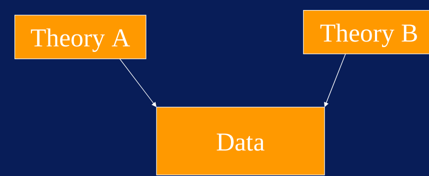
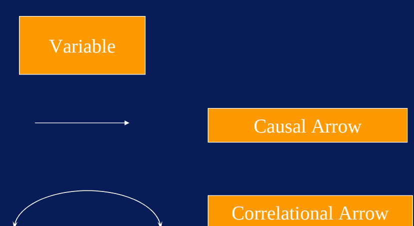
Effective Connectivity

- Intro to SEM
- SEM and fMRI
- DBN

- Theory driven process
  - Theory is specified as a model
- Alternative theories can be tested
  - Specified as models



The Joy of Path Diagrams



Doing “Normal” Statistics

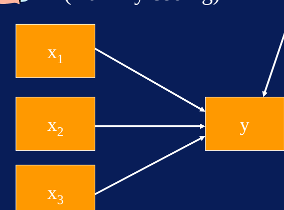
Correlation

Doing “Normal” Statistics

T-Test

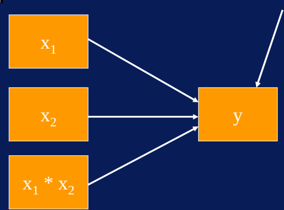
Doing “Normal” Statistics

One way ANOVA
(Dummy coding)



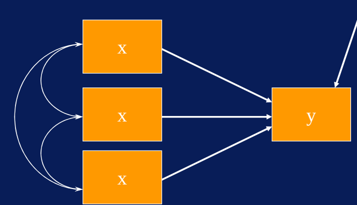
Doing "Normal" Statistics

Two- way ANOVA
(Dummy coding)



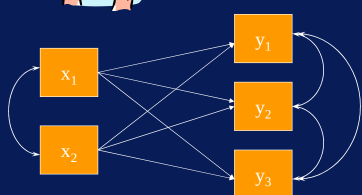
Doing "Normal" Statistics

Regression



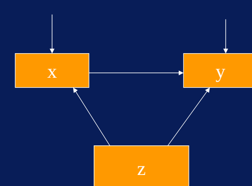
Doing "Normal" Statistics

MANOVA



Doing "Normal" Statistics

ANCOVA



Sampling Variation and χ^2

- Equations and numbers
  - Easy to determine if its correct
- Sample data may vary from the model
  - Even if the model is correct in the population
- Use the χ^2 test to measure difference between the data and the model
  - Some difference is OK
  - Too much difference is not OK

Example 1

- $R_{ab} = 0.3$, N = 100

- Estimate = 0.3, SE = 0.105, C.R. = 2.859
- The correlation is significantly different from 0

- Model

- Tests the hypothesis that the correlation in the population is equal to zero
  - It will never be zero, because of sampling variation
  - The χ^2 tells us if the variation is significantly different from zero
- Force the value to be zero
  - Input parameters = 1
  - Parameters estimated = 0

- The program gives a χ^2 statistic
- The significance of difference between the data and the model
  - Distributed with df = known parameters - input parameters
- $\chi^2 = 9.337$, df = 1 - 0 = 1, $p = 0.002$

- So what? A correlation of 0.3 is significant?

Hardly a Revelation

- No. We have tested a correlation for significance. Something which is much more easily done in other ways
- But
  - We have introduced a very flexible technique
  - Can be used in a range of other ways

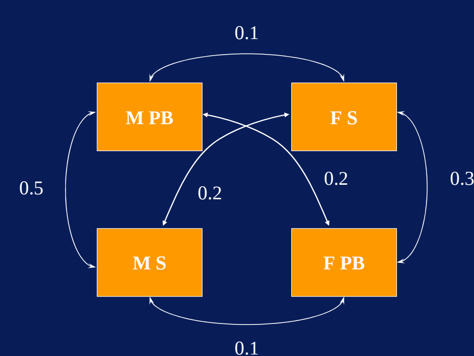
Testing Other Than Zero

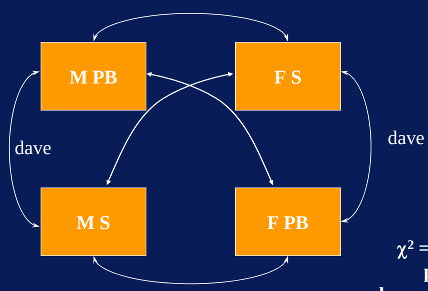
- Estimated parameters usually tested against zero
  - Reasonable?
- Model testing allows us to test against other values

- $\chi^2 = 2.3$, n.s.

