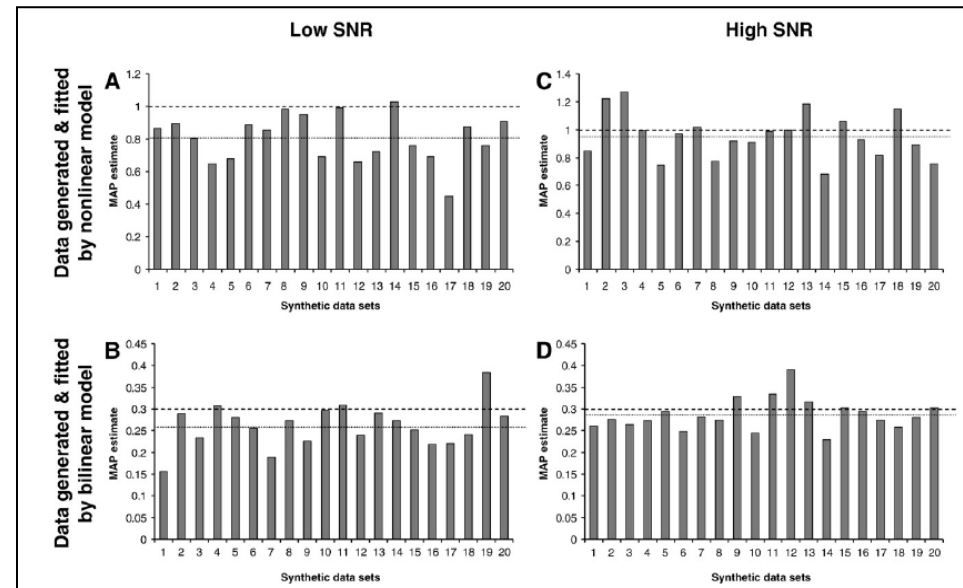
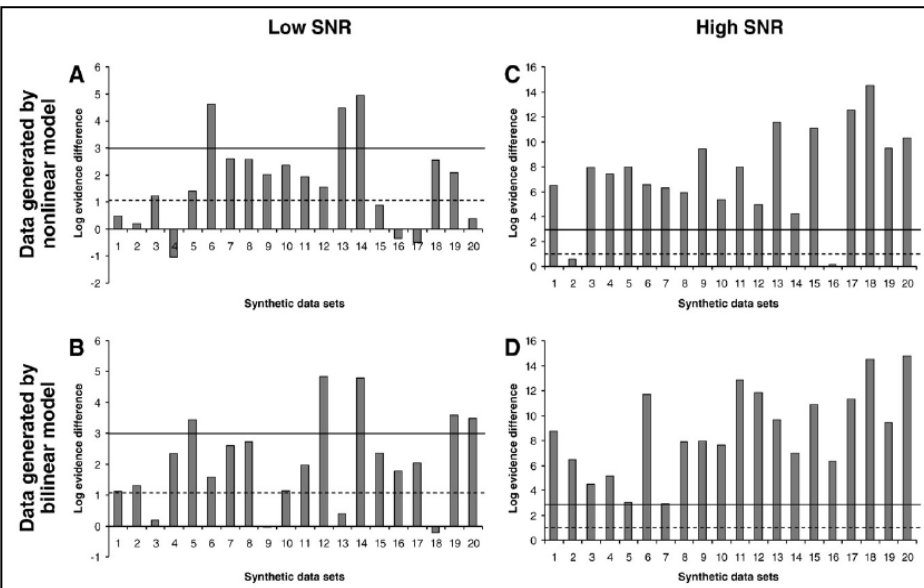


Face validity simulations

“Analyses of synthetic data show that nonlinear and bilinear mechanisms can be distinguished”

Model comparison

Parameter estimation



Positive evidence ----- True parameter values

Strong evidence ——— Average estimates

Construct validity

- Do we reach similar conclusions with other constructs ?

