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Exploratory Data Modeling of Traumatic Brain Injury

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http://www.pdx.edu/sysc/research_dmm.html

Bethesda, June 9, 2015

- [RaDaR](#) (raw data analysis)-[Occam](#) subproject
 - Martin Zwick, Tracie Nettleton
 - Hugo duCoudray Forrest Alexander, Naghmeh Daneshi, Peter Olson
- Brain Trauma Evidence-Based Consortium ([BTEC](#))
- [Dr. Nancy Carney](#), OHSU, head
- Funded by DoD via Brain Trauma Foundation, Stanford

1. Objectives, exploratory modeling

2. Preece data; approach

3. Some results on Preece dataset

1. Objectives, exploratory modeling

- Exploratory modeling (**data mining**)
using Reconstructability Analysis (**RA**)
on multiple data sets to contribute to:
 - a clinically useful TBI **classification** system
 - other BTEC subprojects, e.g., dynamic modeling
- now **Preece data** on auto accidents
- other data sets to follow

What RA is

- **Reconstructability Analysis (RA)** = Information theory + Graph theory
- RA: a **probabilistic graphical modeling technique**
 - Graph = model: node = variable; link = relationship
 - Hypergraphs = **associations** between **>2** variables
- RA can detect **many-variable** or **non-linear** interactions ***not hypothesized in advance***
- RA **model** = a (conditional) probability distribution **simpler** (fewer df) than data, **capturing much** of the **information** in the data

Why RA & Occam software

- Explicitly designed for **exploratory** modeling
 - Analyzes both **nominal** & **continuous** (binned) variables
 - **Easily interpretable** method & output
 - **Standard** text **input**; Occam **emails** results to user
 - **Occam** web-accessible; **available** for research use
- Related statistical & machine-learning methods (log-linear, logistic regression, Bayesian networks, classification trees, support vector machines, neural nets) **not well designed for exploration**, *or* have **limited model types** *or* **difficulty** with **nominal** variables or **stochasticity**

2. Preece data; approach

- 52 variables
- Variable types
 - P = **patient** characteristics (17 variables)
 - Y = **symptoms** (25): subjective reports
 - G = **signs** (4): objective indicators
 - C = **cognitive** deficits (5)
 - N = **neurologic** deficits (1)
- N = 337; reduces to 175 or less if exclude missing data

Variables (1/3)

- Patient (P) variables (17)

pinjgrp,5,	pj	Injury Group patient or control			
page,7,	pag	age			
psex,2,	psx	sex			
pyred,6,	pye	years of education			
pedlevel,8,	ped	highest level of education			
puhrsleap,5,	pul	usual # of hrs of sleep: less than or greater than normal (8 hr)			
precentill,3,	pri	recent illness 0 no 1 yes			
pmedication,3,	pmd	current medications 0 no 1 yes			
ppainkllr,3,	ppk	currently on painkillers 0 no 1 yes			
ppreheadinj,3,	pph	have they had previous head injury 0 no 1 yes			
pprecon,3,	ppc	previous concussion 0 no 1 yes			
pnumprecon,8,	pnp	how many previous concussions			
pdbqerror,13,	pqe	Driver Behavior Questionnaire self reported driving errors/violator			
pdbqviol,14,	pqv	Driver Behavior Questionnaire violations			
plitigat,4,	plg	was the case litigated			
prespacc,6,	pac	who was responsible for the accident			
pfsiq,5,	piq	full scale IQ calculated from national adult reading test			

Variables (2/3)

