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Seminar for International students

Paper 01:

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

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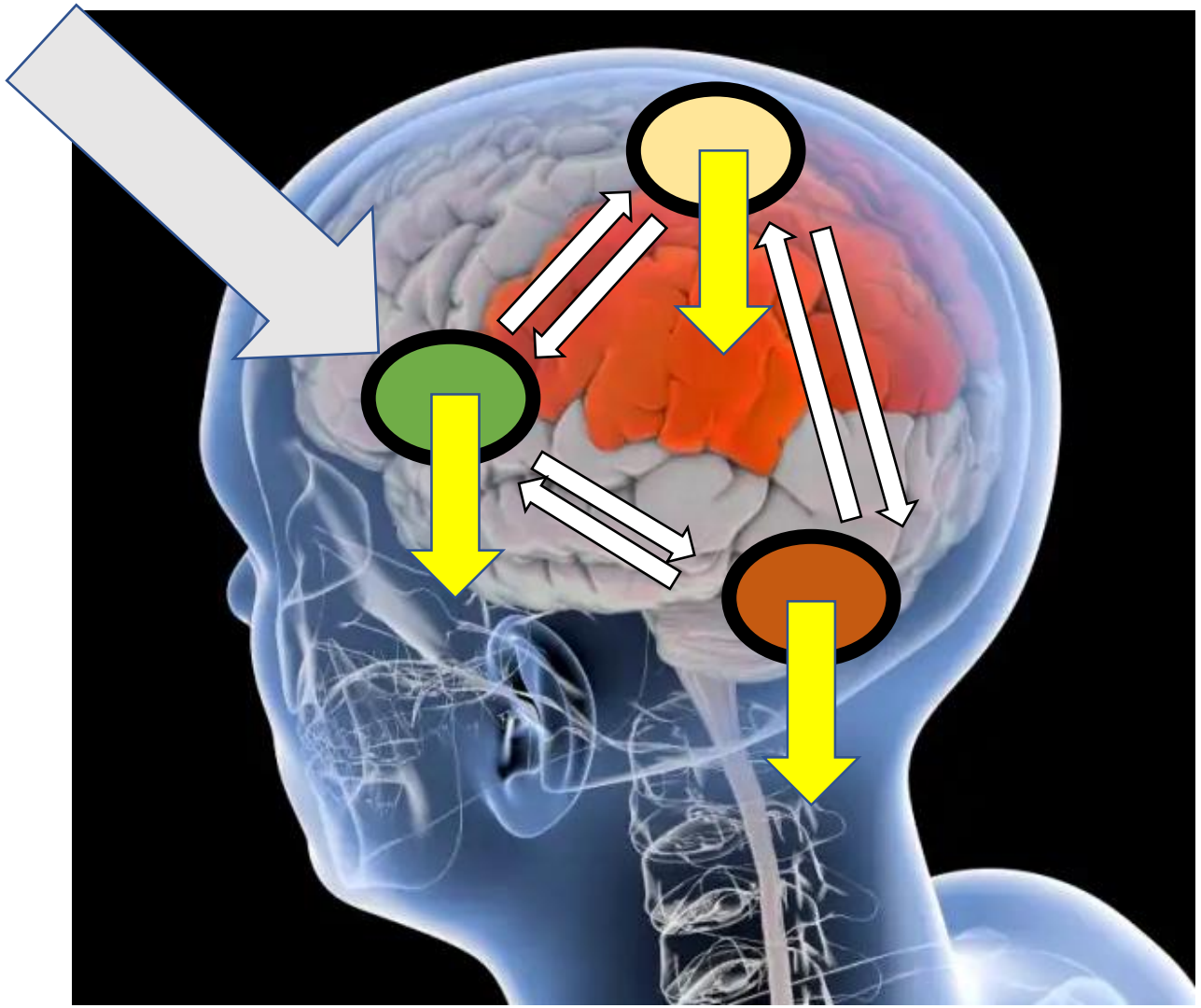
Content

- Background and Motivation of the paper
- What is the Effective connectivity
- Structural Equation Model (SEM)
- Dynamic Causal Model (DCM)
- Comparison of two models
- My Research application

Background



Motivation

- Understanding about the two models ; SEM and DCM by modelling the effective connectivity among the states using fMRI time series data.(fMRI Functional magnetic resonance imaging)
  - How those models are different from each other
  - How modulating variables are affected on connectivity and How state activities are changed according to those mediations.

Previous applications – Brain region analysis

Principal component analysis

- PCA can be used to decompose this high dimensional data into a set of modes or components that capture the most important patterns of variation in the data.