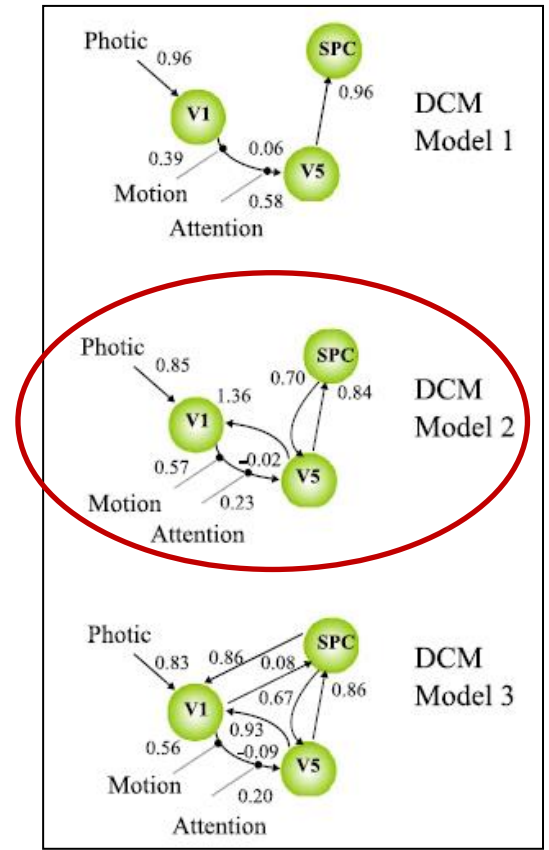
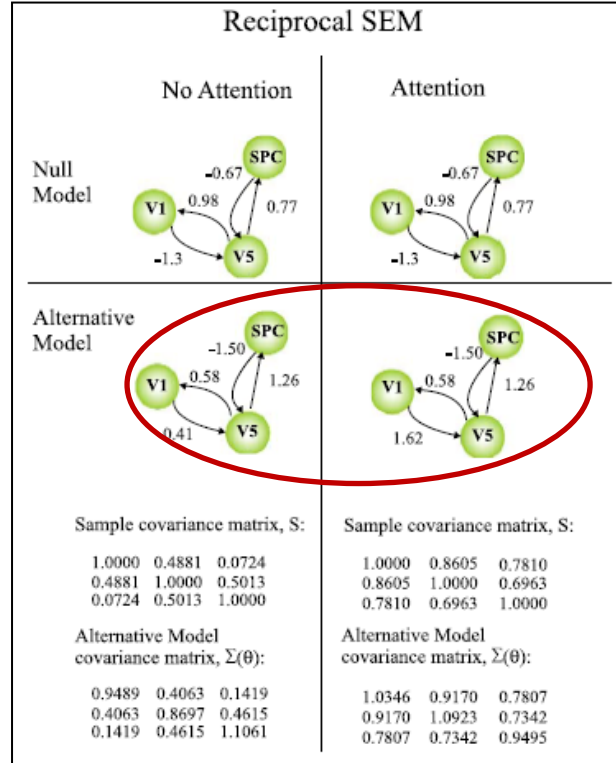
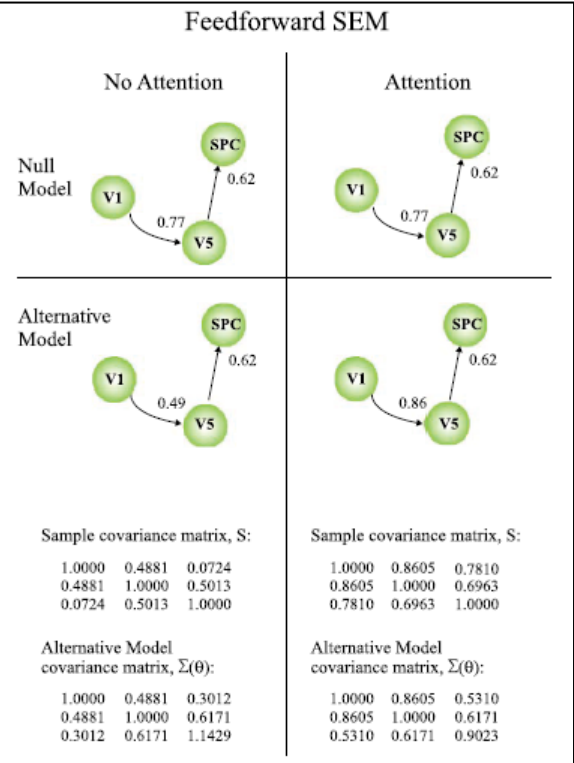
Construct validity

comparing DCM and SEM

NeuroImage 23 (2004) S264–S274

Modelling functional integration: a comparison of structural equation and dynamic causal models

W.D. Penny,* K.E. Stephan, A. Mechelli, and K.J. Friston



Predictive validity

- Do DCM predictions fit with independent knowledge of the same phenomenon ?

Predictive validity

comparing DCM with iEEG

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PLOS BIOLOGY

Identifying Neural Drivers with Functional MRI: An Electrophysiological Validation