Example 2: Comparing correlations

- 4 variables
  - `mothers' sensitivity`
  - `mothers' parental bonding`
  - `fathers' sensitivity`
  - `fathers' parental bonding`
- Does the correlation differ between mothers and fathers?





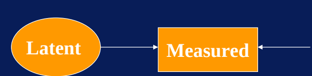
χ^2 = 1.82, df = 1
p = 0.177
dave = 0.41 (s.e. 0.08)

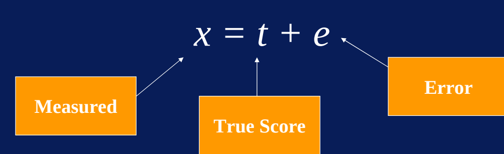
Latent Variables

- The true power of SEM comes from *latent variable modelling*
- Variables in psychology are rarely (never?) measured directly
  - the effects of the variable are measured
  - Intelligence, self-esteem, depression
  - Reaction time, diagnostic skill

Measuring a Latent Variable

- Latent variables are drawn as ellipses
  - hypothesised causal relationship with measured variables
- Measured variable has two causes
  - latent variable
  - "other stuff"
    - random error

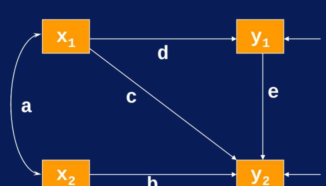




- *Reliability is:*
  - the square root of proportion of variance in x that is accounted
  - the correlation between *x* and *e*

The Multivariate Case

- Much more complex and unpredictable

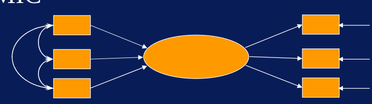


Value of a Car

- Causes
  - type, size, age, rustiness
  - no reason they should, or should not, be correlated
- Effects
  - assessment of value by people who know

Level of Depression

- Questionnaire items
  - causes or effects?
    - been feeling unhappy and depressed?
    - been having restless and disturbed nights?
    - found everything getting 'on top' of you?
- MIMIC

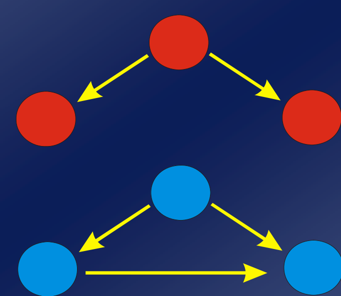


SEM & fMRI

Theory to Analysis

- Examine the influences between brain areas
  - Interregional correlation (Horwitz, et al, 1984)
  - Structural equation modeling (McIntosh & Gonzalez-Lima, 1991, Buchel & Friston, 1997)
  - Multiple regression and extensions (e.g., Kalman filters, Buchel & Friston, 1998)
  - Bayes networks (Dynamic Causal Modeling, Friston, Penny, et al, 2003)
- Identification of interacting regions
  - Partial Least Squares (McIntosh, Bookstein, et al, 1996)
  - Canonical Variates Analysis (Strother et al, 1995)
  - Independent Components Analysis - 32 flavours (McKeown et al, 1998, Calhoun et al, 2001, Beckmann, Smith, et al., 2002)

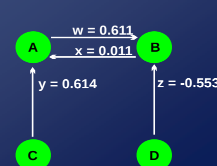
Functional and Effective Connectivity



Structural Equation Modeling

- Multivariate multiple regression
- Combines interregional covariances with anatomical framework
- Provides means to assess whether effective connections are modified by task-demands or differ between groups
- Is not meant to be a model test in the coventional sense
  - Goodness of fit not as relevant

