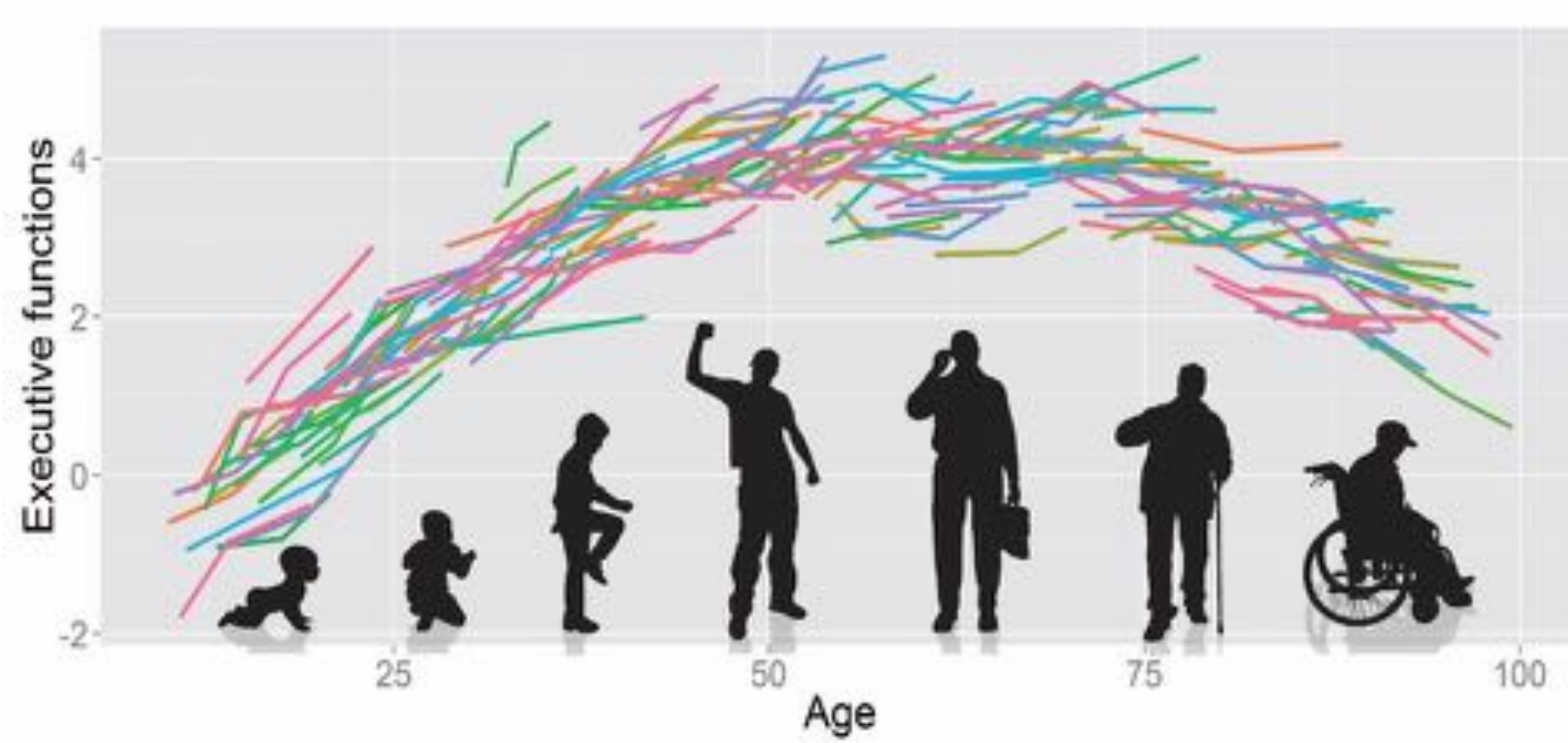
Structural equation modelling of brain and behaviour

Principles and practice



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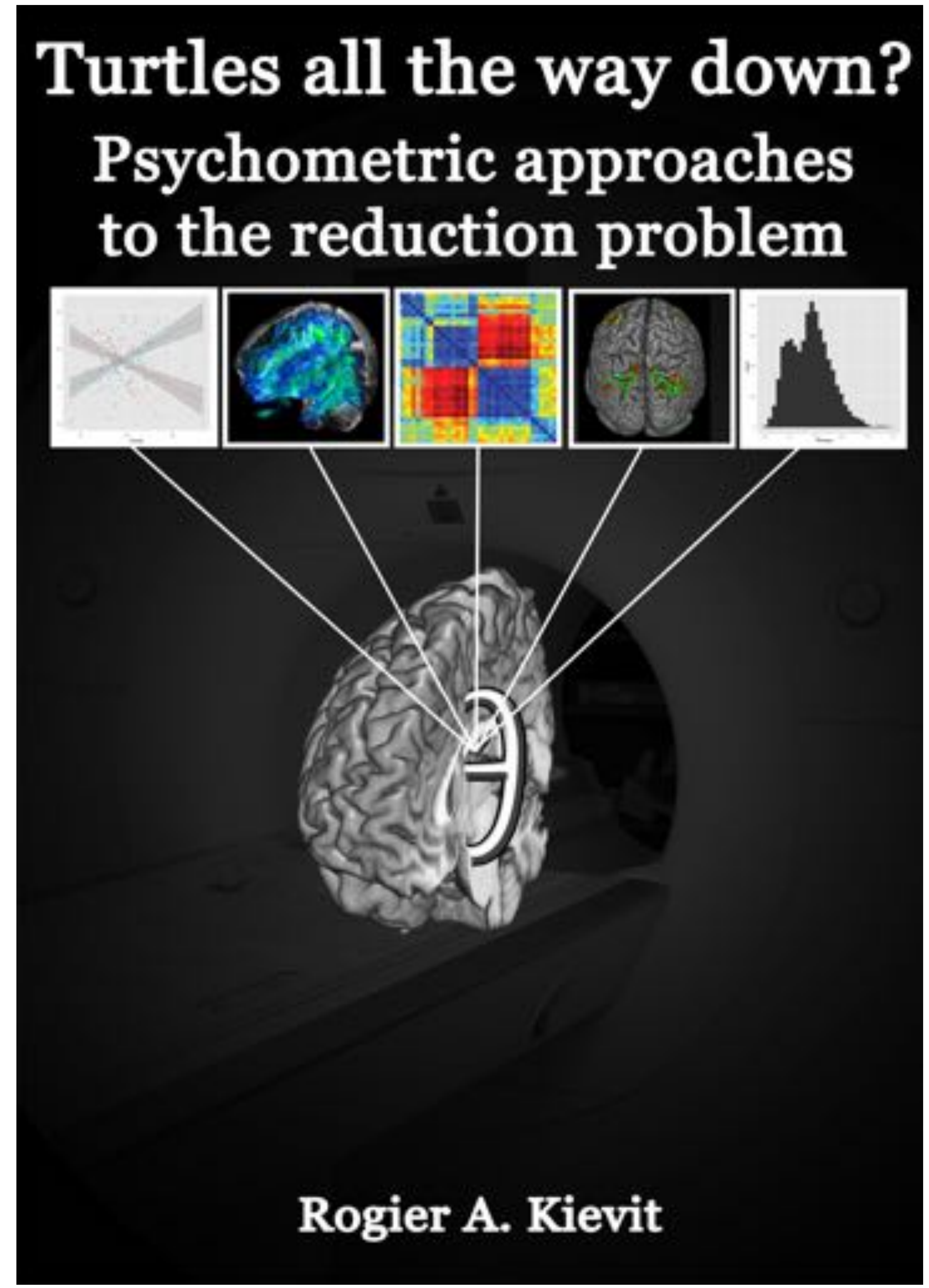
Ringberg 2016