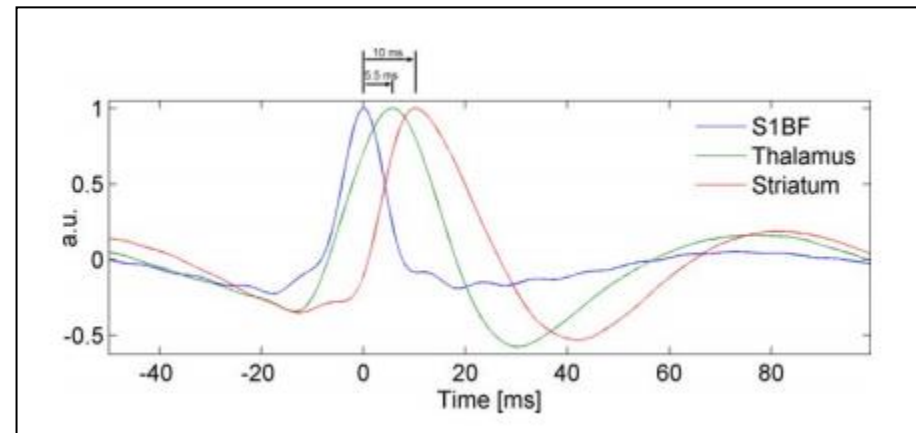
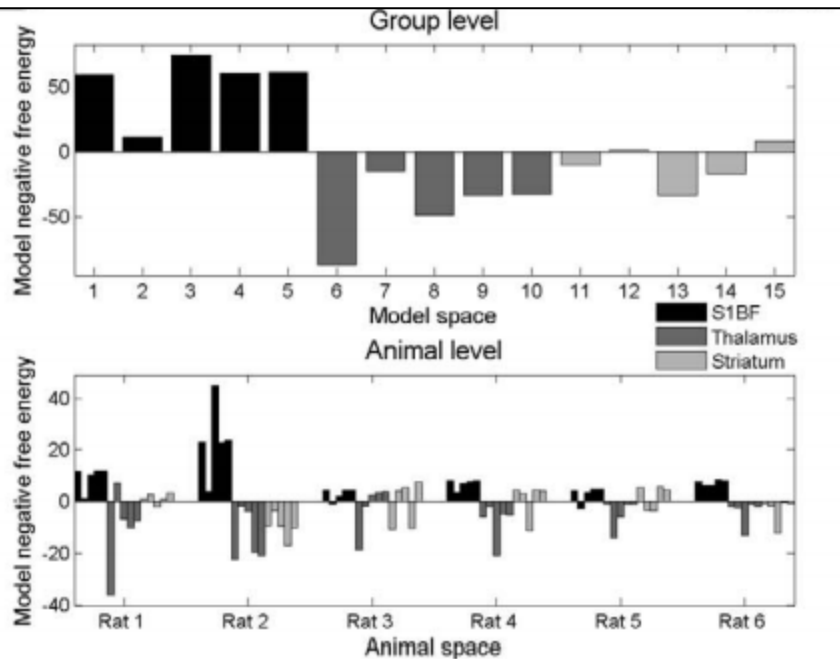
Olivier David^{1,2*}, Isabelle Guillemain^{1,2}, Sandrine Saitlet^{1,2}, Sebastien Reyt^{1,2}, Colin Deransart^{1,2}, Christoph Segebarth^{1,2}, Antoine Depaulis^{1,2}

2008

DCM model comparison

- 6 rats (absence epilepsy model)
- simultaneous EEG/fMRI
- iEEG later on

Temporal precedence inferred from iEEG



Predictive validity

the importance of hemodynamic deconvolution

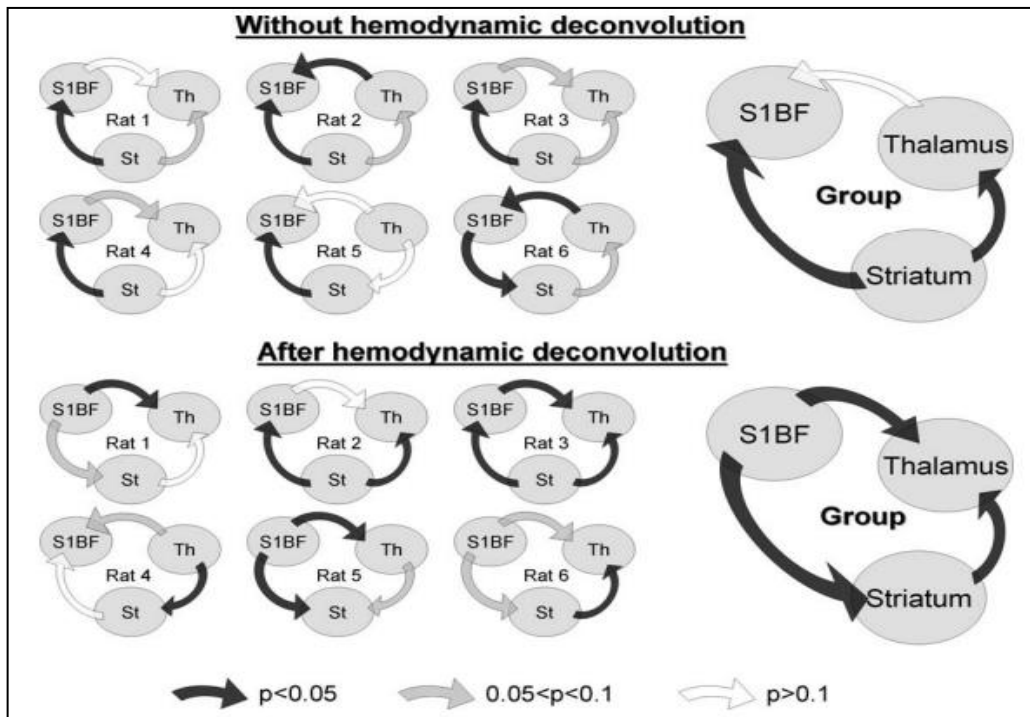
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2008



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- simultaneous EEG/fMRI
- iEEG later on