Canonical variate analysis

- Multivariate extension of PCA is defined as CVA

Independent component analysis

- ICA is a data-driven approach that can identify patterns of activity in a sparsely distributed network, which may not be easily identifiable using other methods.

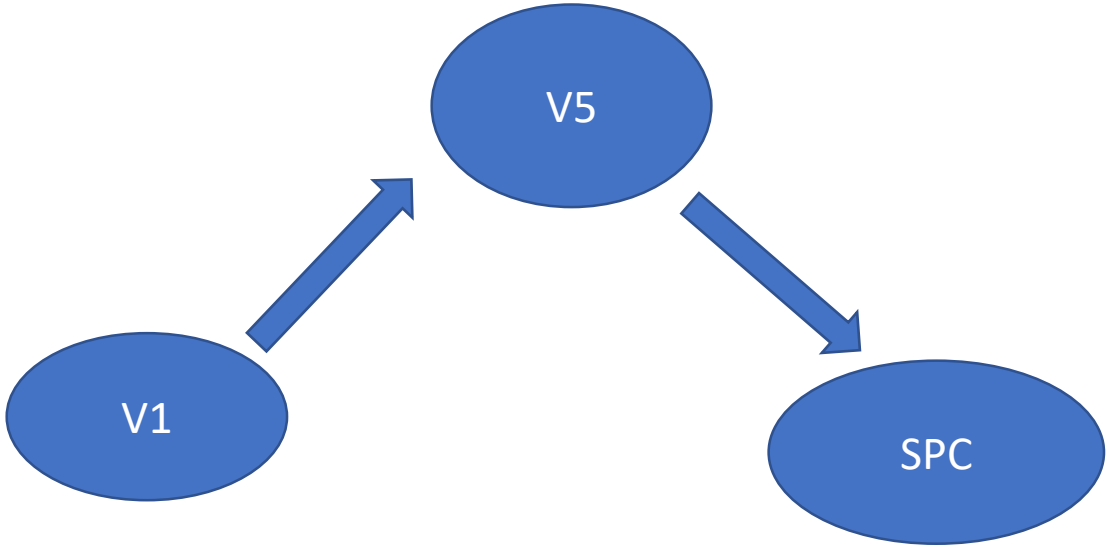
Effective connectivity analysis

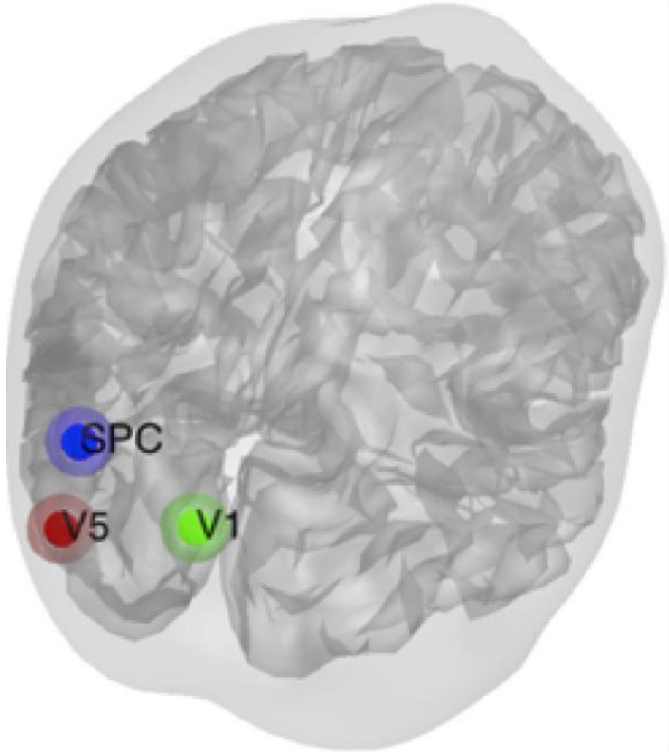
Structural equation modeling

Dynamic causal modeling

Effective connectivity

- Regions in the brain specific for some activities.
- Directed influence of one brain region on physiological activity recorded in other brain region.
- Effective connectivity analyses are hypothetical driven rather than data driven.
- Claims to make statements among tasks and regions.