Outline

- 1) Philosophical foundations
- 2) Using SEM to test theories in neurocognitive aging
- 3) Longitudinal SEM
- 4) Summary and future directions

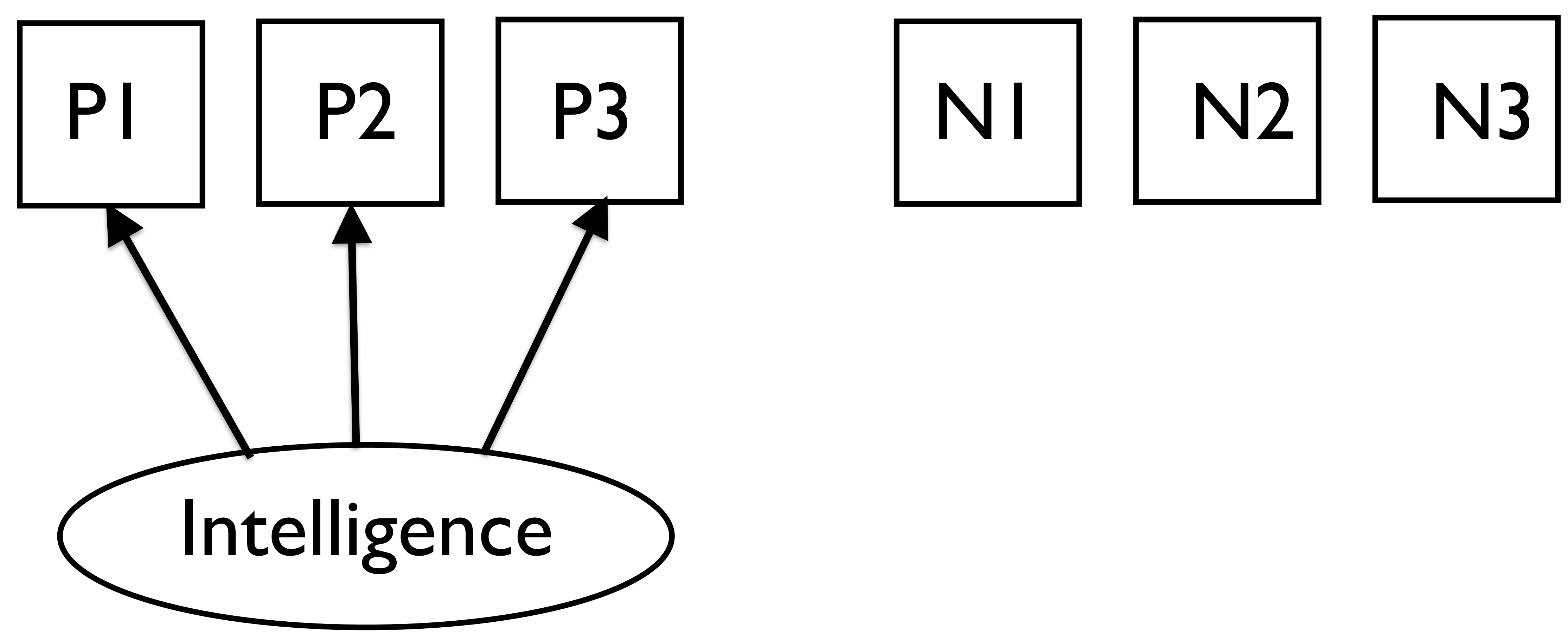
1) Philosophical foundations

- Basic challenge in cognitive neuroscience: two types of measurements
  - Psychological measurements (P)
  - Neurological measurements (N)
- Reduction problem (how do brains relate to minds) is a ***measurement problem***
- Philosophical accounts about the relationship between brain and mind *empirical questions*
- *Project: translate philosophical positions into testable models*



Candidate 1: Identity theory model

- Identity theory (Place, 1956; Smart, 1959)
- A psychological state is identical to a (type of) neural state
- Psychological and neural measurements are measuring the same underlying (latent) property
- Reflective factor model



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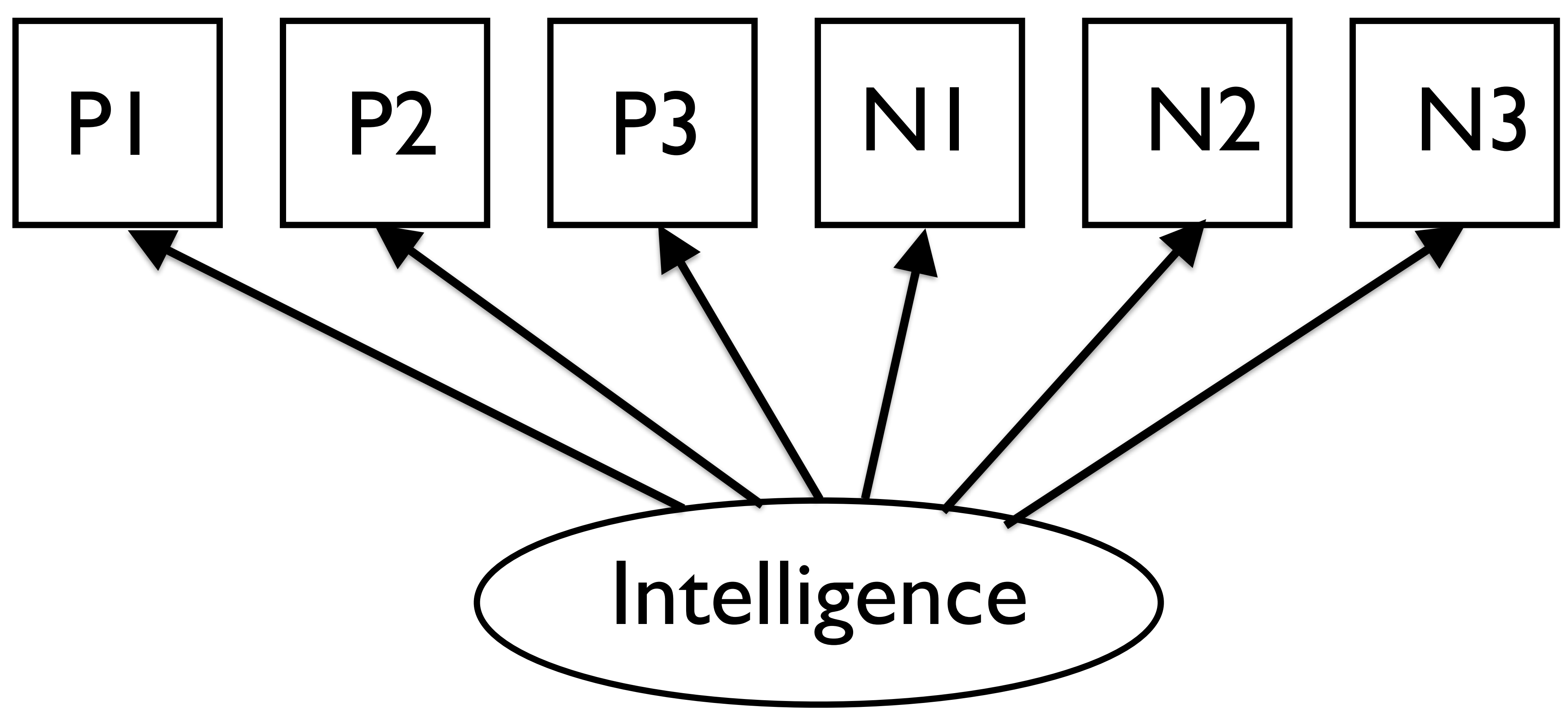