Oriented networks estimated from Granger Causality

Studying pathology: a few recent examples

Within subject differences

An fMRI study of motor imagery and execution in upper limb amputees

doi:10.1093/brain/awr337

Brain 2012; 135; 582–595 | 582

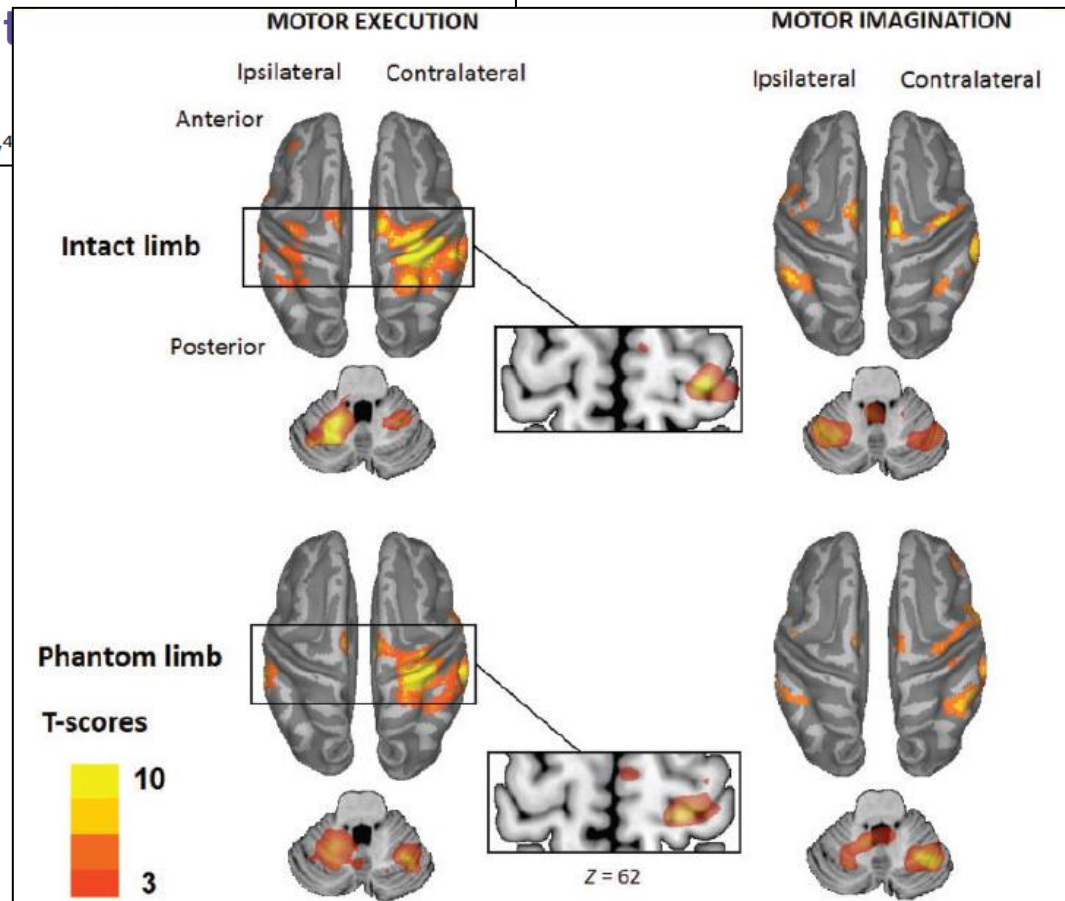
BRAIN
A JOURNAL OF NEUROLOGY

Are phantom limb movements closer to motor imagery or motor execution ?