Structural Equation Modelling
Model formation

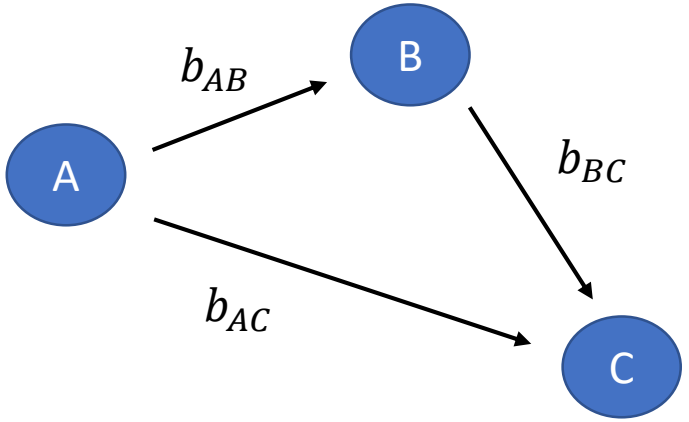
- Structural equation models (SEMs) were developed in the field of econometrics and first applied to imaging data by McIntosh and Gonzalez-Lima (MacIntosh and Gonzalez-Lima, 1991)

- Consists **with set of regions and set of directed connections** and path coefficients are defined between nodes.

Network Formation

Consider a networks comprising N regions in which the activity at time t is given by the N X 1 vector yt.
If there are T time points and Y is an N X T data matrix comprising t = 1...T.

$$\begin{bmatrix} y_A \\ y_B \\ y_C \end{bmatrix} = \begin{bmatrix} 0 & 0 & 0 \\ b_{AB} & 0 & 0 \\ b_{AC} & b_{BC} & 0 \end{bmatrix} \begin{bmatrix} y_A \\ y_B \\ y_C \end{bmatrix} + \begin{bmatrix} e(1) \\ e(2) \\ e(3) \end{bmatrix}$$



$$y_t = My_t + e_t$$

M – *Connectivity matrix*
e_t – *Errors of covariance R*
y_t – *Observed time series*

Key assumption:
network activity is independent from sample to sample

$$p(Y|\theta) = \prod_{t=1}^{T} p(y_t|\theta)$$ Likelihood of the model

Structural Equation Modelling
Model Estimation & Comparison

Estimation

For given data connectivity matrix is optimized by considering maximum likelihood using Pseudo-Newton algorithms or simplex methods.

Since, probabilities are too small, log value is considered as follow.

$$L(\theta) = \log p(Y|\theta) \quad = \sum_{t=1}^{T} \log p(y_t|\theta)$$

Likelihood ratio (LR)

LR can be used to compare two models by using their likelihood values. For model m=I and m=j , R_{ij} can be defined as follow

$$R_{ij} = \frac{p(Y|\theta, m = i)}{p(Y|\theta, m = j)}.$$

Structural Equation Modelling
Model Estimation & Comparison

1. It can be done using partitioning original data based on some experimental factor.

2. Make inferences on connectivity using moderator variables.

- Dummy regions are created to involve the influence about the changes in effective connectivity.

Ex: to test the connectivity from A to B, dummy region C will be created by considering the experimental factor data and region A data. As per the paper This is formally identical to the explanatory variable in psychophysiological interactions.

Attention on connectivity

- In this research, data preparation has been done based on attention data and no attention data.
- After that comparison has been proceed based on two models ,such as null model and alternative model. In null model path coefficients are constrained to be equal in both experimental levels and in alternative model, coefficients of interest can be different.

Structural Equation Modelling chi-squared value

- chi-squared has been used to test the model whether or not attention changes the effective connectivity.

$$L(\theta) = -\frac{T-1}{2}\left(\log|\Sigma(\theta)| + \mathrm{Tr}\left(S\Sigma(\theta)^{-1}\right)\right)$$

$$L_1 = -\frac{T-1}{2}\left(\log|S| + \mathrm{Tr}\left(SS^{-1}\right)\right)$$

- [In the alternative model, sample covariance equals to model covariance]

$$= -\frac{T-1}{2}(\log|S| + N).$$

T – Time period
S – Sample covariance
N – Number of regions

The corresponding (log) likelihood ratio is

$$\log R_{01} = -\frac{T-1}{2}\left(\log|\Sigma(\theta)| + \mathrm{Tr}\left(S\Sigma(\theta)^{-1}\right) - \log|S| - N\right)$$

which in turn has a corresponding chi-squared value

$$\chi^2 = (T-1)F(\theta)$$

where

$$F(\theta) = \log|\Sigma(\theta)| + \mathrm{Tr}\left(S\Sigma(\theta)^{-1}\right) - \log|S| - N.$$

Structural Equation Modelling chi-squared value

- Chi squared is estimated to evaluate the parameters and If P value is less than, for example, 0.05 model is rejected.

$$\chi^2 = (T-1)F(\theta)$$

where

$$F(\theta) = \log|\Sigma(\theta)| + \mathrm{Tr}\left(S\Sigma(\theta)^{-1}\right) - \log|S| - N.$$

- Model comparison can be proceed to make some inference about the changes in effective connectivity. (Stacked model approach)
- Null model and Alternative model is defined for assessing the models.