$$y_i = \lambda_i \eta + \varepsilon_i$$

Kievit et al., 2011a; Kievit et al., 2011b

Supervenience theory

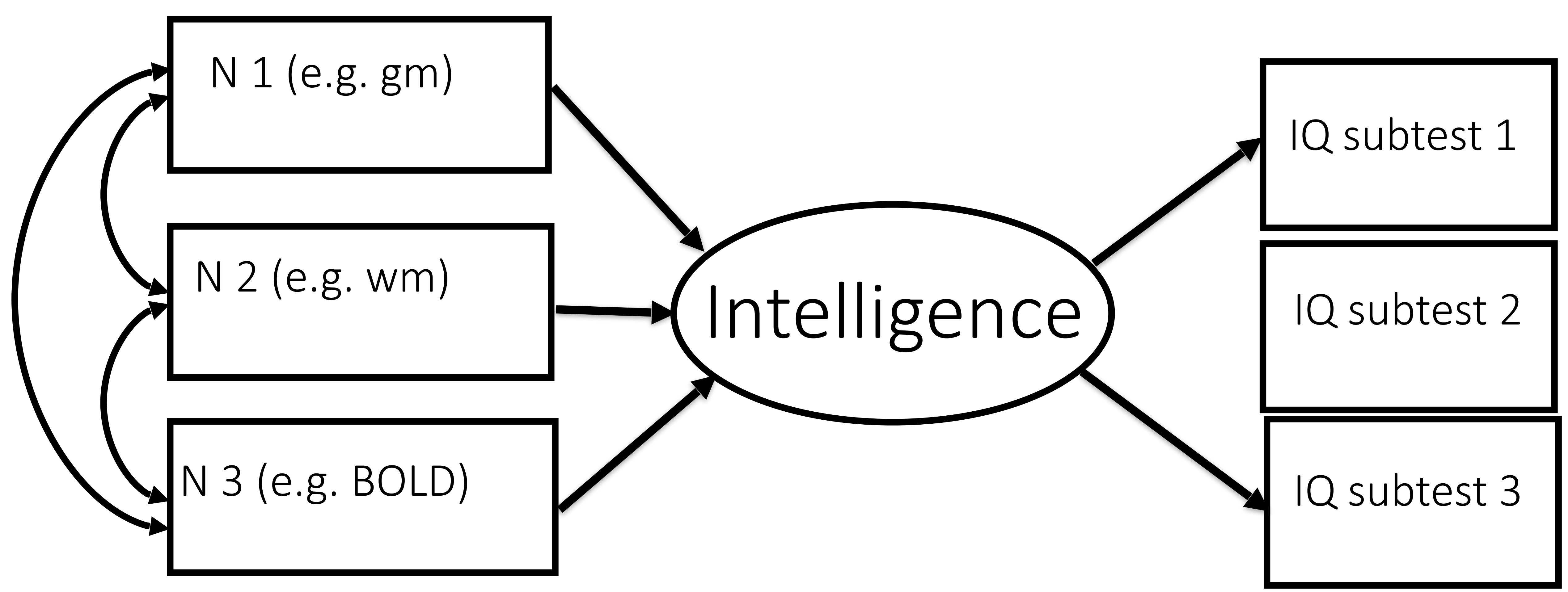
- Higher property ***causally dependent*** on lower properties
- e.g. ‘being moral’, or ‘having socio-economic status X’
- Psychological states/properties ***supervene on*** structure/function of the brain (e.g. Kim, 1984, 1986)
- Fundamentally asymmetrical relationship: Same psychological state can have multiple realizations
- Empirical translation: formative model (MIMIC, Multiple indicators, Multiple causes)