Disentangling motor execution imagery with the phantom

Estelle Raffin,^{1,2} Jérémie Mattout,^{3,4} Karen T. Reilly⁴

Activation results



Within subject differences

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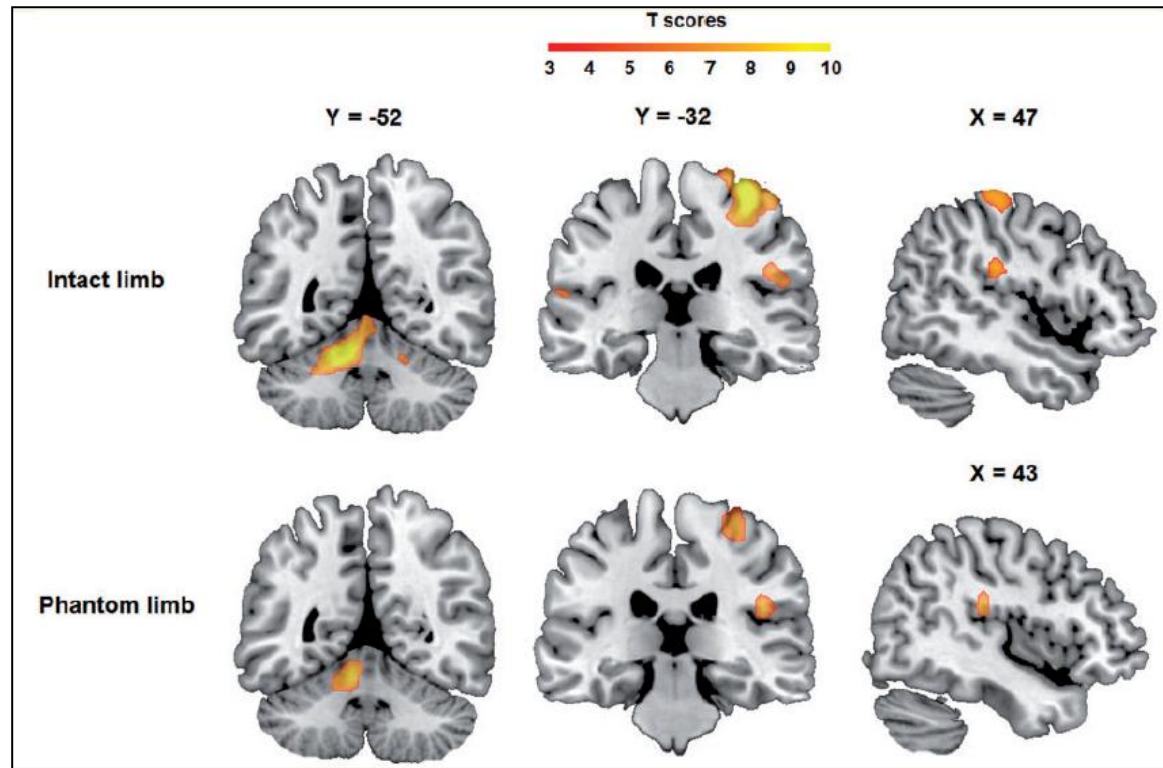
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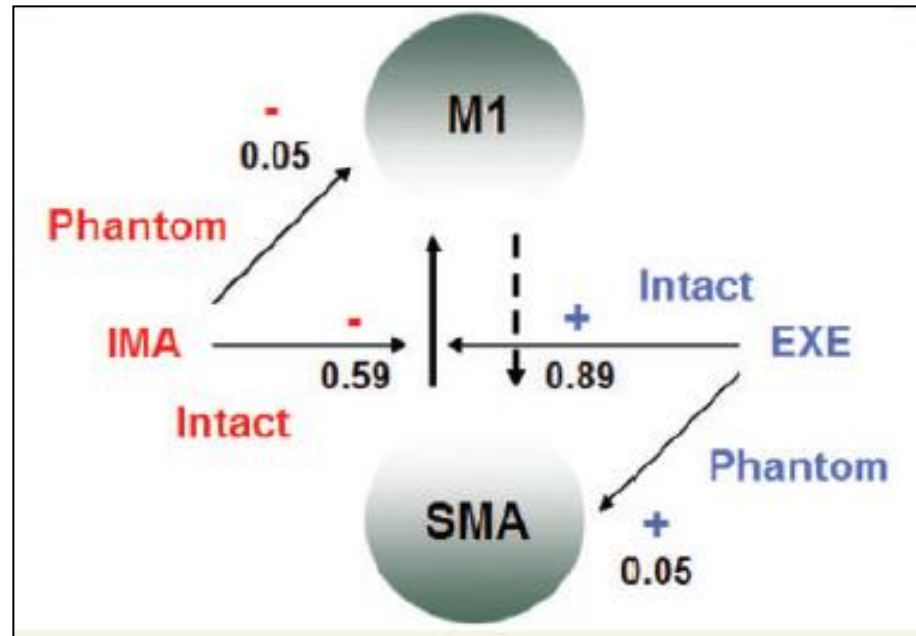
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Are phantom limb movements closer to motor imagery or motor execution ?

Effective connectivity results



Model based decoding of individual clinical status

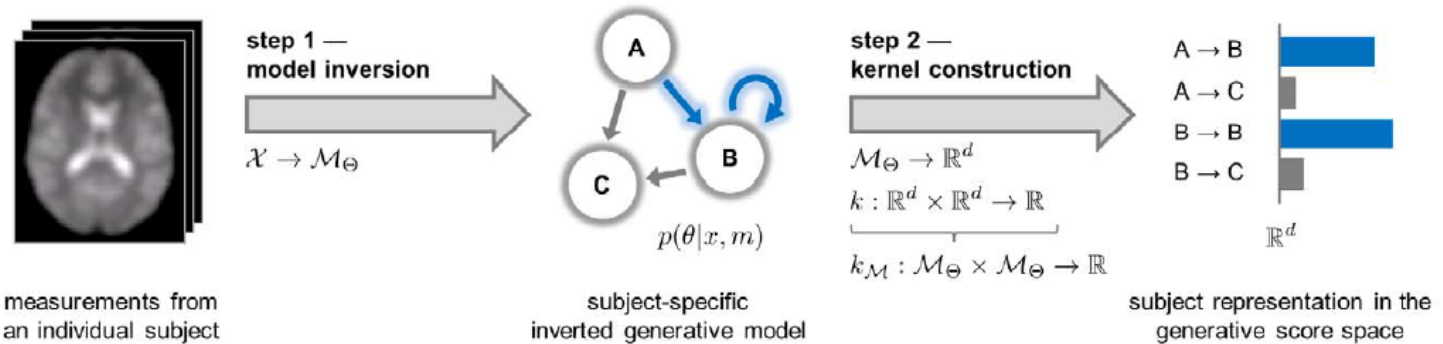
DCM-based classification, an fMRI study in mild aphasia