- Symptom (Y) variables (25)

ypainscale,5,	ypn	standard painscale used by hospitals					
yemoscale,5,	yem	sacle defining emotional state(0 no problems 1 few 2 moderate 3 many problems)					
ydassd,5,	ydd	Depression Anxiety Stress Scales: depression					
ydassa,6,	yda	Depression Anxiety Stress Scales: anxiety					
ydasss,4,	yds	Depression Anxiety Stress Scales: stress					
yheadache,6,	yhs	Rivermead headache					
ydizz,5,	ydz	Rivermead dizzy					
ynausea,5,	yna	Rivermead nausea					
ynoisesens,6,	yns	Rivermead noise sensitivity					
yslpdis,6,	ysd	Rivermead sleep disorder					
yfatigue,6,	yfa	Rivermead fatigue					
yirritable,6,	yir	Rivermead irritable					
ydepressed,5,	ydp	Rivermead depressed					
yanxious,6,	yax	Rivermead anxious					
yfrustrated,5,	yfr	Rivermead frustrated					
yforgetful,6,	yfg	Rivermead forgetful					
ypoorconc,6,	ycn	Rivermead poor concentration					
ylongthink,6,	ytk	Rivermead long time to think					
yblurredvis,6,	ybr	Rivermead blurred vision					
ylightsens,5,	yls	Rivermead light sensitivity					
ydoublevis,6,	ydv	Rivermead double vision					
yrestless,6,	yrs	Rivermead restless					
ydazed,5,	yaz	Rivermead dazed					
yrivermead,5,	ym	summation of Rivermead post concussion symptom questionnaire					
ycorrectedvis,3,	ycv	corrected vision					

Variables (3/3)

- Sign (**G**) & Deficit (**C, N**) variables (4, 5, 1)

ghrssleep,5,	ghl	number of hours of sleep, divided in less than normal normal=8hr and greater than normal							
ggcs,4,	ggc	Glasgow coma scale a measure of level of unconsciousness; lower = deeper unconsciousness							
gextcause,8,	gxc	external cause of the injury							
gpta,3,	gpt	post traumatic amnesia							
chazpt,10,	chp	hazard perception test measures how quickly potential driving hazards are predicted							
cnormsrt,6,	cnr	Spatial Reaction Time normalized for age and sex							
cspatialreac,6,	csr	Spatial Reaction Time tests how quickly patient responds to a visual stimuli							
cdgtcorrect,7,	cdg	Digit Symbol Substitution neuropsychological test							
cstarcan,4,	csc	Star Cancellation Test a test of spatial neglect							
nlogmar,4,	nlr	LogMAR Logarithm of the Minimum Angle of Resolution: a visual acuity test							

Approach (1/3)