Structural Equation Modeling

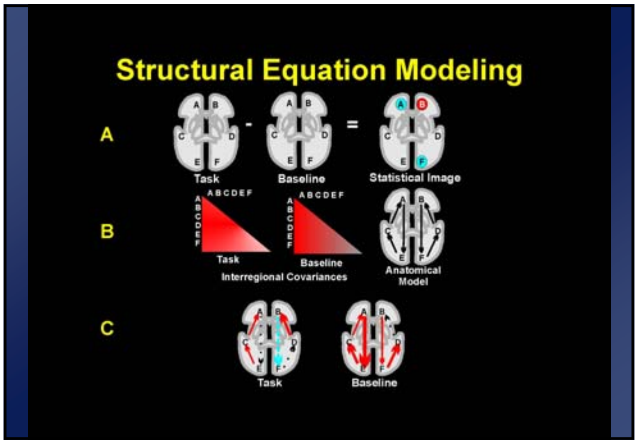


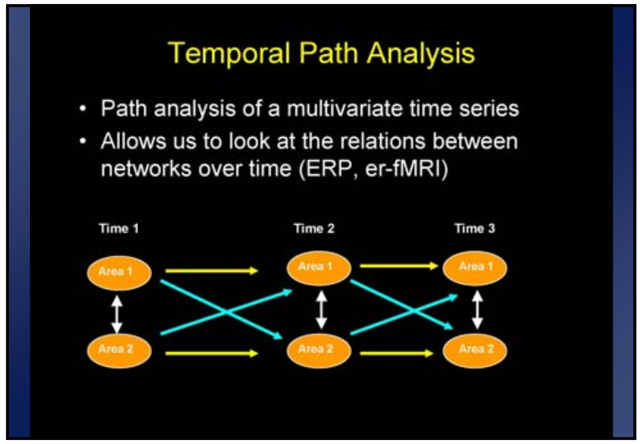
	A	B	C	D
A	1.00			
B	0.48	1.00		
C	0.62	0.16	1.00	
D	0.24	-.41	0.06	1.00

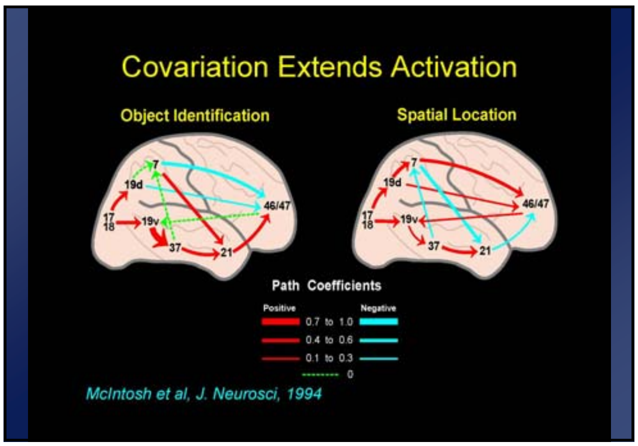
Structural Equations

$A = xB + yC + \psi$

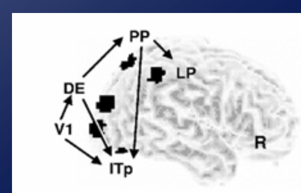
$B = wA + zD + \psi$

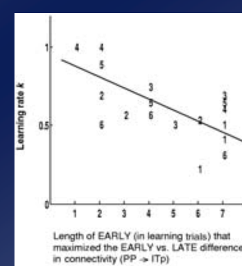






Relation of "effective connectivity" changes to behavior





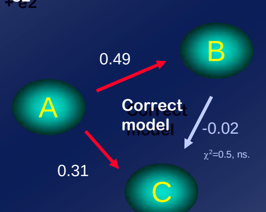
Buchel, Coull, Friston, Science, 1999

Effective vs. functional connectivity

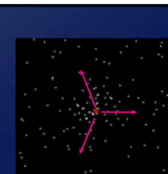
Model:
A = V1 fMRI time-series
B = 0.5 * A + e1
C = 0.3 * A + e2

Correlations:

A	B	C
1		
0.49	1	
0.30	0.12	1



Dynamic changes in effective connectivity
Attentional modulation of V5 responses to visual motion



Stimuli
250 radially moving dots at 4.7 degrees/s

Pre-Scanning
5 x 30s trials with 5 speed changes (reducing to 1%)
Task - detect change in radial velocity

Scanning (no speed changes)
6 normal subjects, 4 100 scan sessions;
each session comprising 10 scans of 4 different condition

e.g. F A F N F A F N S ....

