Dynamic Causal Modeling and Structural Equation Models on fMRI Experiments. A Meta-Analytic Approach

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Abstract

In the last ten years, a large number of papers have been generated about the statistical models applied to the modelization of brain connectivity. Among them, we have the use of Structural Equation Models and the approximation of Dynamic Causal Models (DCM) based on data obtained from the registration of Functional Magnetic Resonance Image (*f*MRI) activations in the face of several cognitive tasks. They use different designs and statistical models and they also pay attention to specific functioning brain areas called Regions of Interest (ROI's). However, there has been little reflection on the properties of the statistical models used from a strictly statistical viewpoint. That is, we know little about whether the conditions of application and assumptions of SEM and DCM are properly met, whether the conditions of order and range, as well as the identification of complex models, fit the statistical properties, or whether, in the different papers, they are properly listed for a correct assessment of statistical guarantees. Therefore, the goal of this study is to analyze, through a meta-analysis, the results obtained in some of the studies on brain connectivity published during the 2001-2012 period, especially in the case of SEM. After a bibliographical inquiry fitting the precepts of meta-analytic techniques, the SEM models with the best fits were selected following the χ^2 criterion and, from each of them, some relevant variables were collected (sample size, number of ROI's, design type, hypothesis mechanism, etc.). Also, the effect size, for lack of other more usual values like the Determination Coefficient, has been estimated based on the study of the structural parameter (β_{ij} or γ_{ij} depending on the case) with the highest statistical value, be it with a positive or negative loading, considered as an absolute value. The results obtained show some significant effects in the sense that the SEM models offer higher parameters than Unified SEM or than designs with only one group, and, by comparing tasks, they make it possible to estimate greater impact parameters.

Key Words: Brain Connectivity, *f*MRI, Meta-Analysis, Structural Equation Models.

1. Introduction

Since the appearance of Bertalanffy's proposals for the study of the organization of the structure and dynamics of systems and, as a result, the idea of the phenomenon as whole being more complex than the sum of its parts, this particular view of nature has become a source of models to represent reality analogically. The contributions from various fields of knowledge, ranging from Wiener cybernetics to Prigogine's Dissipative Structures, have been used to generate options for the analysis of many phenomena. In recent years, these subjects have spread widely and have come to contribute analyses and methodological advances in research on neuroscience brain connectivity. The problem is to capture network effects on neuronal activity and to establish analog models to show the structural relationships between brain locations. Many of these approaches, though based on some understanding of the complexity, are still based on very concrete and specific statistical aspects such as Independent

Component Analysis (ICA) estimates or models like Structural Equation Models (SEM).

These details lead us to the consideration of what has been called Quantitative & Computational Neuroscience as a field of methodological advances. Computational models can be found in all cognitive domains, but with results sometimes implausible around brain functioning. The objective of this contribution is to show some recent results derived from the use of the Structural Equation Models as a statistical model to recognize the complexity, and the dynamic causal model (DCM) to represent the connectivity of brain activities based on the *f*MRI paradigm and experimental designs. An example of this type of approach can be found in numerous papers, but the best way to show how the SEMs are commonly used in this domain is shown in Figure 1.

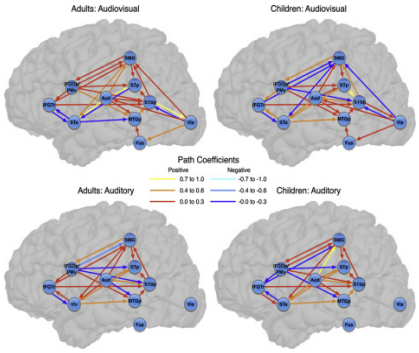

Figure 1. SEM approach to estimate brain connectivity between several ROI's (Dick et al., 2010).

As can be seen, this is a complex model with recursive and non-recursive effects between ROI's which uses, for parameter estimation, the correlations between those ROI's obtained in groups of subjects. Each of the ROI's is defined from the neuroanatomic structure and the statistically significant activations found in each *voxel* defining a three-dimensional matrix for each brain volume analyzed. Figure 2 displays a usual Path Diagram in the case of SEMs.