2 types of model searches

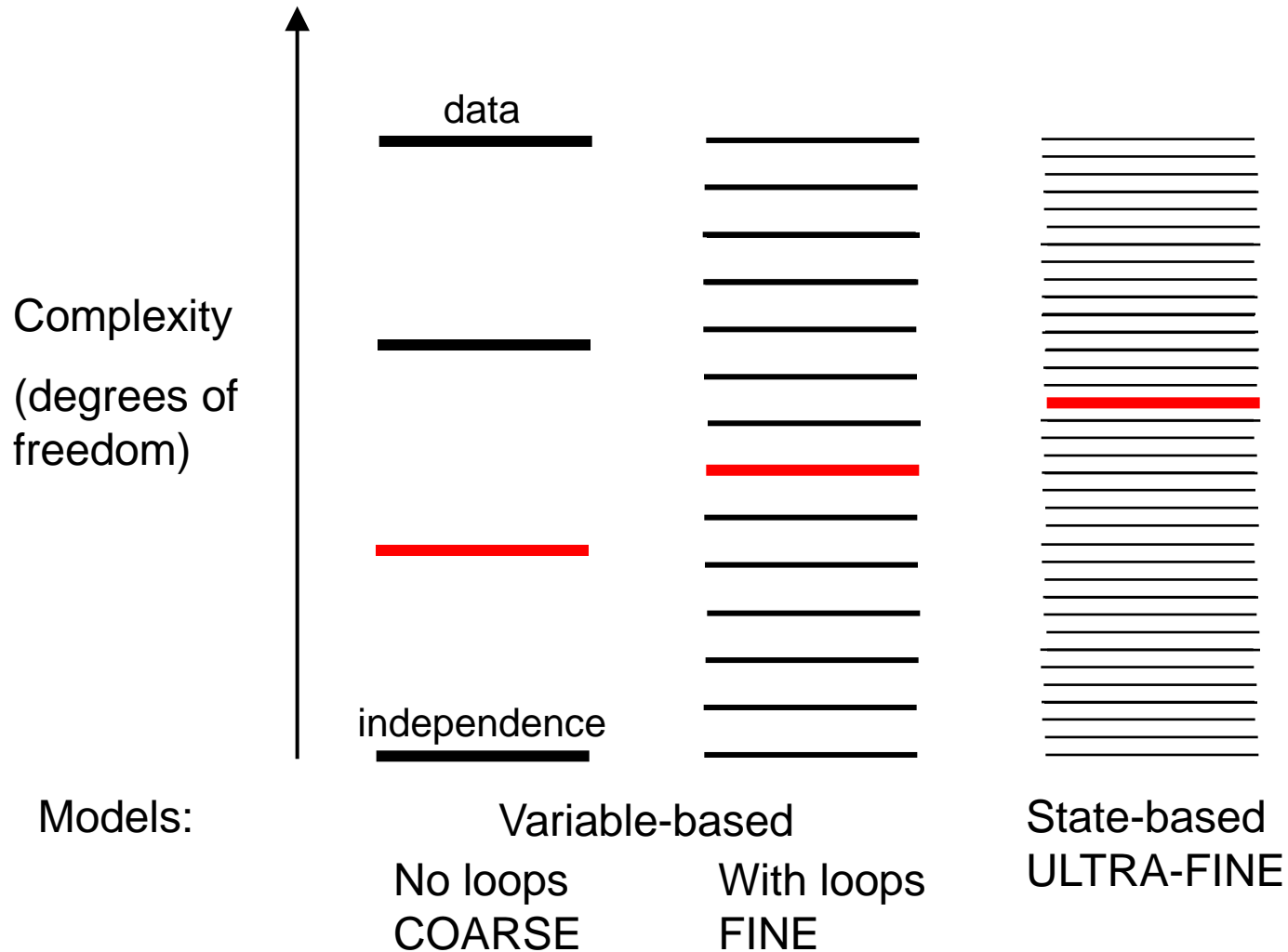
- *Neutral*: find relationships among all variables ('clustering')
- *Directed*: predict C, N variables from P, Y, G ('classification')
 - reference = independence model
 - **predictive success** (information captured) measured by
 - $\% \Delta H = \% \text{reduction of uncertainty}$: (information-theoretic measure)
 - Uncertainty is *like* variance
 - Rule of thumb: $\% \Delta H = 8\%$ *can be* a sizeable effect
 - $\% c = \% \text{correct}$ (general measure)
 - want low model **complexity** = Δdf

Approach (2/3)

3 degrees of search refinement (IVs: A,B,C...; DV: Z)

- *Coarse search*: variable-based models w/o loops, e.g., $A B z, \dots$
Fast, can handle *many* variables
- *Fine search*: variable-based models w' loops, e.g., $A B z : B C z$
Slow, can handle 100s of variables
- *Ultra-fine search*: state-based models, e.g., $A_2 B_1 z : B_0 z$
Very slow, less than 10 variables

Three degrees of search refinement



Approach (3/3)

3 model selection criteria (information-complexity tradeoff)

- *Conservative:* Bayesian Information Criterion (**BIC**)
- *Aggressive:* Akaike Information Criterion (**AIC**)
- Incremental p-value (**IncrP**)
- AIC & BIC: **linear combinations** of error (opposite of information) & complexity; BIC penalizes more for complexity: weights it by $\ln(N)$
- IncrP uses **Chi-square p-values** to pick models whose difference from -- & every **incremental** step from -- independence is statistically significant