Structural Equation Modelling
Bayesian approach

- **Parameter Estimation**

Bayesian approach where priors are placed over model parameters and the aim of estimation is to find the maximum posterior (rather than maximum likelihood) parameters.

Bayesian approach starts with prior knowledge about the model structure. (Prior distribution)

Next update the parameters based on observed data and obtain posterior probabilities over parameters.

$$p(\theta|y,m) = \frac{p(y|\theta,m)p(\theta|m)}{p(y|m)}.$$

I. model prediction errors are minimized
II. the parameters are close to their prior values.

Dynamic Causal Modelling
Model formation

- Dynamic causal modelling (DCM) (Friston et al., 2003) has been **specifically designed for the analysis of functional imaging time series.**

- DCM is typically used to estimate the coupling among brain regions and the changes in coupling due to experimental changes

Idea : Brain is dynamic system and external inputs causes changes in neural activities which is caused to make some effect on measured outputs as blood oxygen level dependent (BOLD) signals.

- DCM models consists with two models (bilinear model) ; Neuronal model, Hemodynamic model.

Dynamic Causal Modelling
Model formation

Experimental design

In DCM , brain regions are evoked by the external inputs

- Driving Inputs
- Modulating Inputs

Driving inputs - Direct inputs on regions.

Modulating inputs - Modulating coupling among the regions

Model specifications

❖ Which links should be switch on or off

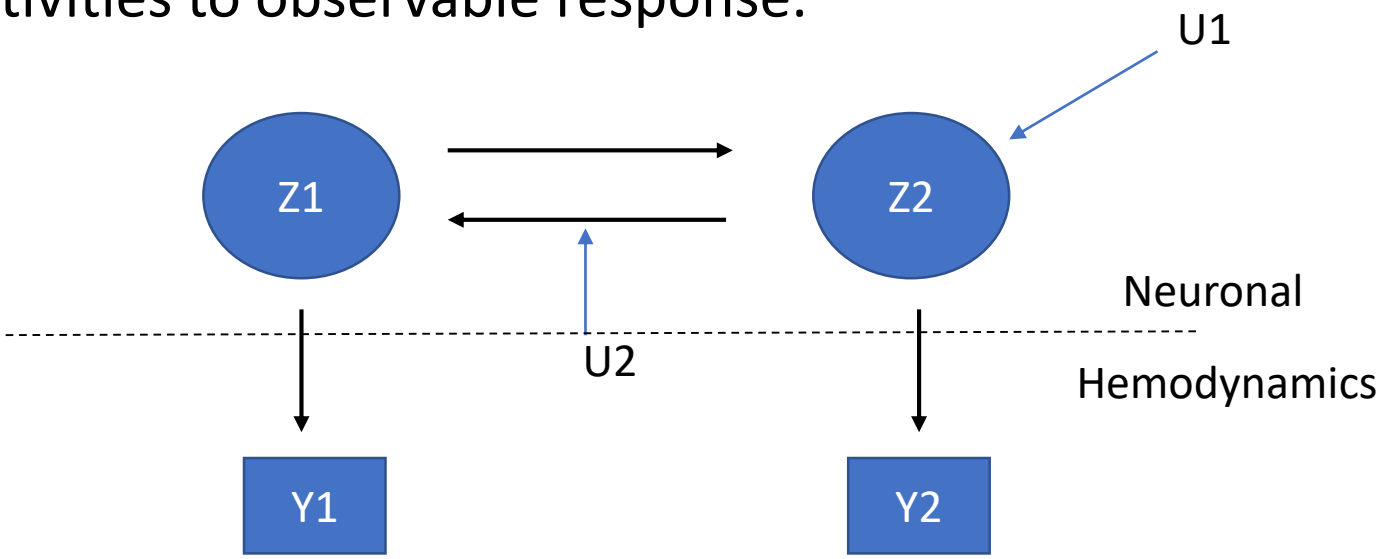
❖ What are the priors over the parameters

Dynamic Causal Modelling
Model formation

- With DCM, there is no need to partition the time series into selected periods of interest as inferences about changes in connectivity can be made based on the strength of modulatory connection.
- In DCM neuronal model will be used to interact with regions and used a forward model which will be transferred neuronal activities to observable response.

