Model-based analysis of functional connectivity during associative learning in schizophrenia

Mihály Bányai, Vaibhav Diwadkar and Péter Érdi

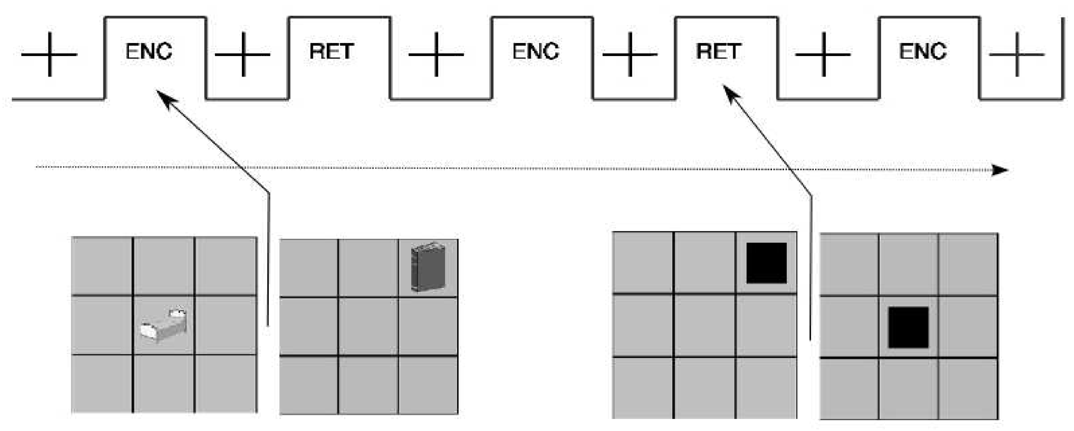
KFKI Research Institute for Particle and Nuclear Physics of the Hungarian Academy of Sciences
Budapest, Hungary

Wayne State University
School of Medicine
Detroit, MI, USA

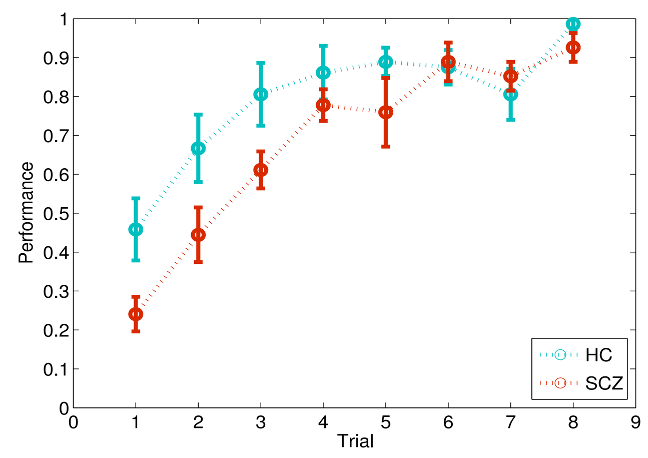
Center for Complex Systems Studies,
Kalamazoo College
Kalamazoo, MI, USA

BUDAPEST CNS GROUP

The experiment



Task
- 11 subjects with schizophrenia and 11 healthy controls
- visual associative learning task: objects in the cells of a 3-by-3 grid
- Encoding phase: the objects were shown in their places one by one
- Retrieval phase: only cues were given, patients had to tell what was the object in the cell
- phases were separated by resting periods.
- 8 learning epochs in a row



Behavioural differences
- Schizophrenia patients were able to learn the task
- their learning curve converges slower compared to healthy controls