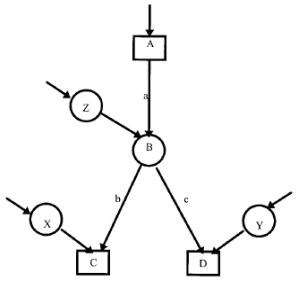

Figure 2. Path Diagram in SEM approach to estimate brain connectivity (Taylor et al. 2000)

This type of models follows a similar structure between SEM and DCM given certain common characteristics between them both. In summary, these are the essential elements for SEM:

- General Model $\eta = \beta\eta + \zeta$
- Adaptation $\eta = [I - \beta]^{-1}\zeta$
- Parameter Estimation: $E(\eta\eta') = [I - \beta]^{-1}\psi[I - \beta]^{-1}$
- ψ is the Var-Covar matrix of residual variance of η
- No C matrix in SEM
- In SEM $\beta = A$

In the case of DCM, these are the properties:

- Model: $Z_t = (A + \Sigma u_{t(j)} B^j) Z_t + C u_t$
  t is continuous time
  Z_t is the neuronal activity
  $u_{t(j)}$ is the j input at time t
  A, B^j and C are the connectivity matrix
- A = Intrinsic connections
- B = Modulatory Connections
- C = External Connections

But in both versions, SEM or DCM, if a series of conditions are met, both models are identical. These are those conditions:

- Neurodynamics are directly observable ($y_i = z_i$)
- The direct inputs are stochastic ($\zeta = Cu_t$)

In this case, DCM can appear as a SEM model and adopt the general form of SEM models in LISREL notation, that is,

$$y_t = \beta y_t + \zeta_t$$

For this purpose, we selected the works published in the last ten years that have applied SEM to study brain connectivity, analyzing the effect of applying these models in such studies. Variables such as the number of ROI's, the parameter estimation techniques, or the properties of the observed distributions, among others, have been analyzed through a meta-analytic approach.

2. Method

Work selection: We analyzed the databases of indexed publications (Science Citation Index and Social Science Citation Index) during the 2001-2012 period. Obviously papers of this type exist prior to 2001, but the increase has come about in the last ten years. We selected the works containing the following Key Words: Structural Equation Model, fMRI, brain connectivity. Out of the works selected, we kept those meeting the following inclusion criteria:

- Presenting standardized estimates. Non-standardized estimates were rejected because neither of them offered the standard errors estimates either.
- Focusing on the study of healthy populations, since connectivity estimates focus on different aspects with samples of diagnosed patients.
- Some papers offer results from several models. In those cases, we selected the SEM model with the best fit, complying with χ^2 values, as is usual.

Following this criterion, we obtained 31 papers or SEM models applied to brain connectivity in healthy subjects. The following table described the models studied.

Table 1. Descriptive characteristic of the n=31 SEM models analyzed.

VARIABLE	DESCRIPTION
Year of publication	2001-2004: 7 models 2005-2008:11 models 2009-2012:13 models
Recursive effects	NO: 15 models

	YES: 16 models
Estimation technique	No Information: 3 models Bootstrap: 1 model Maximum Likelihood: 27 models
Normal multivariate distribution of observed variables	YES: 6 models NO: 2 models No information: 23 models
Statistical conditions	Well conditioned: 4 models No Information: 27 models
The paper has the initial R correlation matrix	YES: 3 models NO: 28 models

Because they were standardized estimates of the free parameters, we used, in every case, the maximum value of all the estimates in an absolute sense, that is, positive and negative values of β_{ij} or γ_{ij} (in LISREL notation). The sign of the parameter is obviously relevant in neuroanatomic terms, but not statistically. For each variable, we estimated the effect size based on the consideration of the highest parameter, bearing in mind the sample size and considering those parameters as linear correlation coefficients. Actually, although it does not appear in 28 models, the R matrix was used in every case for the estimation process in SEM. For each model, we evaluated a series of variables to estimate the effect size, and others as moderating variables. Table 2 shows the corresponding descriptives.

Table 2. Statistical Description of variables included in the meta-analysis.