F - fixation point only
A - motion stimuli with attention (detect changes)
N - motion stimuli without attention
S - no motion

Structural equation modelling (SEM)

Minimise the difference between the observed (S) and implied (Σ) covariances by adjusting the path coefficients (a, b, c)

The implied covariance structure:

$x \quad = x.B + z$

$x \quad = z.(I - B)^{-1}$

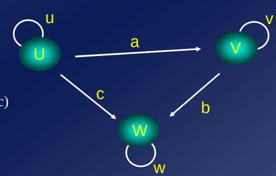
x : matrix of time-series of regions U, V and W

B: matrix of unidirectional path coefficients (a,b,c)

Variance-covariance structure:

$x^T . x = \Sigma \quad = (I-B)^{-T} . C.(I-B)^{-1}$

where $C \quad = z^T z$

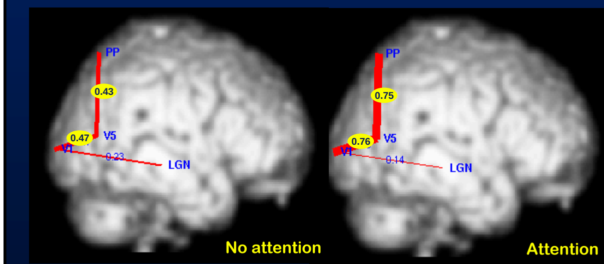


$x^T.x$ is the implied variance covariance structure Σ

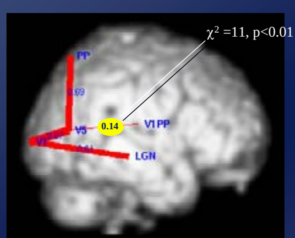
C contains the residual variances (u,v,w) and covariances

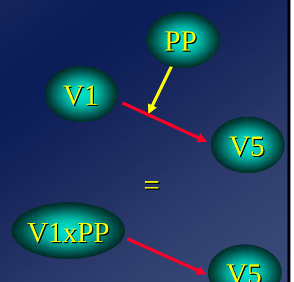
The free parameters are estimated by minimising a [maximum likelihood] function of S and Σ

Attention - No attention



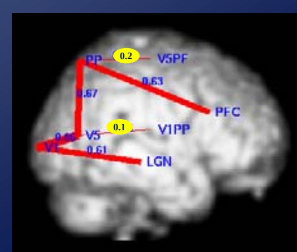
The use of moderator or interaction variables

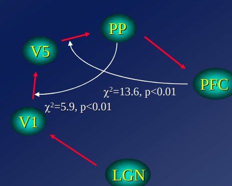




Modulatory influence of parietal cortex on V1 to V5

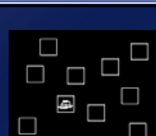
Hierarchical architectures

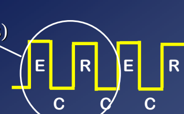


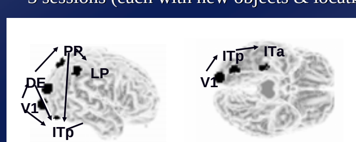


Changes in effective connectivity over time: Learning

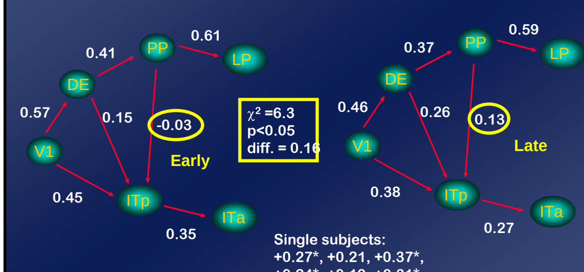
- Paired associates learning
- Pairing
  - Object (Snodgrass) with
  - Location
- fMRI, 48 axial slices, TR 4.1s, 8 scans/cond
- 8 cycles (E)ncoding (C)ontrol (R)etrieval
- 3 sessions (each with new objects & locations)