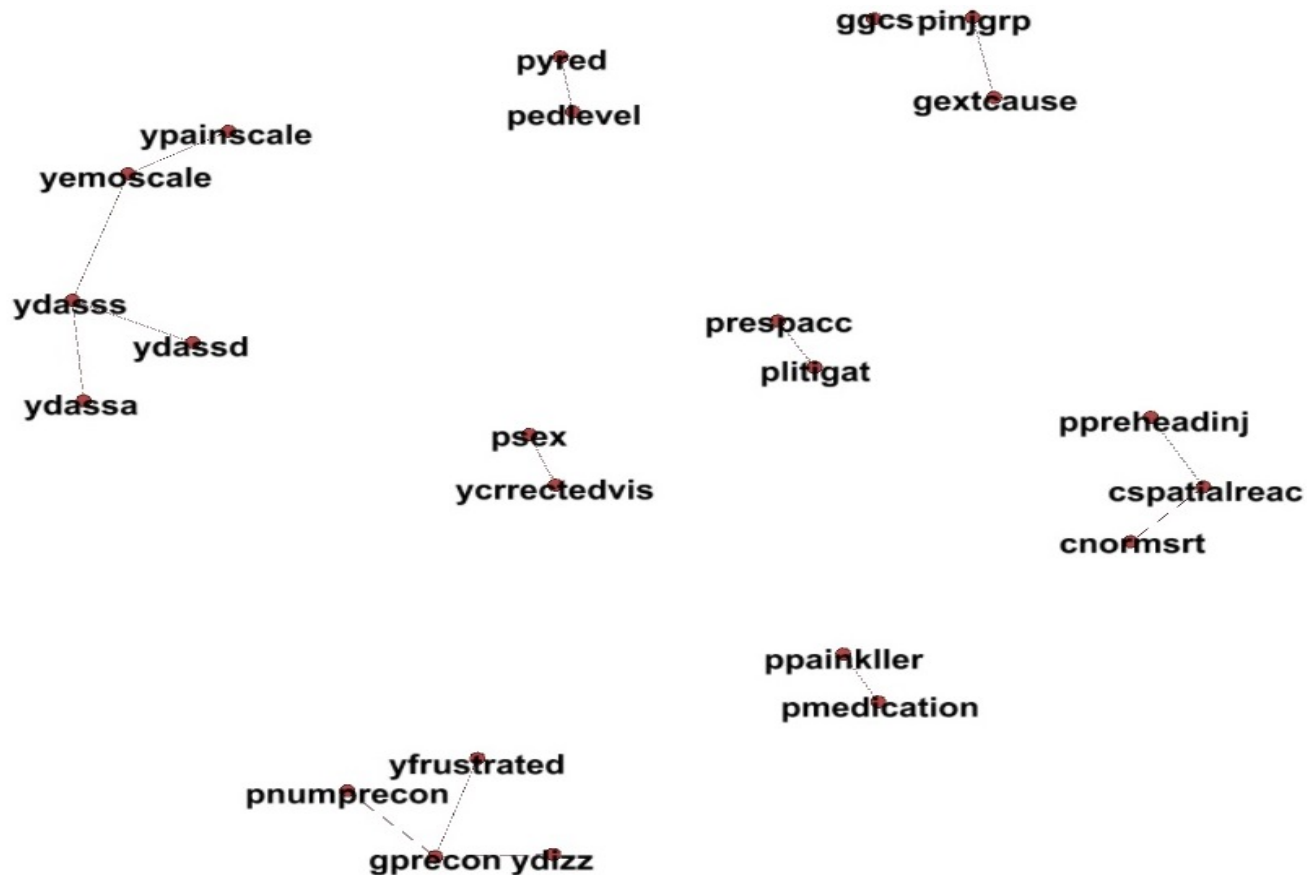
Some **issues**: binning, missing data, small N, validation

3. Results on Preece dataset

- **Neutral** *coarse searches*
 - find **associations** among all P, Y, G, C, N variables
- **Directed** *coarse, fine, ultra-fine searches*
 - **predict** C, N from P, Y, G & from *other* C, N variables

Neutral coarse search (graph of associations)

- 15 $p \leq 0.05$ associations in BIC model (2 involve C)



Neutral coarse search (15 associations)