$$\eta = \sum_i \gamma_i x_i + \zeta$$

Sum of weights i * indicators i

Latent variable

Disturbance/error term



$$x_i = \lambda_i \eta_1 + \varepsilon_i$$

Factor loading i

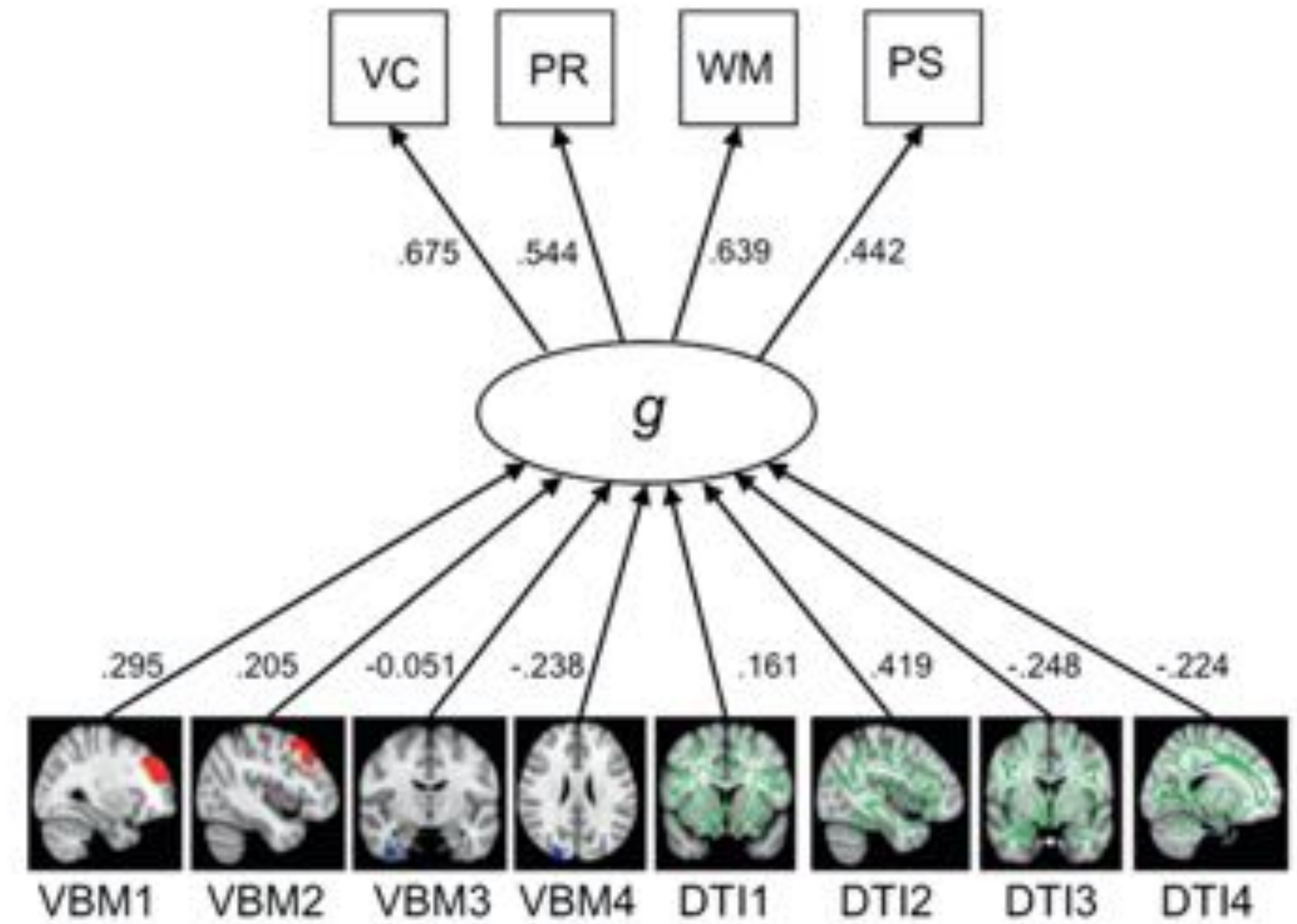
Observed score i

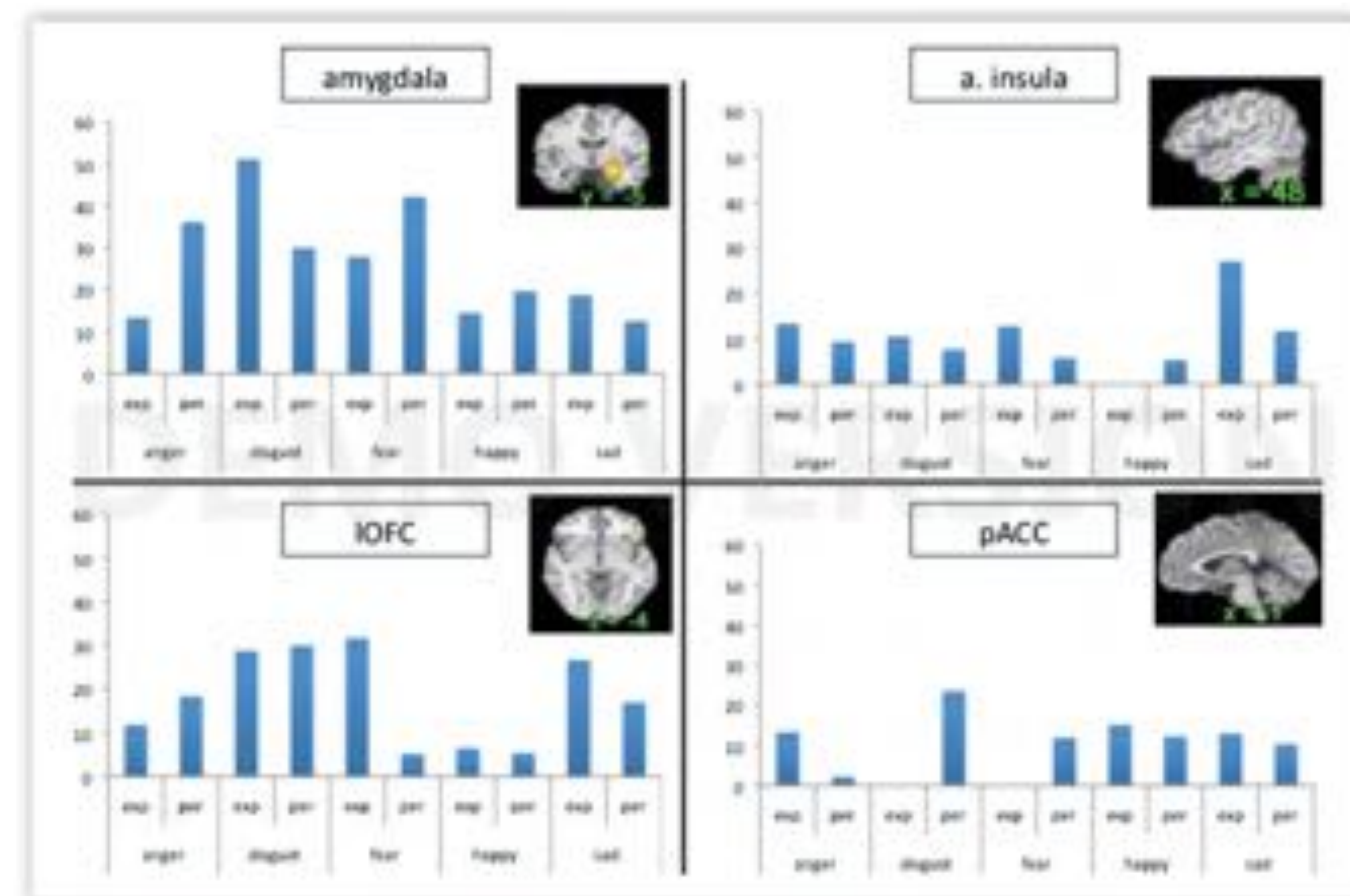
Error term i

Latent variable

Empirical tests

- Across several datasets supervenience (MIMIC model) outperforms other candidates
- Intelligence (Kievit et al. 2011a; Kievit et al. 2012, Ritchie et al. 2015)
- Emotional states (Lindquist et al., 2012)
- Psychological state/level is the best seen as consequence of weighted combination of neural properties (not one ‘dedicated’ system)