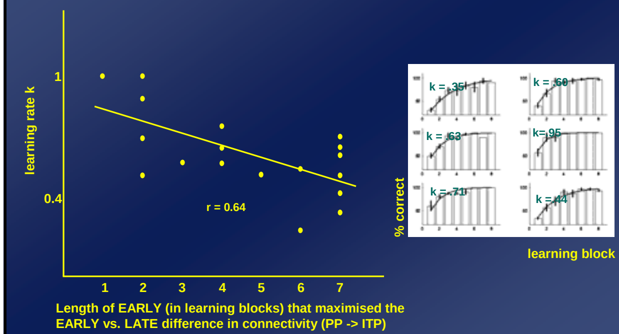
SEM: Encoding Early vs. Late



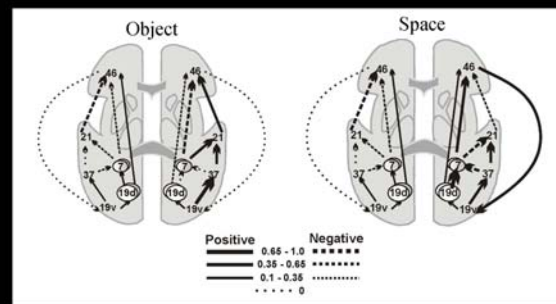
Single subjects:
+0.27*, +0.21, +0.37*,
+0.24*, +0.19, +0.31*

* p < 0.05

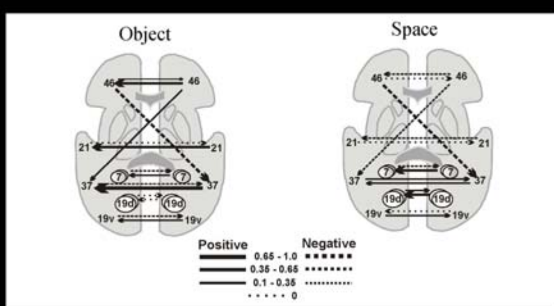
Changes in effective connectivity predict learning



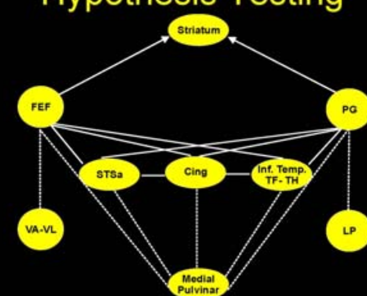
Interhemispheric interactions



Interhemispheric interactions

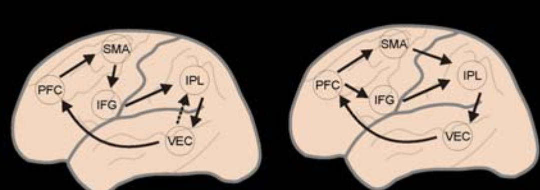


Hypothesis Testing



Network for Directed Attention (Mesulam, 1981)

Hypothesis Testing



Theory-driven Model

Data-driven Model

Bullmore, et al, NeuroImage, 2000

Dynamic Bayes Networks

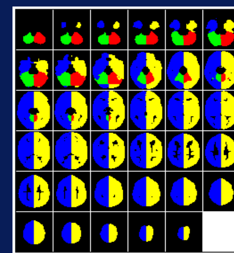
Goals

- Machine learning techniques applied to neuroimaging problems
- Analyze Buckner et al.'s fMRI dementia data[1]
  - Dartmouth fMRI Data Center
- How do neural networks change with dementia?
- How to model networks of relationships?
- Create classifiers to discriminate between healthy and demented patients

1) Buckner, R. L., Snyder, A., Sanders, A., Marcus, R., Morris, J. (2000). *Journal of Cognitive Neuroscience*

Prepping the Data

- Too many voxels
- Use Talairach Database
  - Lancaster et al., U of Texas[2]
- Average activity across regions
- Table of regional time series
- How to model time series?