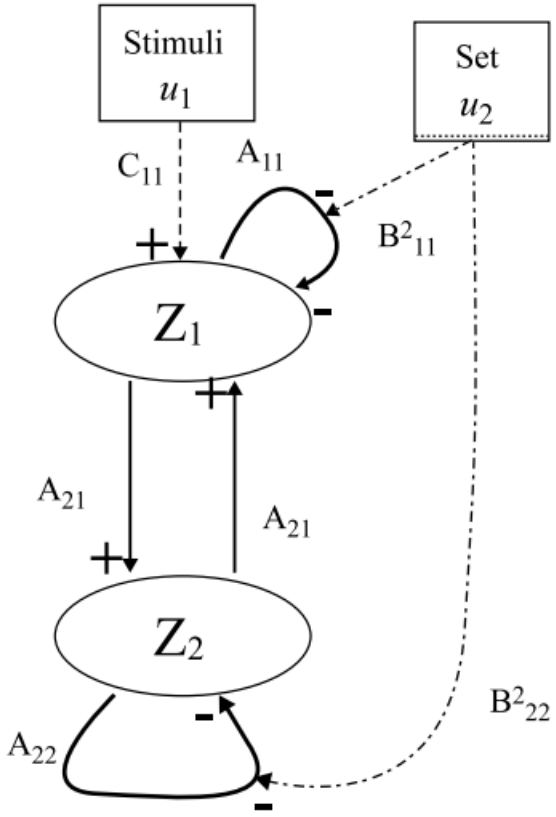
$$\dot{z}_t = \left(A + \sum_{j=1}^{J} u_t(j) B^j\right) z_t + C u_t$$

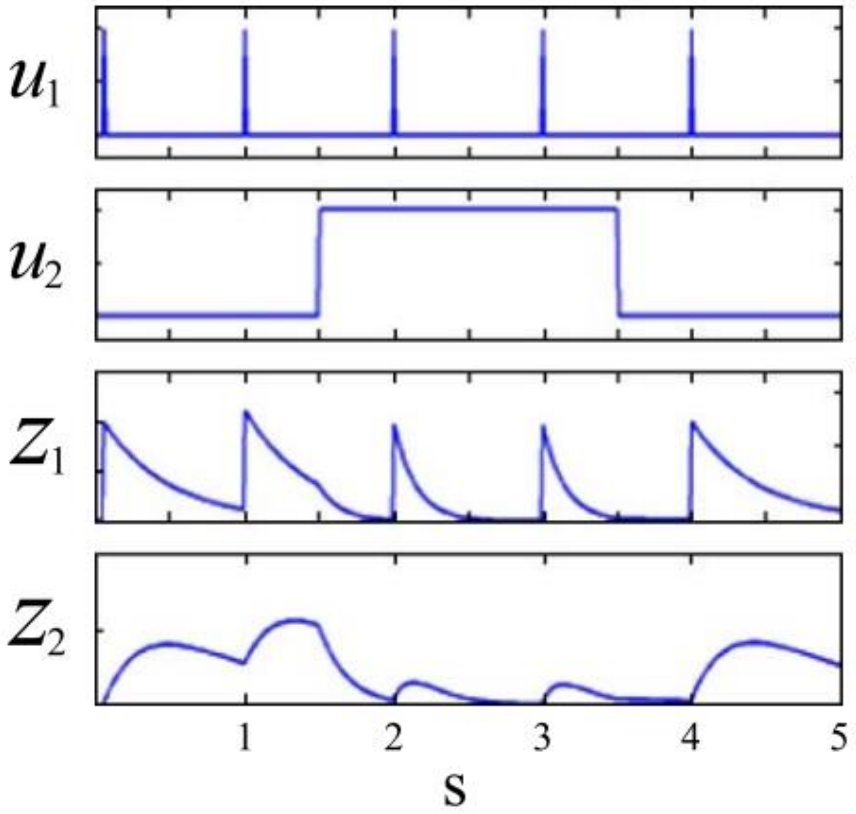
A – Intrinsic connections
B - Modulatory connections
C – Inputs for regions



$$y = h(\theta, u) + X\beta + w$$

Dynamic Causal Modelling
Neuro dynamic model





The input variable u1 drives neuronal activity z1. Informally, neuronal activity in this region then excites neuronal activity z2, which then reactivates activity in region 1.