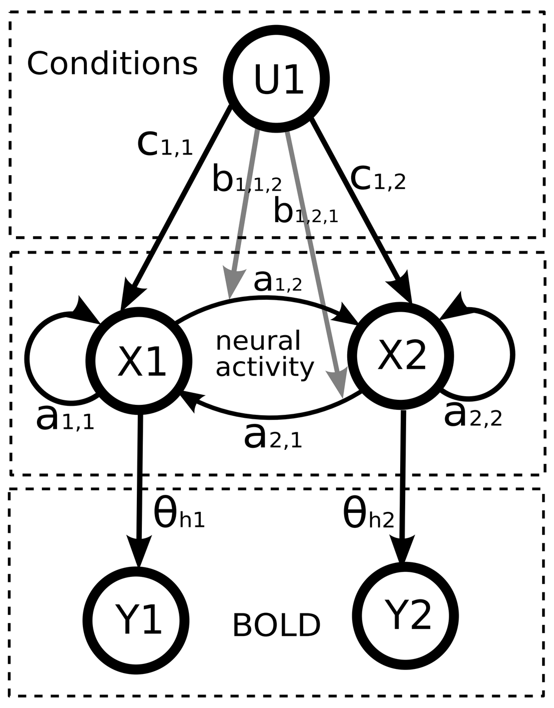
Data preparation
- fMRI data were preprocessed and analysed using a standard processing sequence
- Time series were extracted using a thresholded effects of interest contrast
- stereotactic region-of-interest maps

Dynamic Causal Modelling

Neural activity dynamics considering the effects of experimental conditions

$$\dot{x}=\left(A+\sum_{i=1}^{N}u_jB^j\right)x+Cu$$
$$y=\lambda(x,\theta_h)$$

Mapping from neural activity to BOLD signal (nonlinear)



Bayesian parameter estimation:

$$p(\theta|y,M)=\frac{p(y|\theta,M)\,p(\theta|M)}{p(y|M)}\qquad \theta=\{A,B,C,\theta_h\}$$

Assumption: all distributions are Gaussian
Approximation method: Expectation Maximization

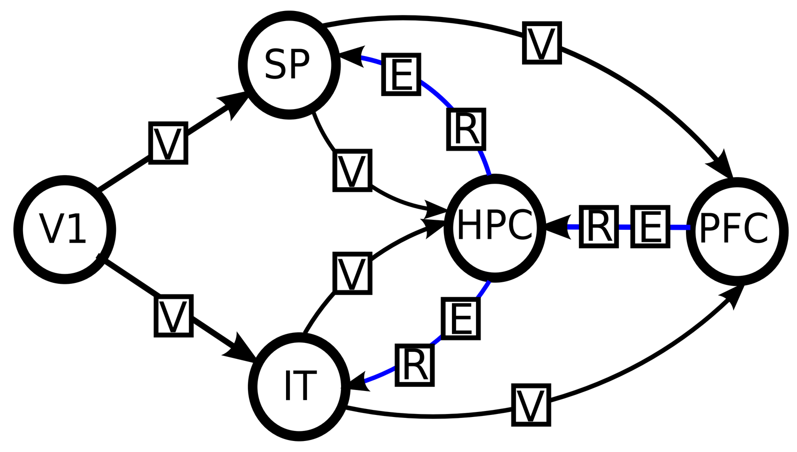
Model comparison:

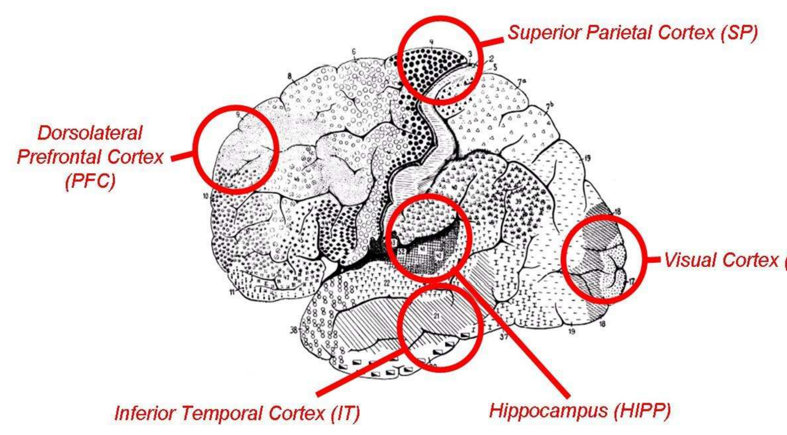
Goodness measure: model evidence

$$p(y|M)=\int p(y|\theta,M)\,p(\theta|M)\,d\theta$$

Approximation method: variational Bayesian

Models to compare



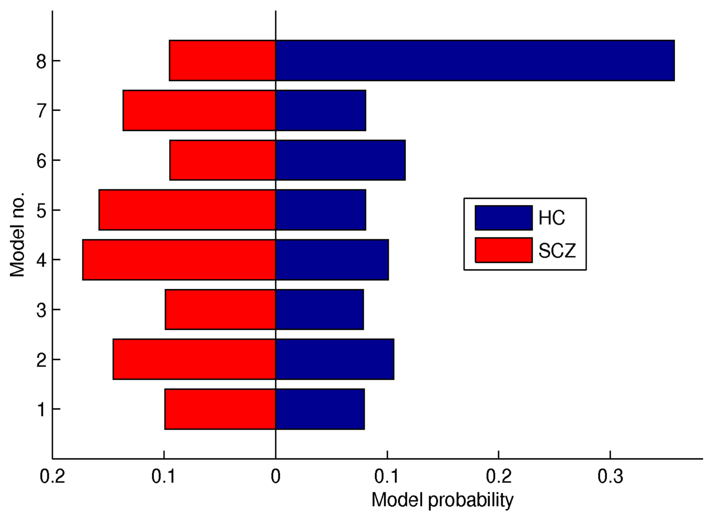


Input conditions: presence of a visual stimulus (Visual), encoding phase (Encoding), retrieval phase (Retrieval) and the epoch number (Time)

Two streams of connections:
data stream: lower level -> higher level, black on above figure, fixed in the models
control stream: higher level -> lower level, black on above figure, varied in the models

First model set: different intrinsic connectivity combinations (A matrix in DCM)
Second model set: different modulatory effects of input conditions (B matrix in DCM)

Results

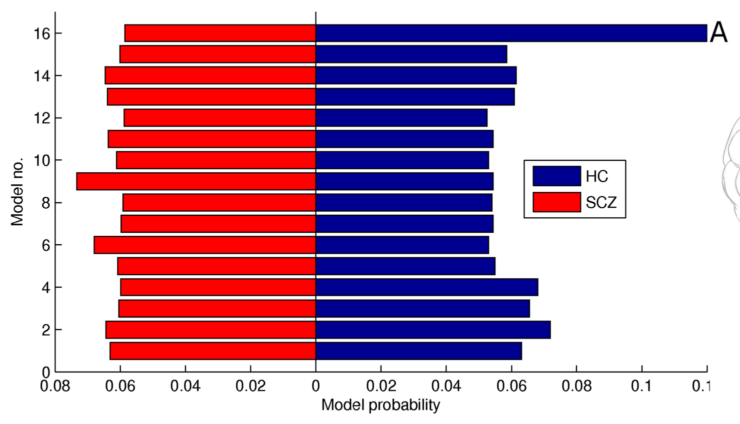


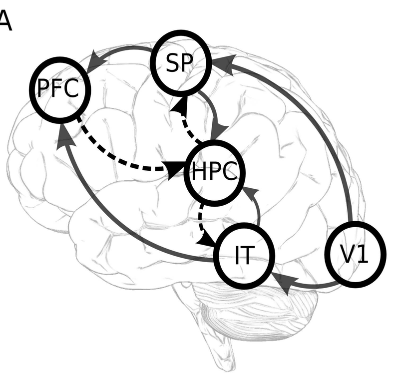
Model structure level analysis

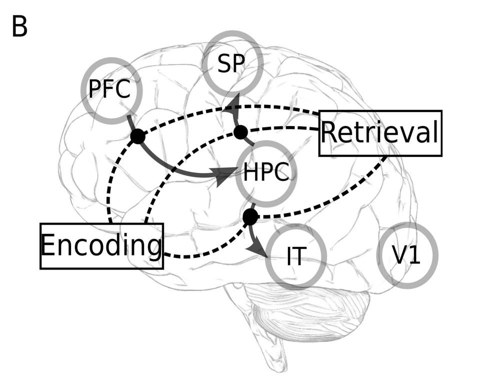
- Model evidences -> Posterior probabilty densities over the model sets
- subjects within group are not assumed to have the same structure