- Predictive success ($\% \Delta H$, $\Delta \% C$ relative to independence) ($p \leq 0.05$)

v1	v2	$\% \Delta H(2 1)$	$\% \Delta H(1 2)$	p-value	N	$\Delta \% C(2 1)$	$\Delta \% C(1 2)$	v1	v2
Ggc	Pij	34.5	86.5	0.000	196	9.7	7.7	glasgow coma scale	Injury patient/control
Gxc	Pij	32.9	12.6	0.000	280	20.4	14.3	external cause	Injury patient/control
Ped	Pye	41.3	34.8	0.000	248	32.3	27.4	highest educ level	years of education
Yem	Ypn	6.4	6.1	0.000	218	5.0	2.3	emotional problems	painscale
Yds	Yem	6.0	27.8	0.000	210	3.8	0.0	stress	emotional problems
Ydd	Yds	43.6	26.0	0.000	210	1.4	1.9	depression	stress
Yda	Yds	54.7	32.6	0.000	210	0.0	2.9	anxiety	stress
Pmd	Ppk	50.7	57.6	0.000	230	28.3	15.7	current medications	painkillers
Gpc	Pnp	57.0	100.0	0.000	52	11.5	30.8	previous concussion	# previous concussion
Pac	Plg	26.5	12.3	0.000	201	0.0	12.4	caused accident	case litigated
Cnr	Csr	48.6	48.3	0.000	210	34.3	31.0	reaction time norm	reaction time
Psx	Ycv	6.5	8.8	0.000	197	2.0	0.0	sex	corrected vision
Gpc	Ydz	13.7	21.9	0.003	52	0	9.6	previous concussion	dizzy
Csr	Pph	5.3	2.3	0.010	187	5.3	4.8	reaction time	previous head injury
Gpc	Yfr	9.1	17.3	0.011	52	1.9	9.6	previous concussion	frustrated

Directed searches: DVs = deficit variables

- Priorities (Dr. Carney): focus here on predicting **Cdg, Cnr**
- #bins excludes missing values ; will often aggregate states into fewer bins

	#bins		N	
cdgtcorrect	6	Cdg	255	Digit Symbol Substitution neuropsychological test
				Most important/reliable test
cnormsrt	6	Cnr	210	Spatial Reaction Time normalized for age and sex
cspatialreac	6	csr	214	Spatial Reaction Time test: how quickly patient responds to visual stimuli
nlogmar	3	Nlr	209	LogMAR Log of Minimum Angle of Resolution (visual acuity)
				Less important/reliable
cstarcan	3	csc	50	Star Cancelation Test a test of spatial neglect
chazpt	9	chp	282	Hazard perception test: how quickly potential driving hazards are predicted

Cdg directed coarse, fine, ultra-fine searches

Predict Cdg: digit symbol substitution test (rebin |Cdg| = 2: ~ 50-50)

MODEL (IV component omitted)	Δdf	p	% ΔH	%c			
COARSE, single predictors					ΔBIC	N=240	
Pij _{Cdg}	3	0.00	11.9	68.3	47.6	patient injury type	
Ped _{Cdg}	7	0.00	11.7	65.0	5.9	education level	
Ggc _{Cdg}	3	0.00	5.6	65.0	18.3	Glasgow coma scale	
Cnr _{Cdg}	5	0.00	3.5	60.8	6.1	spatial reaction, normalized	
Pye _{Cdg}	1	0.00	3.0	68.3	27.9	years education	
Csr _{Cdg}	5	0.00	2.5	63.3	0.4	spatial reaction	
<i>Cdg (independence=reference)</i>	0	1.00	0.0	50.8	0		
FINE					Criterion	N=240	Cnr =6, incl missing
Pij _{Cdg} : Pye _{Cdg}	4	0.00	25.5	72.9	BIC		
Pij _{Cdg} : Pye _{Cdg} : Cnr _{Cdg}	9	0.00	32.8	76.7	AIC		
Pij _{Cdg} : PSX _{Cdg} : Pye _{Cdg} : Cnr _{Cdg}	10	0.00	32.9	76.3	IncrP	sex	
ULTRA-FINE (state-based model)						N=175	Cnr =2, no missing
Pij₂ Cnr₁ Cdg : Pye₀ Cdg	2	0.00	13.5	68.6	BIC		
<i>Cdg (independence=reference)</i>	0	1.00	0.0	50.9			

Cdg ultra-fine (state-based) model 3/3

Model: $P_{ij_2} Cnr_1 Cdg : Pye_0 Cdg$

Odds (high is good) = $Cdg_1/Cdg_0(\text{model}) = p(\text{high digit score})/p(\text{low score})$