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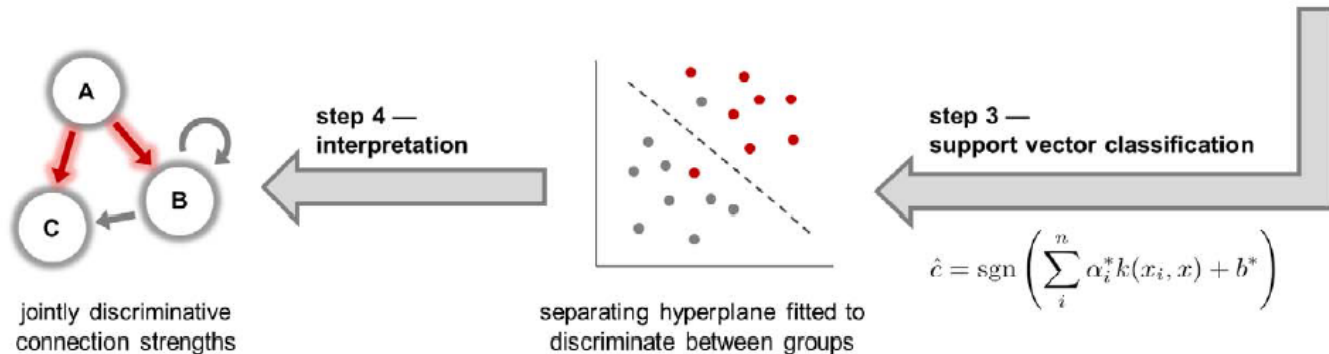
PLOS COMPUTATIONAL BIOLOGY

Generative Embedding for Model-Based Classification of fMRI Data

Kay H. Brodersen^{1,2*}, Thomas M. Schofield³, Alexander P. Leff³, Cheng Soon Ong¹, Ekaterina I. Lomakina^{1,2}, Joachim M. Buhmann¹, Klaas E. Stephan^{2,3}



General principle



Model based decoding of individual clinical status

DCM-based classification, an fMRI study in mild aphasia

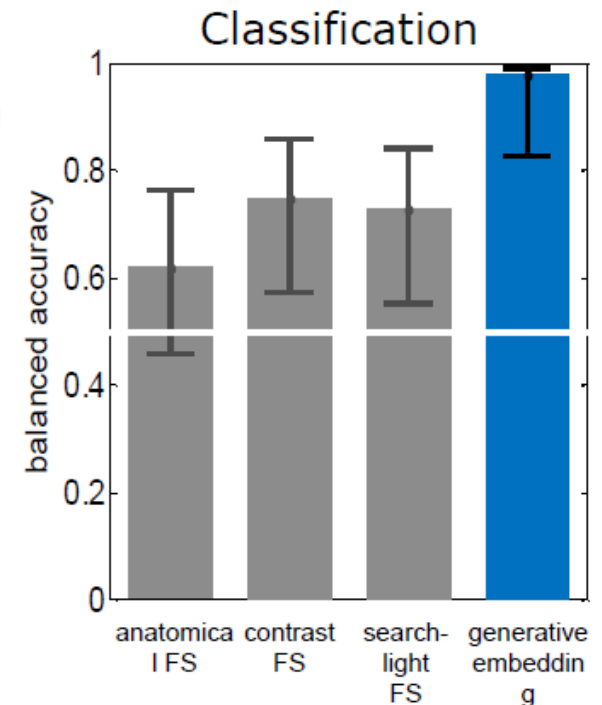
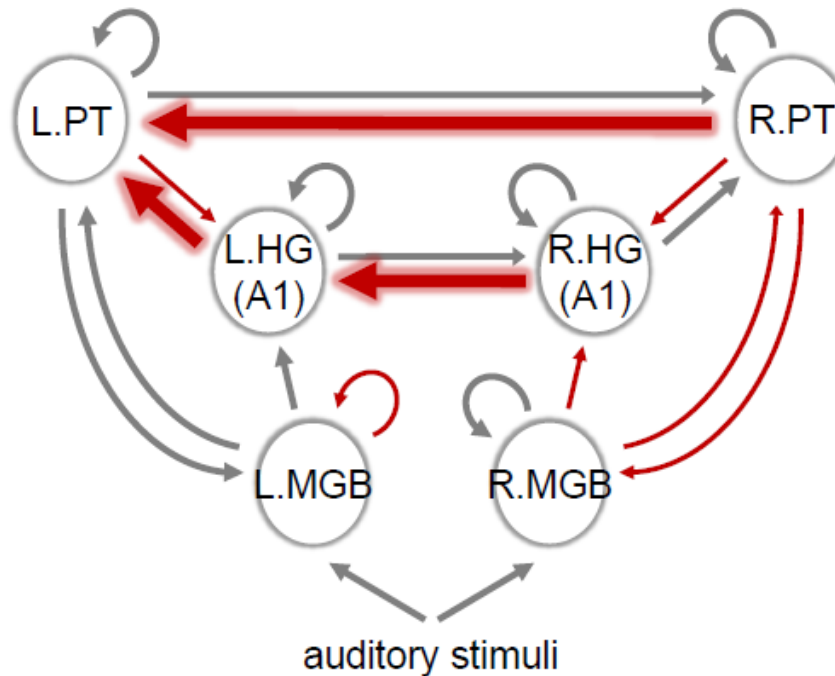
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Results
in mild aphasia