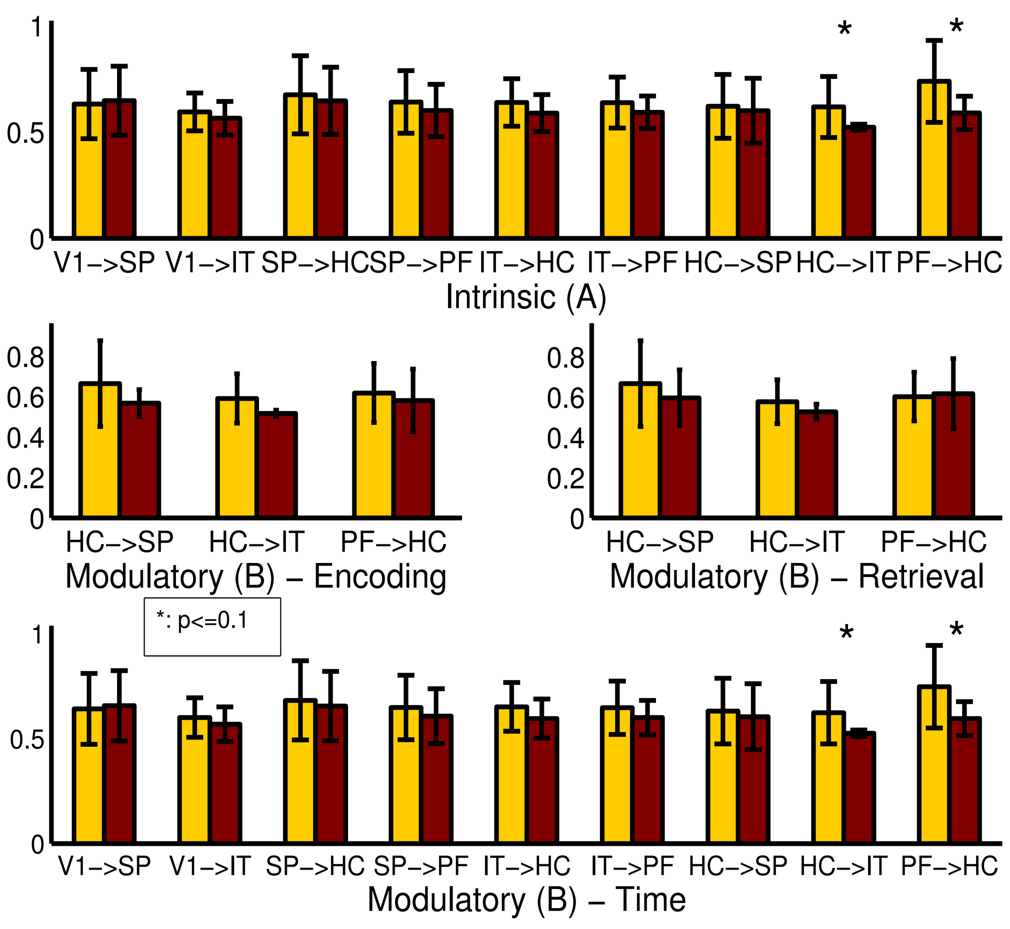
Control group:
- clear winner
- the model containing most connections

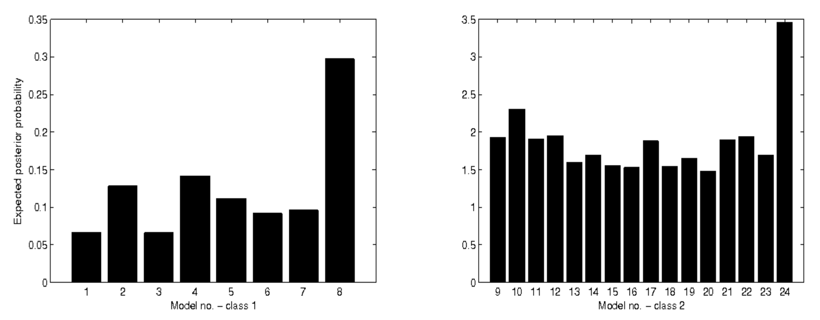
Patient group:
- no clear winner
- most probable models lack connections in the control stream