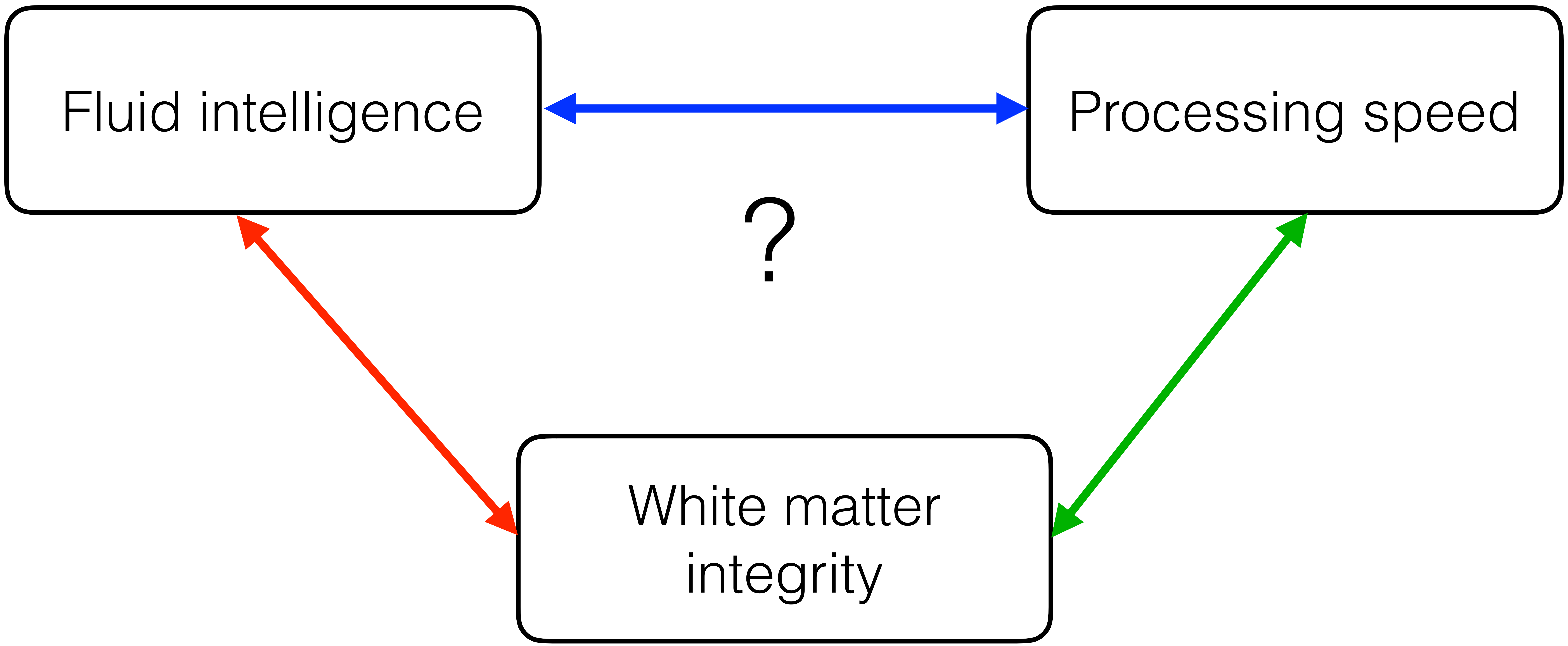




2) Using SEM to test theories in neurocognitive aging

- Philosophical theories about mind-body relations can be tested empirically
- Testing theories in (cognitive neuroscience of) aging
- Often poorly formalized

A watershed model for fluid intelligence



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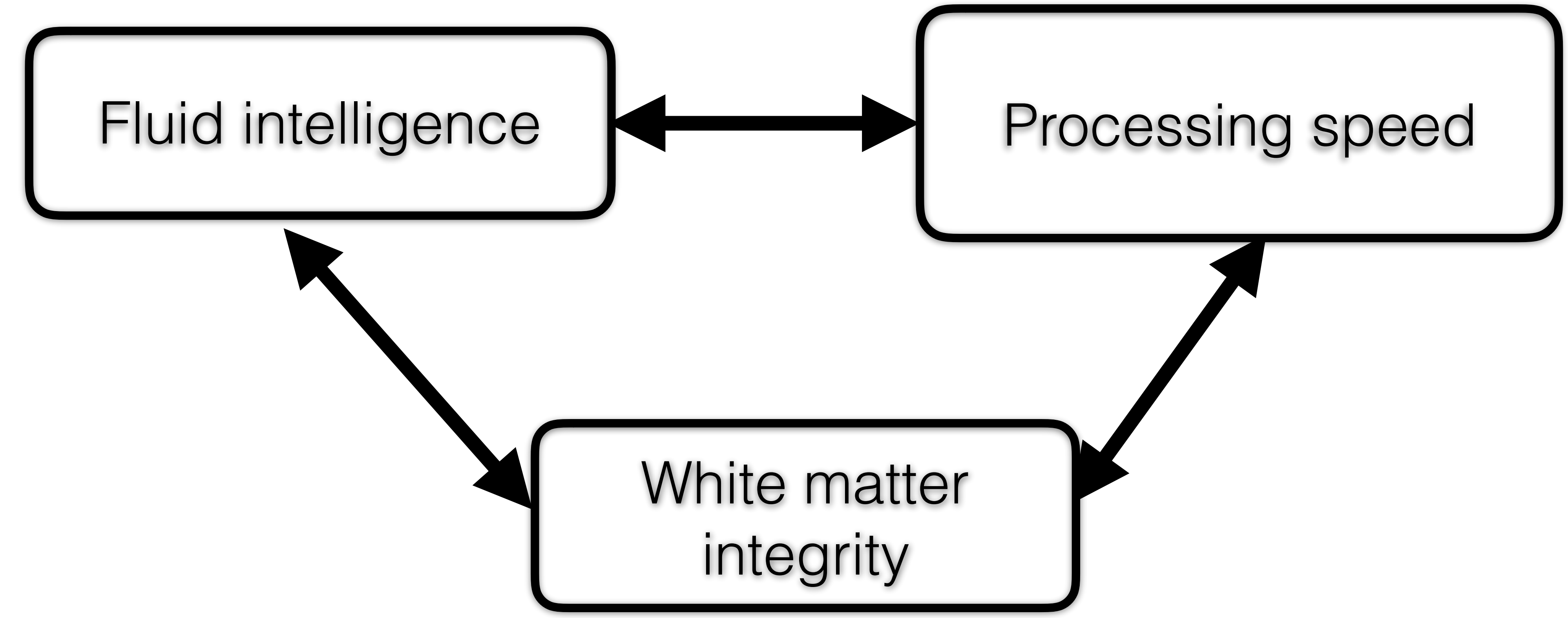
Quite well established