Model based decoding of individual clinical status

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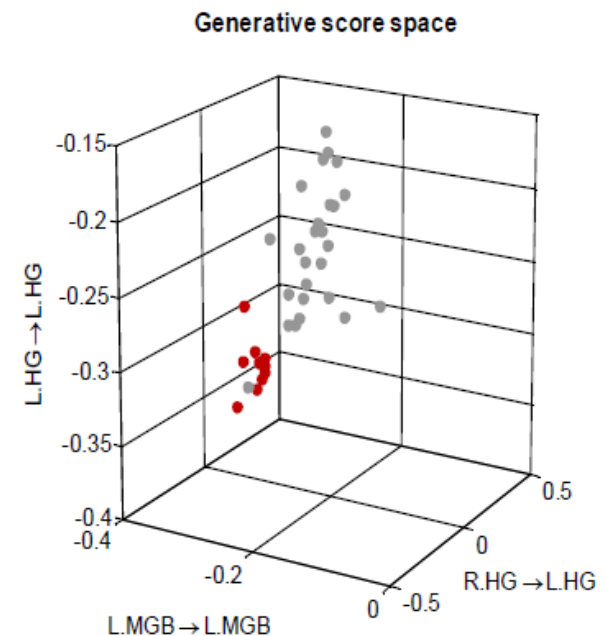
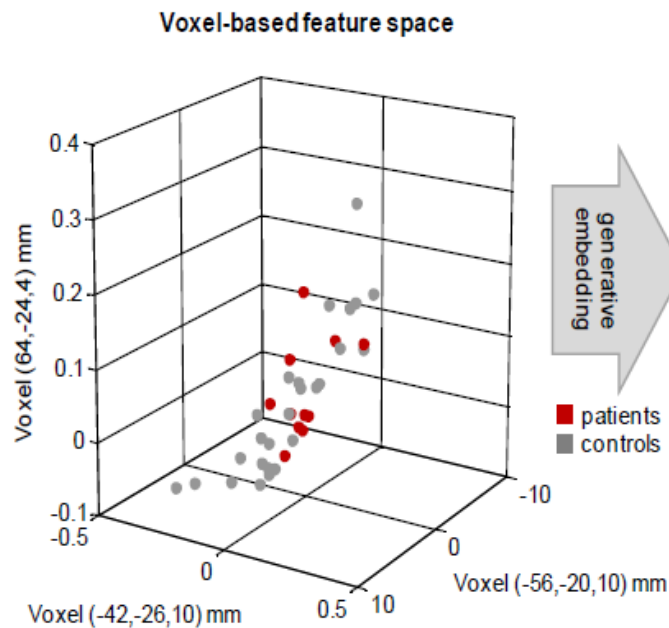
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Multivariate searchlight classification analysis

Generative embedding using DCM

Results
in mild aphasia



Group level differences

MMN study in disorders of consciousness

Preserved Feedforward But Impaired Top-Down Processes in the Vegetative State

Melanie Boly,^{1,2*} Marta Isabel Garrido,² Olivia Gosseries,¹ Marie-Aur lie Bruno,¹
 Pierre Boveroux,³ Caroline Schnakers,¹ Marcello Massimini,⁴ Vladimir Litvak,²
 Steven Laureys,¹ Karl Friston²

Science 332, 858 (2011)

Scalp level effect

RESPONSE TO DEVIANTS

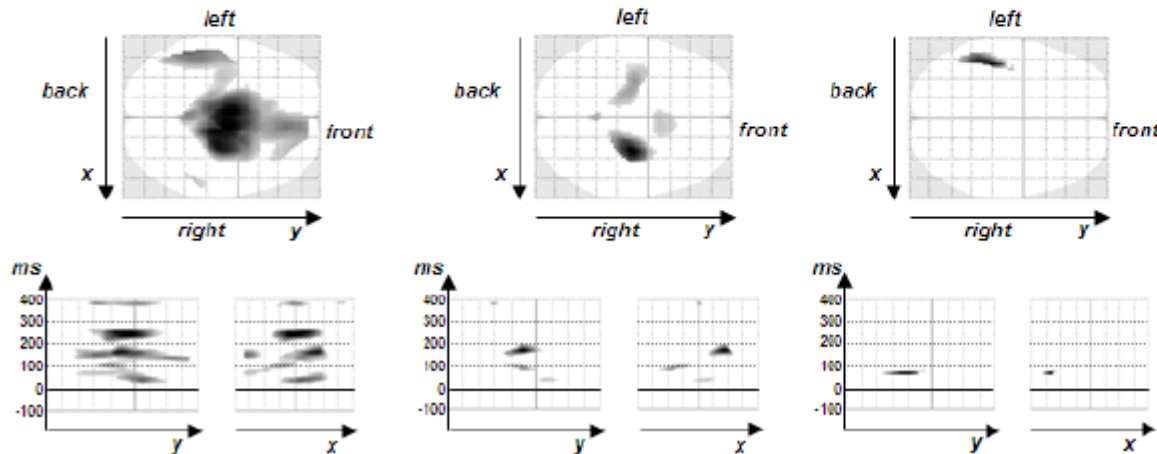
A.