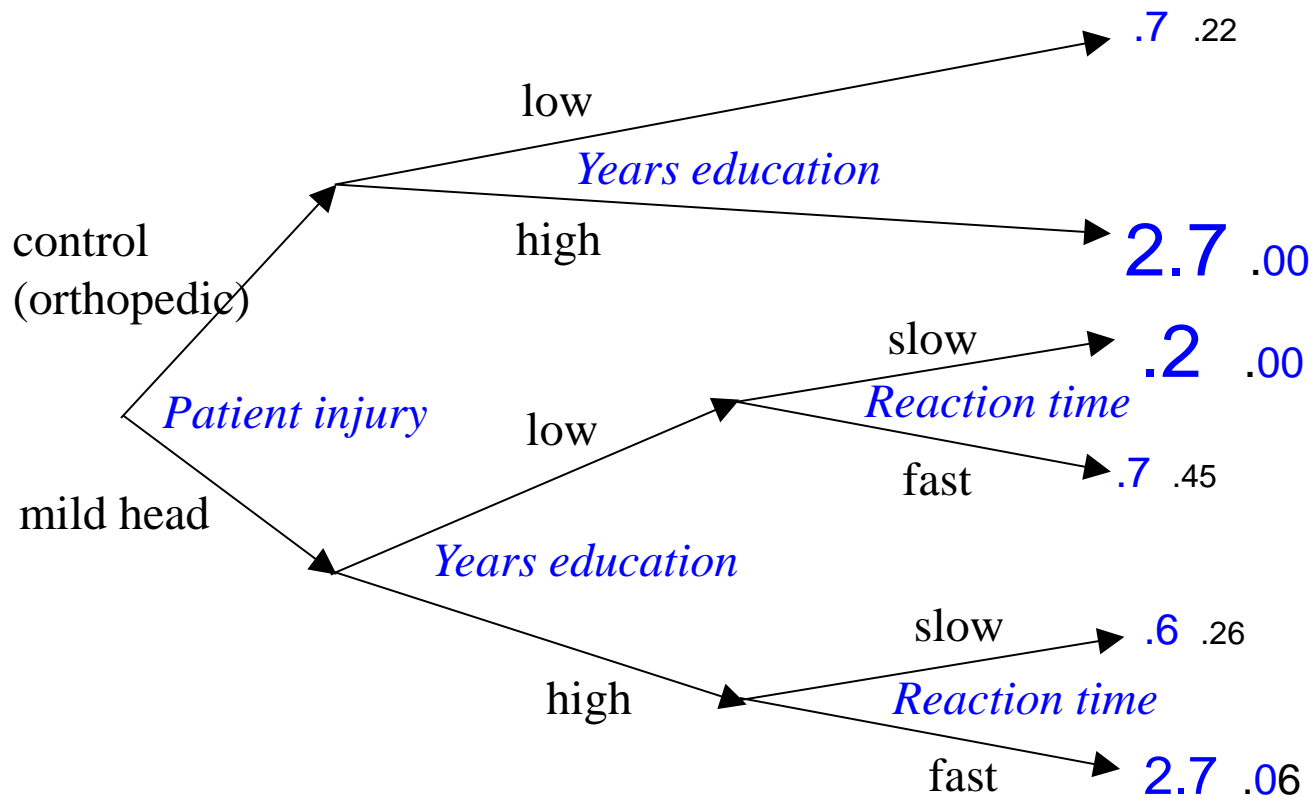
P_{ij_1} control, P_{ij_2} mild head injury; Pye_0 low years educ.; Cnr_0 = fast reaction

conditional probabilities of DV

IV states				data		model			
Pij	Pye	Cnr	N	Cdg ₀	Cdg ₁	Cdg ₀	Cdg ₁	Odds	p
1	0	0	18	0.50	0.50	0.59	0.41	0.7	.41
1	0	1	22	0.68	0.32	0.59	0.41	0.7	.36
1	1	0	38	0.21	0.79	0.27	0.73	2.7	.01
1	1	1	20	0.35	0.65	0.27	0.73	2.7	.05
2	0	0	15	0.53	0.47	0.59	0.41	0.7	.45
2	0	1	24	0.88	0.13	0.86	0.14	0.2	.00
2	1	0	18	0.33	0.67	0.27	0.73	2.7	.06
2	1	1	20	0.60	0.40	0.62	0.38	0.6	.26
			175	0.49	0.51	0.49	0.51	1.0	