Parameter level analysis

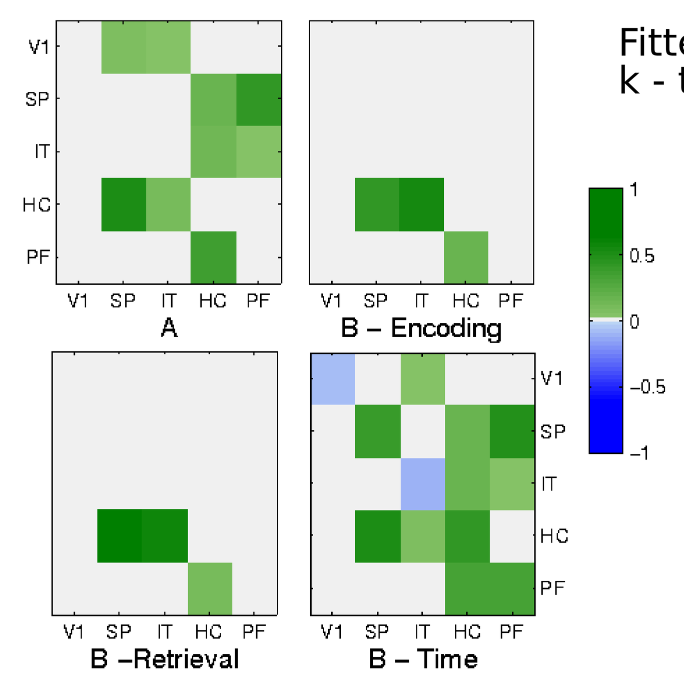
- comparing effective connectivity parameters
- reference model was selected (above)

The significance values come from two-sided t-tests on the samples of the two groups.

Significant differences:
- prefronto-hippocampal pathway
- hippocampo-inferior temporal pathway
- the context-dependent modulation of those by the learning procedure

Correlation with behaviour

How are the DCM model parameters correlated with learning performance of the subjects?



Fitted to performance data
k - the learning rate:

$$l(t)=1-e^{-kx}$$

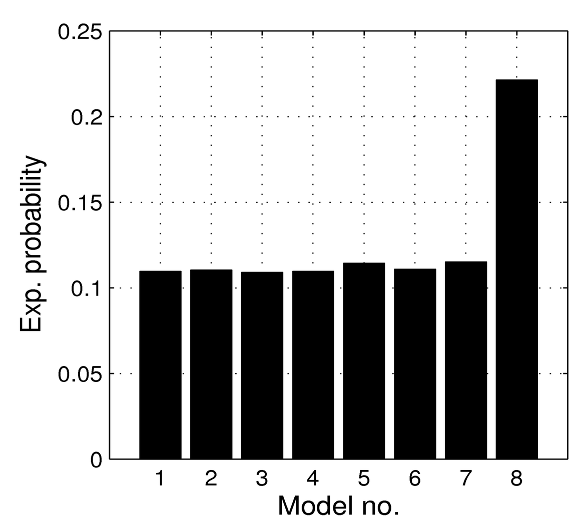
- Spearman rank correlation
- averaged over subjects

most correlated:
- hippocampo-parietal pathway
- hippocampo-inferior temporal connectivity during encoding

Illnes or slow learning?

Common probelm in learning experiments:
are the differences there due to the disorder, or some subjects are naturally slow learners?

- subjects in control group with no better performance than patients (3 people).
- model comparison for these subjects separately



Posterior probability distribution of models:
- same as for control group
- different from patient group

The method is capable of:
- capturing the underlying structure of the illness
- separate it from slow learning despite of the similar performance

Conclusions

- An associative learning task was performed by schizophrenia patients and healthy controls, patients performed worse.
- Several connectivity models of the BOLD signal generation were defined by DCM and fitted to measurement.
- The information processing neworks implemented by patients proved to be fundamentally different than the controls'.
- Impairment in the prefronto-hippocampal and hippocampo-inferiontemporal pathways, which play an important role in the cognitive control of associative memory formation.
- The connection strengths are positively correlated with learning performance.
- The method is able to differentiate natural slow learning and illness.