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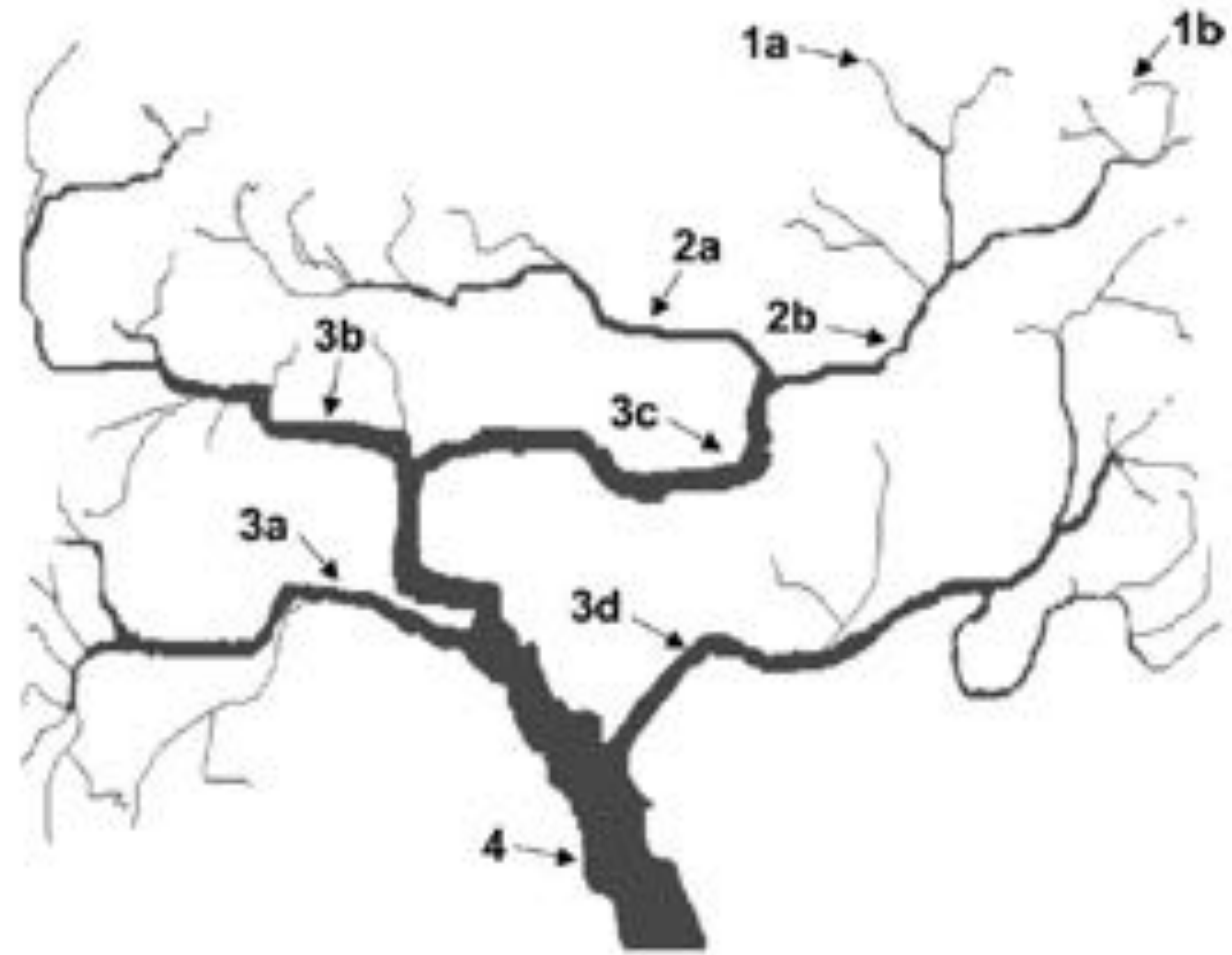
Watershed model

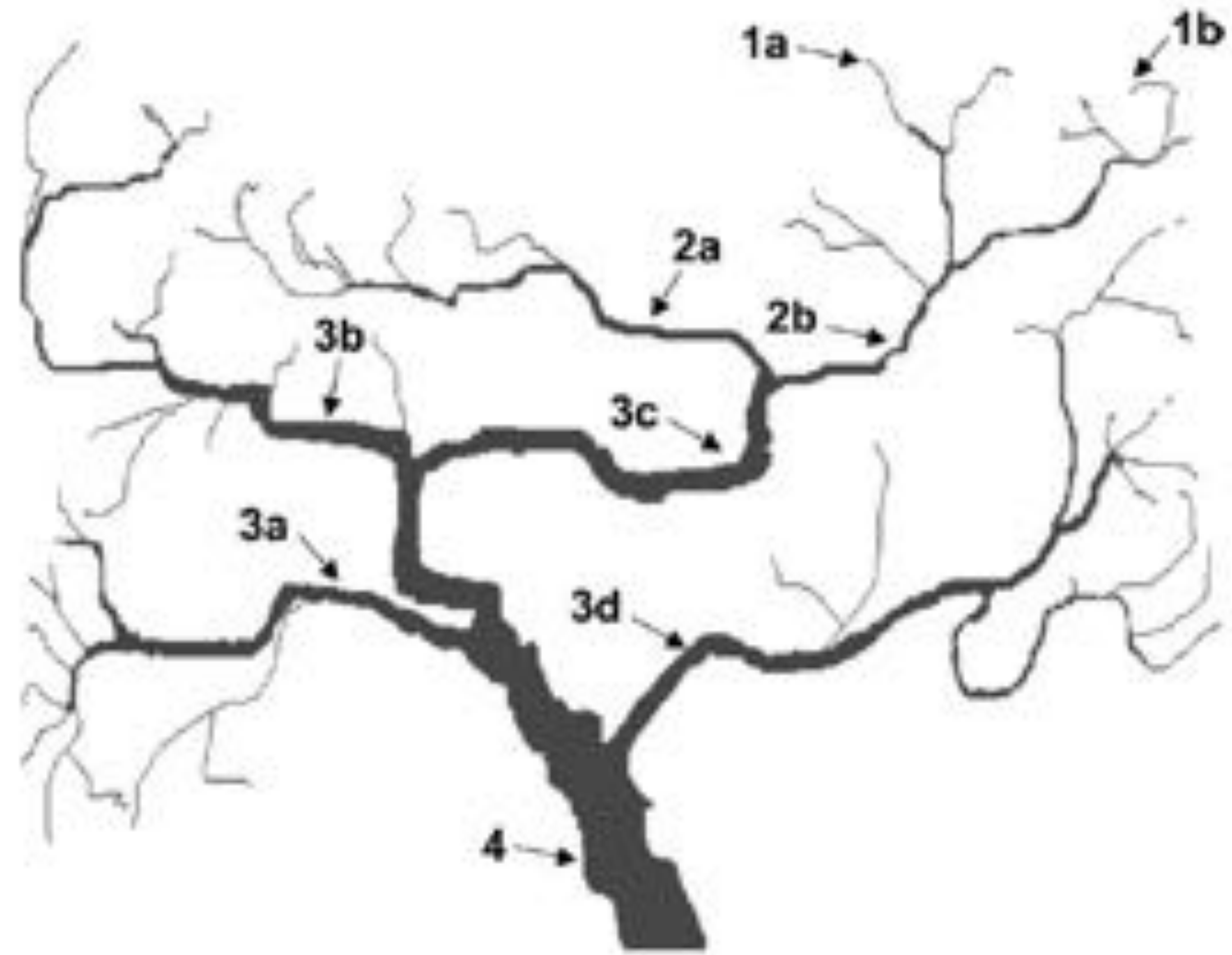
- Cannon & Keller (2006)
- Used to explain schizophrenia
- Hierarchical, many-to-one cascade of partially independent effects



- 4: phenotype (schizophrenia)
- 3a:d: ‘high’ endophenotype (e.g. working memory deficits)
- 2a:2d: ‘low’ endophenotype (e.g. dopaminergic regulation in the prefrontal cortex)
- 1a:1n: genotype