Individual population results

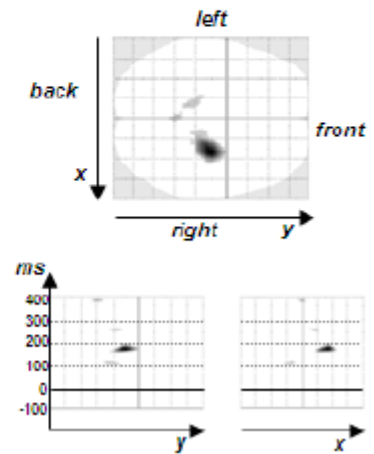
Controls

MCS

VS



B. Level of consciousness effect



Group level differences

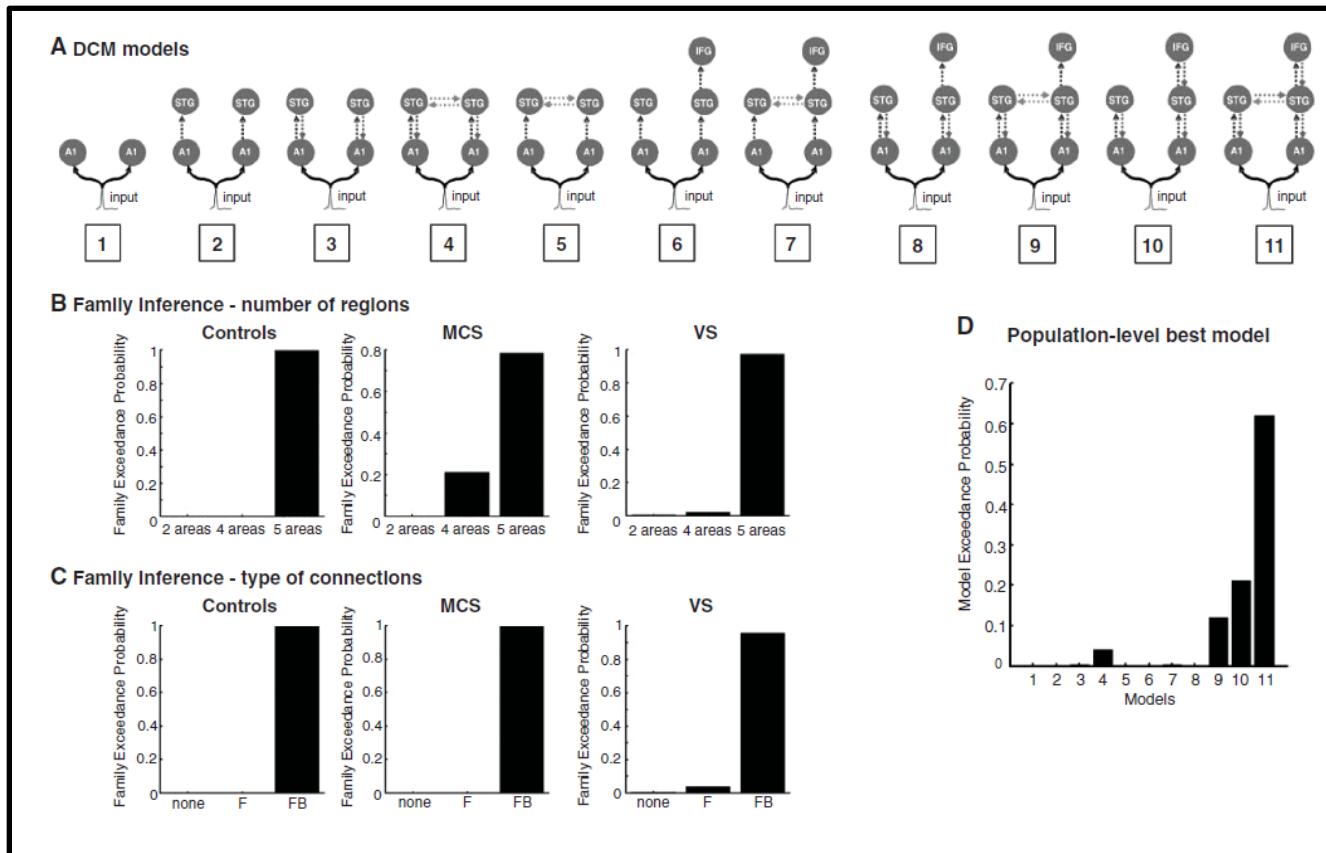
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Model selection



Group level differences

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Science 332, 858 (2011)

Group difference in connection strength

Impairment of backward connectivity from frontal to temporal cortices in Vegetative State as compared to Minimally Conscious State and controls

Vegetative State