VARIABLES FOR THE EFFECT SIZE ESTIMATION			
	Mean	Standard Deviation	Standard Error
Sample Size	36.39	78.402	14.081
Absolute Maximum Parameter Estimation	0.6472	0.36908	0.04833
MODERATOR VARIABLES			
CATEGORICAL			
Design	Box Car one Group: 23 models Box Car more one Group: 2 models Complex Event Related: 1 model Simple Event Related: 5 models		
Statistical Model	Extended Unified SEM: 1 model Path Analysis: 2 models SEM: 26 models Unified SEM: 2 models		
Analysis	Between Groups: 2 models Only subjects: 5 models Tasks: 22 models Task and Groups: 2 models		
Models generation	Data Driven: 16 models Hypothesis Driven: 11 models Mixture: 4		
QUANTITATIVE			
	Mean	Standard Deviation	Standard Error
Number of ROI's	6.68	3.754	0.674
Number of Paths	9.23	5.402	0.970

For the 31 models analyzed, we estimated the effect size value based on the value of the most significant parameter and, with the sample size value, we estimated the standard error associated to each of them in order to define the corresponding confidence intervals. Since they were standardized parameters, any other transformation was unnecessary for the corresponding comparability between models. The data was treated with the **`meta`** library in the R project and with the CMA software.

3. Results

The analysis yielded a statistically significant effect for a fixed-effects model (Q = 273.289; df = 30; $p < .001$; I^2 = 89.023), which indicates an effect linked to the value of the standardized parameters. Therefore, the results in the different SEM models analyzed are not independent from some of the studies' own characteristics and, consequently, from the moderating variables. The values of the partial effect for each variable appear in table 3.

Table 3. Meta-Analysis Results

VARIABLE	Categories	Q value	df	Significance	I^2
Analysis	Between Groups	0.035	1	.852	No Sig.
	Only subjects	9.695	4	.046	Sig.
	Tasks	222.414	21	.001	58.743
	Task and Groups	0.537	1	.464	90.558 No Sig.
Design	Box Car one Group	107.651	22	.001	79.654
	Box Car more one Group	2.245	1	.134	55.447
	Complex Event Related	--	-	--	--
	Simple Event Related	60.686	4	.001	93.409
Statistical Model	Extended Unified SEM	--	-	--	--
	Path Analysis	12.170	1	.001	91.783
	SEM	250.858	25	.001	90.034
	Unified SEM	0.311	1	.577	No Sig.
Models generation	Data Driven	125.577	15	.001	88.055
	Hypothesis Driven	24.001	10	.008	58.336
	Mixture	112.767	3	.001	97.340
Number of ROI's	Quantitative variable	r = -.1867	29	.314	No Sig.
Number of Paths	Quantitative variable	r = .2288	29	.215	No Sig.

Complementarily, to evaluate the possible bias effect due to the publishing years, we generated the Funnel graph so as to evaluate the study concentration and thus assess the precision of our meta-analysis. Figure 3 displays that graph.

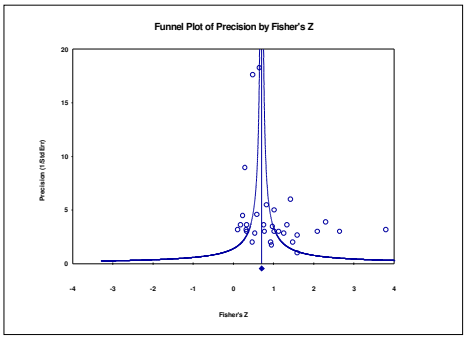

Figure 3. Funnel Graph.

From the graph above, we can infer a concentration in the appropriate area of precision with some exceptions corresponding to high-level works in the estimated parameters which, in some cases, are within the γ_{ij} values and near 0.9. Due to lack of space, we did not include it on ForestPlot to assess each paper's effect and contribution to the general effect size.

4. Conclusions

In light of our results, we can outline the following conclusions:

- Brain connectivity estimated through SEM offers higher estimates in those designs using only contrasts between tasks with just one group. Two-group or factorial design choices do not offer such significant results.
- There is no relevant relationship between the number of ROI's defined and the number of paths established. Obviously this analysis does not imply the neuroatomic importance of those ROI's, which is not the subject of the current work.
- Whatever the form of generation of the connectivity model, high, fitted results are obtained.
- The most relevant effects are used when using SEM and Path analysis classically, whereas that effect is reduced in the strategy of the Unified SEM. The latter case, however, is widely underrepresented and we should be cautious with this idea.
- Likewise, the classical Box-Car and Event Related strategies seem to offer data for better parameter estimations in SEM. The simpler strategies seem to offer better data for the study of connectivity.

Therefore, generally speaking, the form, methodology, and strategy defining the brain signal recording in *f*MRI paradigms is not independent from the best solution we can get when using SEM for estimating brain connectivity.

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[1] To consult the list of works analyzed please contact with the authors.