Watershed model

- Model explains
  - Small genetic effects
  - Lack of success of single cause explanations
  - Non-unitary consequences of e.g. lesions
  - Phenotypical heterogeneity (e.g. 1000 ways to be depressed)
  - Our goal: a watershed model of fluid intelligence



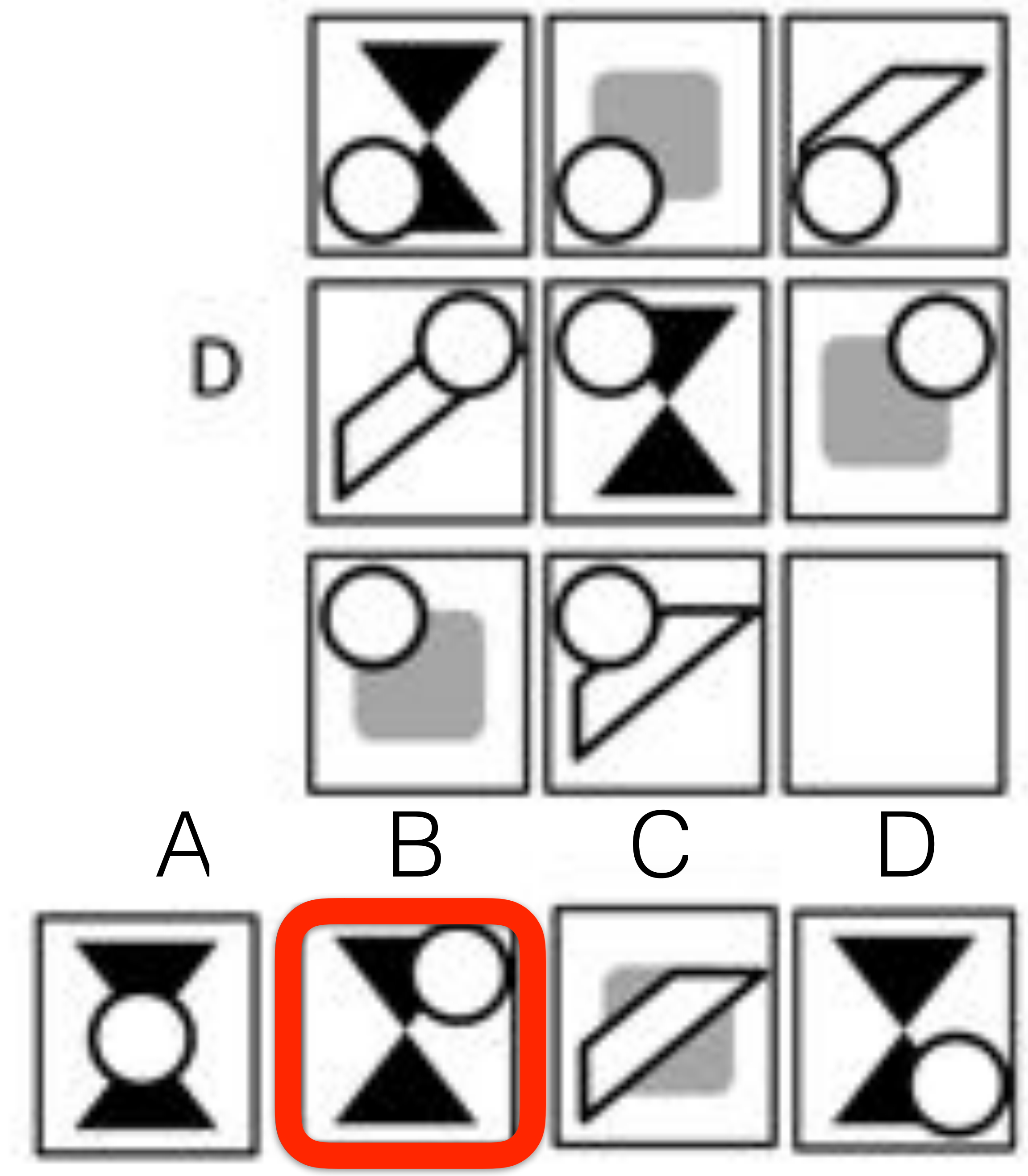
- 4: phenotype (schizophrenia)
- 3a:d: ‘high’ endophenotype
- 2a:2d: ‘low’ endophenotype
- 1a:1n: genotype