Dynamic Causal Modelling
Hemodynamics model

- How neural dynamic model connects hemodynamic model in brain region studies?
- It is decided based on following assumptions.

1. Neural activity increases the metabolic demand for oxygen, which leads to an increase in cerebral blood flow.
2. The increase in blood flow leads to an increase in blood volume, which in turn leads to an increase in the total amount of oxygenated hemoglobin.
3. The increase in oxygenated hemoglobin leads to a decrease in the concentration of deoxygenated hemoglobin.

- During the calculations, parameters are estimated by solving differential equations.

❖ **But in SEM , hemodynamic response directly observe from regions.**

Dynamic Causal Modelling
Estimation

Estimation

As per the Bayes rule, posterior distribution is equal to the likelihood times the prior density divided by the evidence.

$$p(\theta|y,m) = \frac{p(y|\theta,m)p(\theta|m)}{p(y|m)}.$$

Maximum posterior probability is optimized by considering following condtions.

i) model prediction errors are minimized.

ii) parameters are close to their prior values.

Aim:

Estimate mean and covariance of posterior densities

Dynamic Causal Modelling
Model comparison

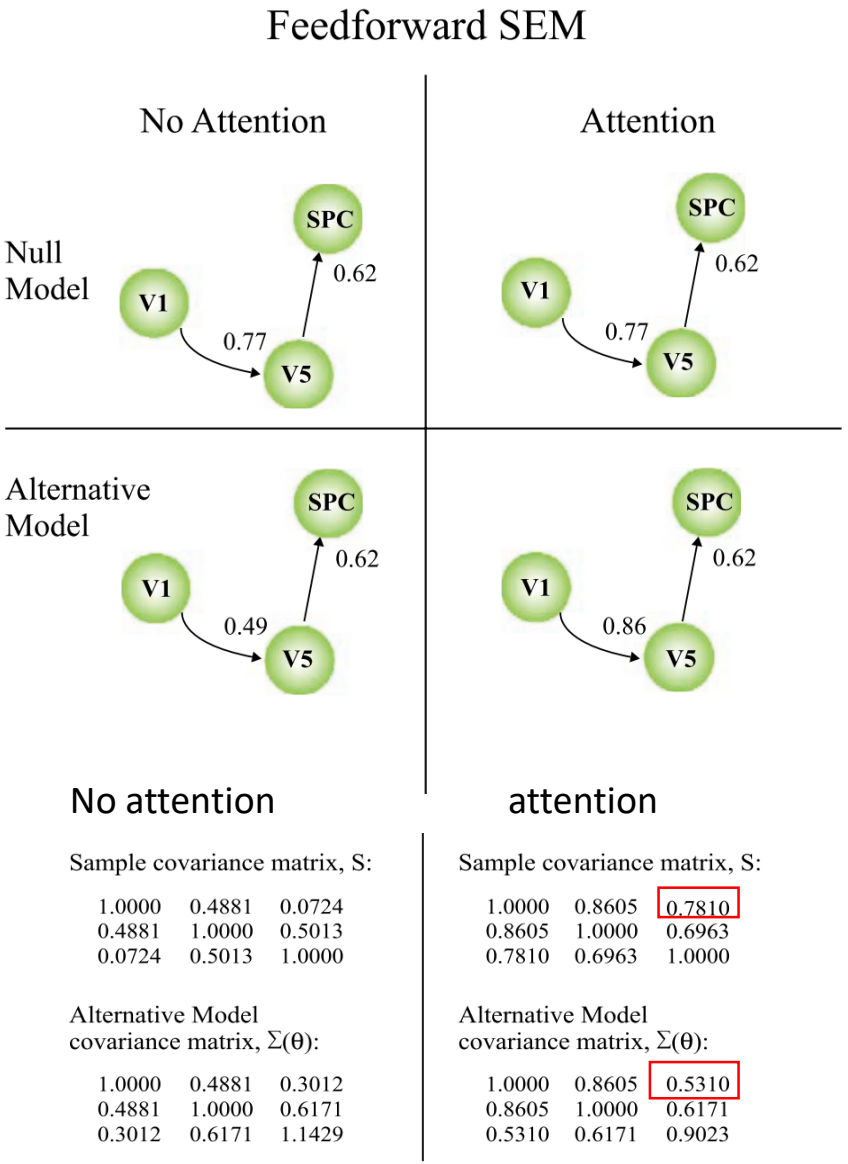
Estimation is extended to model comparison using evidence ratios. Bayes factor for two models i and j is defined as below.