Cdg decision tree from conditional probabilities

Digit Symbol score odds (prob. high performance/ prob. low performance) & p-values relative to marginal prob. (odds = 1):



Cdg decision tree, verbally

- For all patients, **education predicts** performance on **digit symbol** test: more education predicts better performance.
 - Education is a **confounding** variable for digit symbol test in discriminating concussion, & must be controlled for
- For controls (orthopedic), **reaction time** does **not predict** digit symbol score.
- For TBI patients, fast reaction time predicts better digit symbol performance **beyond influence of education**.

Cnr directed coarse, fine, ultra-fine searches

Predict Cnr: reaction time, normalized by age, sex (rebin |Cnr| = 2: ~ 50-50)

MODEL	Δdf	p	% ΔH	%c		N=175		
COARSE, single predictors								
Cdg Gpt Cnr	3	0.00	10.6	64.6	BIC, AIC	Cdg = digit symbol test		
Pph Cdg Gpt Cnr	7	0.00	13.1	66.9	IncrP		Gpt = amnesia	
Cnr (independence=reference)	0	1.00	0.0	50.9			Pph = previous head injury	
FINE								
Cdg Cnr : Gpt Cnr	2	0.00	8.8	64.6	BIC			
Pri Cnr : Pph Cnr : Cdg Gpt Cnr	6	0.00	14.7	70.3	AIC	Pri = recent illness		
Pye Cnr : Pph Cnr : Cdg Gpt Cnr	5	0.00	12.9	67.4	IncrP	Pye = years education		
ULTRA-FINE (state-based model)								
Pph₁ Cdg₁ Cnr : Cdg₀ Gpt₁ Cnr	2	0.00	12.4	64.8	BIC			
Cnr (independence=reference)	0	1.00	0.0	50.9				

Cnr ultra-fine (state-based) model

Model: Pph₁ Cdg₁ Cnr : Cdg₀ Gpt₁ Cnr

Odds (high is good) = **Cnr₀**/**Cnr₁**(model) = p(**fast** = normal reaction)/p(**slow**)