2) Lancaster JL, Woldorff MG, Parsons LM, Liotti M, Freitas CS, Rainey L, Kochunov PV, Nickerson D, Mikiten SA, Fox PT (2000). *Human Brain Mapping*

Relationship Modeling

- Typical analysis methods
  - Generalized Linear Model (GLM)
  - Structural Equation Modeling (SEM)
- Assumptions GLM and SEM frequently make
  - Fixed temporal model
  - Linearity
  - Gaussian distribution
  - Correlation accurately modeled with covariance

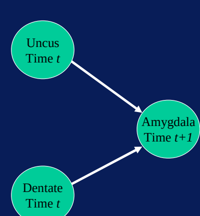
Discrete Multivariate Model

- Use multivariate temporal models
  - Each ROI is discrete temporal random variable
- Requires decimation of data
  - Continuous ROI amplitude mapped to small set of discrete states
  - 12 bit continuous ⟶ 2 bit discrete
  - Multinomials define ROI's behavior
  - Not limited to pair-wise relationships

Amplitude	
Very High	0.1
High	0.4
Low	0.4
Very Low	0.1

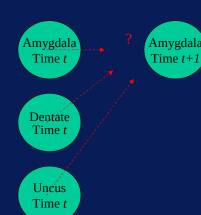
Dynamic Bayesian Network

- Framework for multinomial analysis
- Explicitly models time
- Links indicate correlation
- Example is a DBN *family*
  - *Parents:* Uncus and dentate
  - *Child:* Amygdala
  - *Parents* predict values of *child*



Dynamic Bayesian Network

- One family for every ROI
- Families may share parents
- Which links should be added?
- Correlations vary in strength
- DBN is a set of families



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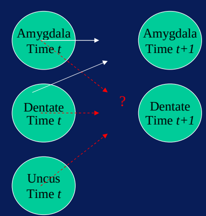

Dynamic Bayesian Network

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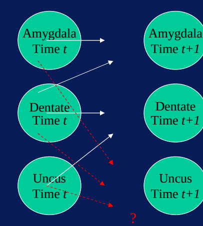
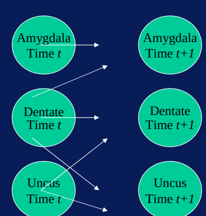


Dynamic Bayesian Network

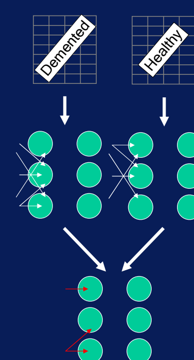
Basic search idea
- Suggest many structures
- "Score" each one
- Score measures correlation strength
- Choose structure with > score

- Issues
  - Too many structures
  - Finding best is "hard"

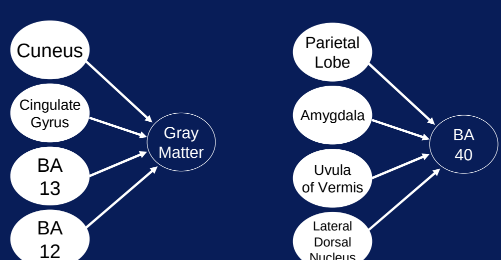


Approach

1. Separate data into:
   - Healthy subjects
   - Diseased patients
2. Learn DBN structure for each group
3. Look for change in DBN structure
4. Classify using likelihood tests



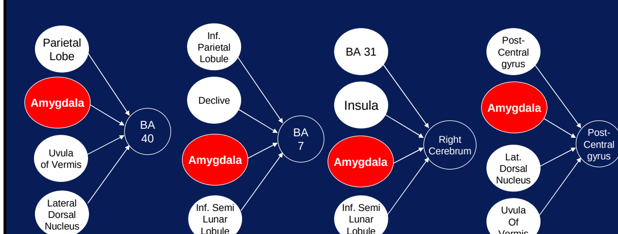
Structure Results



Best healthy family

Best demented family

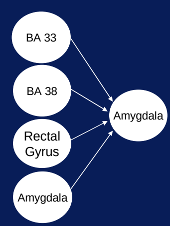
Amygdala Prevalence in Dementia



7 of top 10 families

49% of all families

Amygdala Activity in Healthy



Only in 1 family

Validation

1. Quantify confidence in each family
   - Measure likelihood correlations due to chance
   - Top 10 families all have p values << 0.01
2. Compare classification efficacy with
   - Support vector machines
     - 65% accuracy
   - Gaussian naïve Bayesian networks
     - 73% accuracy
   - DBN
     - 73% accuracy