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

$$B_{ij} = \frac{p(y|m = i)}{p(y|m = j)}$$

- When $B_{ij} > 1$, the data favor model i over model j, and when $B_{ij} < 1$ the data favor model j
- Bayes factors of 20 or more provide strong evidence in favour of one model over another

Structural Equation Modelling Results



No attention

Sample covariance matrix, S:

1.0000	0.4881	0.0724
0.4881	1.0000	0.5013
0.0724	0.5013	1.0000

Alternative Model covariance matrix, Σ(θ):

1.0000	0.4881	0.3012
0.4881	1.0000	0.6171
0.3012	0.6171	1.1429

attention

Sample covariance matrix, S:

1.0000	0.8605	0.7810
0.8605	1.0000	0.6963
0.7810	0.6963	1.0000

Alternative Model covariance matrix, Σ(θ):

1.0000	0.8605	0.5310
0.8605	1.0000	0.6171
0.5310	0.6171	0.9023

Alternative model

Number of regions = 3
Variance parameters (VP) = 6
Path coefficients (b) = 3

Corresponding degree of freedoms = k – q
k = 12 ; q = VP+ b = 9

$X^2 = 24.6$

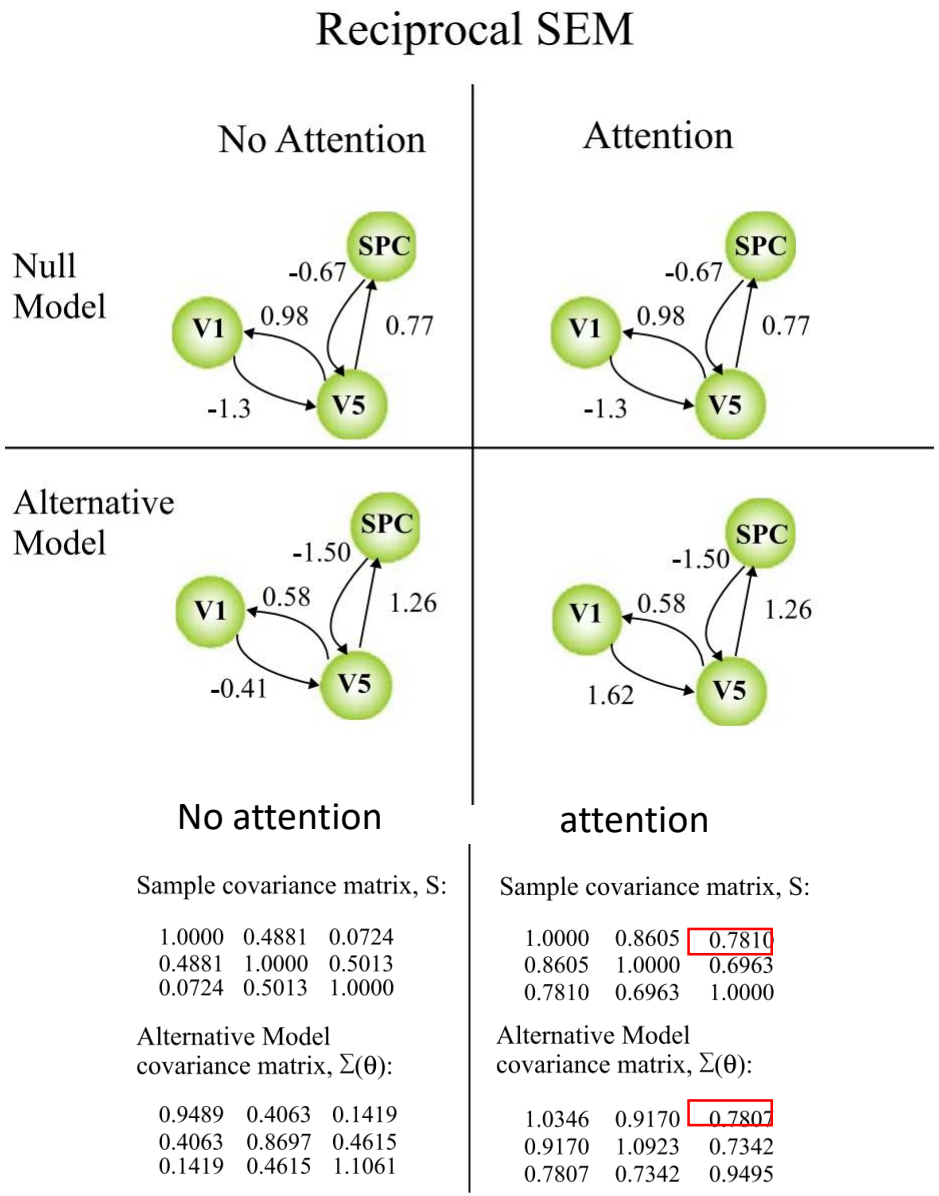
Null model

Number of regions = 3
Variance parameters (VP) = 6
Path coefficients (b) = 2

Corresponding degree of freedoms = k – q
k = 12 ; q = VP+ b = 8

$X^2 = 33.2$

Structural Equation Modelling Results



Alternative model

Number of regions = 3
Variance parameters (VP) = 6
Path coefficients (b) = 5

Corresponding degree of freedoms = k – q
k = 12 ; q = VP+ b = 11

X^2= 3.9

Null model

Number of regions = 3
Variance parameters (VP) = 6
Path coefficients (b) = 4

Corresponding degree of freedoms = k – q
k = 12 ; q = VP+ b = 10

X^2= 23.6

Dynamic Causal Modelling Results

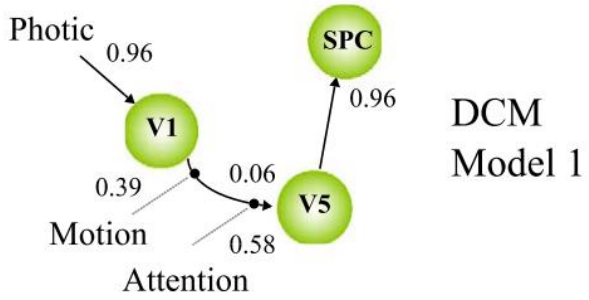
Connectivity modulation

Three experimental variables have been considered as follow. In this study three models have been compared each are different based on their intrinsic connectivity structure;

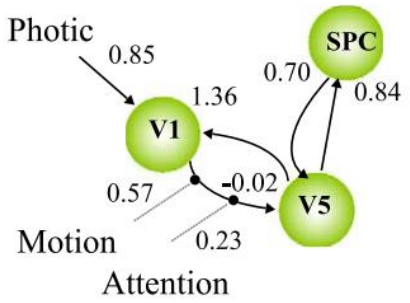
model 1 - feedforward structure