Pph₁ previous head injury, Cdg₁ high digit score; Gpt₁ amnesia

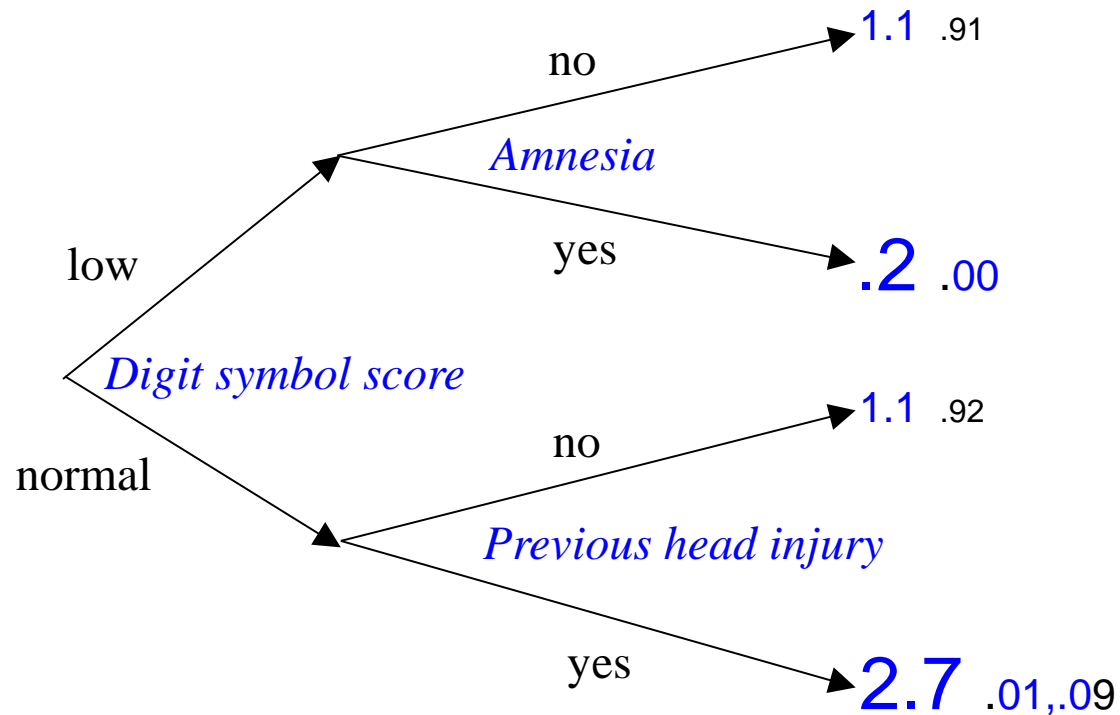
conditional probabilities of DV

IV states				data		model			
Pph	Cdg	Gpt	N	Cnr ₀	Cnr ₁	Cnr₀	Cnr₁	Odds	p
0	0	0	20	0.40	0.60	0.52	0.48	1.1	.92
0	0	1	19	0.16	0.84	0.16	0.84	0.2	.00
1	0	0	30	0.57	0.43	0.52	0.48	1.1	.90
1	0	1	18	0.17	0.83	0.16	0.84	0.2	.00
0	1	0	24	0.50	0.50	0.52	0.48	1.1	.91
0	1	1	13	0.61	0.39	0.52	0.48	1.1	.93
1	1	0	38	0.76	0.23	0.73	0.27	2.7	.01
1	1	1	14	0.64	0.36	0.73	0.27	2.7	.09
			176	0.51	0.49	0.51	0.49	1.0	

Cnr decision tree from conditional probabilities

Reaction time score odds (probability normal/ probability slow)

& p-values relative to marginal prob. (odds = 1)



Cnr decision tree, verbally

- For **low** performance on **digit symbol** test, **amnesia** predicts **slow reaction time**.
- For **normal** performance on **digit symbol** test, **previous head injury** **increases** the probability of fast (**normal**) **reaction time**. THIS IS ANOMALOUS.
 - We need to see if it would be **replicated** in another data set.
 - One possible explanation: prior exposure to Reaction Time test introduces a **practice effect**.
 - If Reaction Time is so vulnerable to a practice effect that it no longer discriminates concussed from non-concussed, then it's probably not an appropriate measure for this purpose.

Future (1/2)

- Provide data a **test bed** for future analyses.
- Results are **preliminary & tentative, illustrative** of *type* of results from exploratory analysis.
- **Need to confirm results** with other data sets or future studies.

Future (2/2)

- Hoping for *more data sets* (accident, military, sports), *higher N*, *fewer missing data*, *additional types* of *variables* (imaging, genomic, proteomic).
- Work to be *fully collaborative* with investigators sharing data.

- THANK YOU

RA (DMM) web page

<http://pdx.edu/sysc/research-discrete-multivariate-modeling>
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Research: Discrete Multivariate Modeling

The methods used are also known in the systems literature as "reconstructability analysis" (RA). RA overlaps significantly with the fields of logic design and machine learning and with log-linear statistical modeling. The papers "Wholes and Parts in General Systems Methodology" and "An Overview of Reconstructability Analysis" listed below offer a concise review of RA methodology.

Projects

Theory/Methodology

- OCCAM: RA software for data analysis & data mining**
 - Occam3 (web accessible; try it out)
 - User manual (PDF)
- EDA: Extended Dependency Analysis**
 - Heuristic RA search for loopless models.
 - Download executable, sample files, and documentation (for Windows)

RA utility programs

Below is the lattice of structures for a 4-variable *directed* system with 1 dependent variable (output). Boxes = relations; lines = variables; bold lines = the dependent variable.