model 2 - reciprocal structure

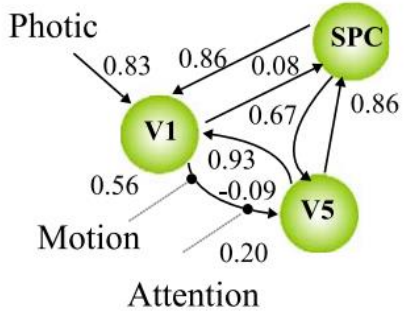
model 3 - fully connected structure



DCM Model 1



DCM Model 2



DCM Model 3

- Connectivity can be made based on the strength of modulatory connections

Converting DCM to SEM

Transferring DCM to SEM

If we assume that

(i) the neuro dynamics are directly observable, that is,. yt = zt

(ii) the direct inputs are stochastic, that is,. $e_t = Cu_t$ then the generative model for DCM becomes,

$$\dot{z}_t = \left(A + \sum_{j=1}^{J} u_t(j)B^j\right) z_t + Cu_t \quad \Rightarrow \quad y_t = My_t + e_t$$

Note:
inputs would be accommodated by splitting the data into different partitions, each partition having its own intrinsic connectivity matrix.

Comparison of two models

SEM	DCM
▪ In SEM, changes in effective connectivity lead directly to changes in the covariance structure of the observed hemodynamics.	▪ Experimental inputs cause changes in effective connectivity expressed at the level of neuro dynamics, which in turn cause changes in the observed hemodynamics
▪ Initially data is divided based on the experiment to check the modulating effect.	▪ There is no data partition and changes in connectivity can be made based on the strength of modulatory connections.
▪ Model comparison is done using likelihood ratio	▪ Model comparison is done using Bayes' factor

Conclusion

Conclusions

(i) reciprocal models are superior to feedforward models,
(ii) models with reciprocal connections provide a good fit to the data
(iii) attention significantly modulates the connectivity between the regions.

DCM is the preferred method for making inferences about changes in effective connectivity from fMRI data. SEM is, however, appropriate for PET data

Advantages of DCM

- It can postulate arbitrarily complex connectivity patterns between regions.
- DCMs are able to work at the neuronal level