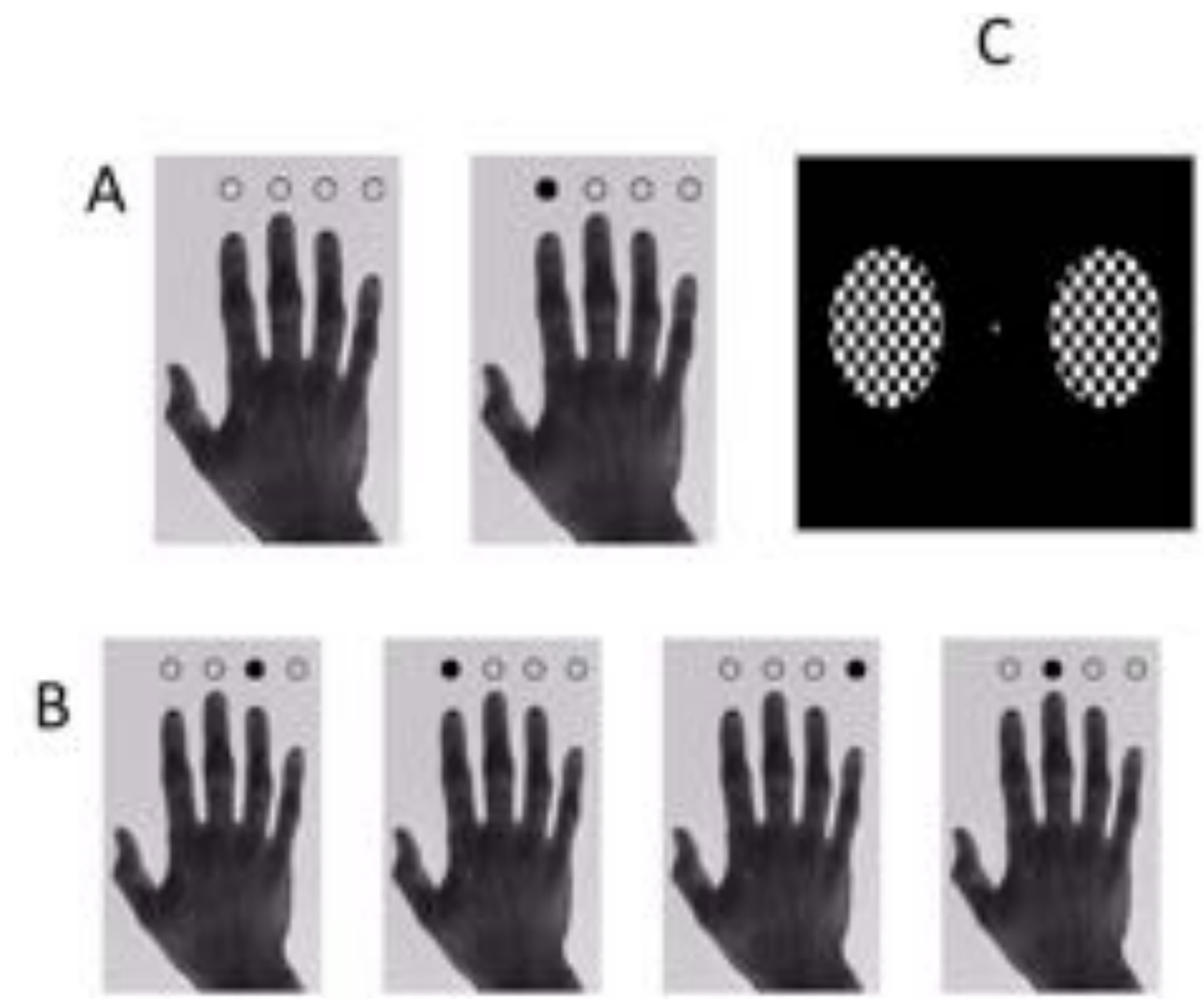
Statistical implications

- ‘Upstream’ measures will have greater statistical dimensionality (partially independent)
- ‘Multiple realizability’ of higher constructs
  - Many-to-one/ Multiple causes at each level
- Hierarchical dependence:
  - (e.g.) fluid intelligence is caused by processing speed
  - .. which is determined by white matter integrity
- Translate predictions into testable SEM

Behavioural measures

- Cam-CAN, N=555
- Cattell Culture Fair test
- Four subtest scores (series completions, odd-one-out, matrices and topology)
- A) Simple RT
- B) Choice RT
- C) Un-cued
- Mean and SD (consistency/variability)

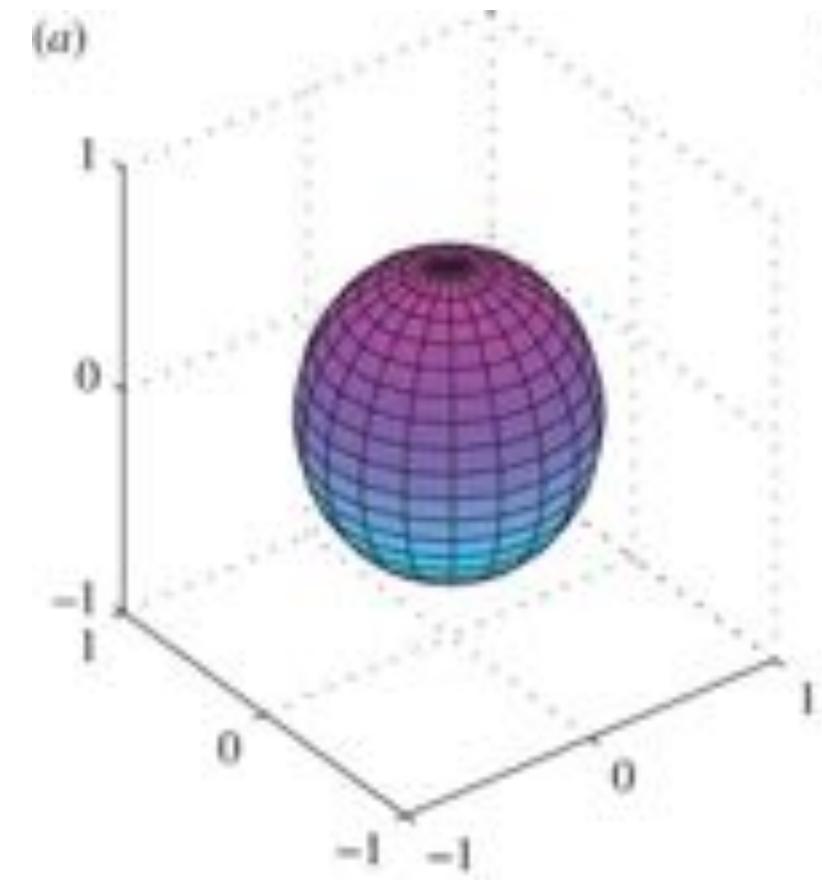




Neural measure

- *Fractional anisotropy*
- (a) measure of white matter integrity
- Reflects directional coherence of water dispersion

- Empirically test of the model



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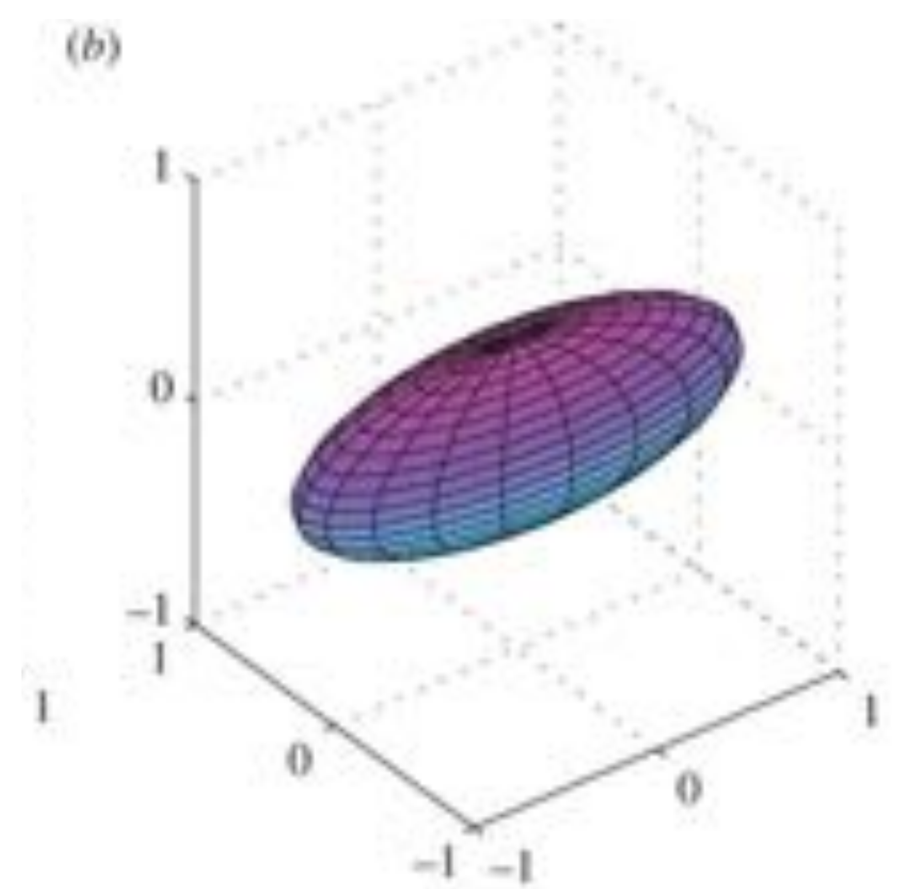

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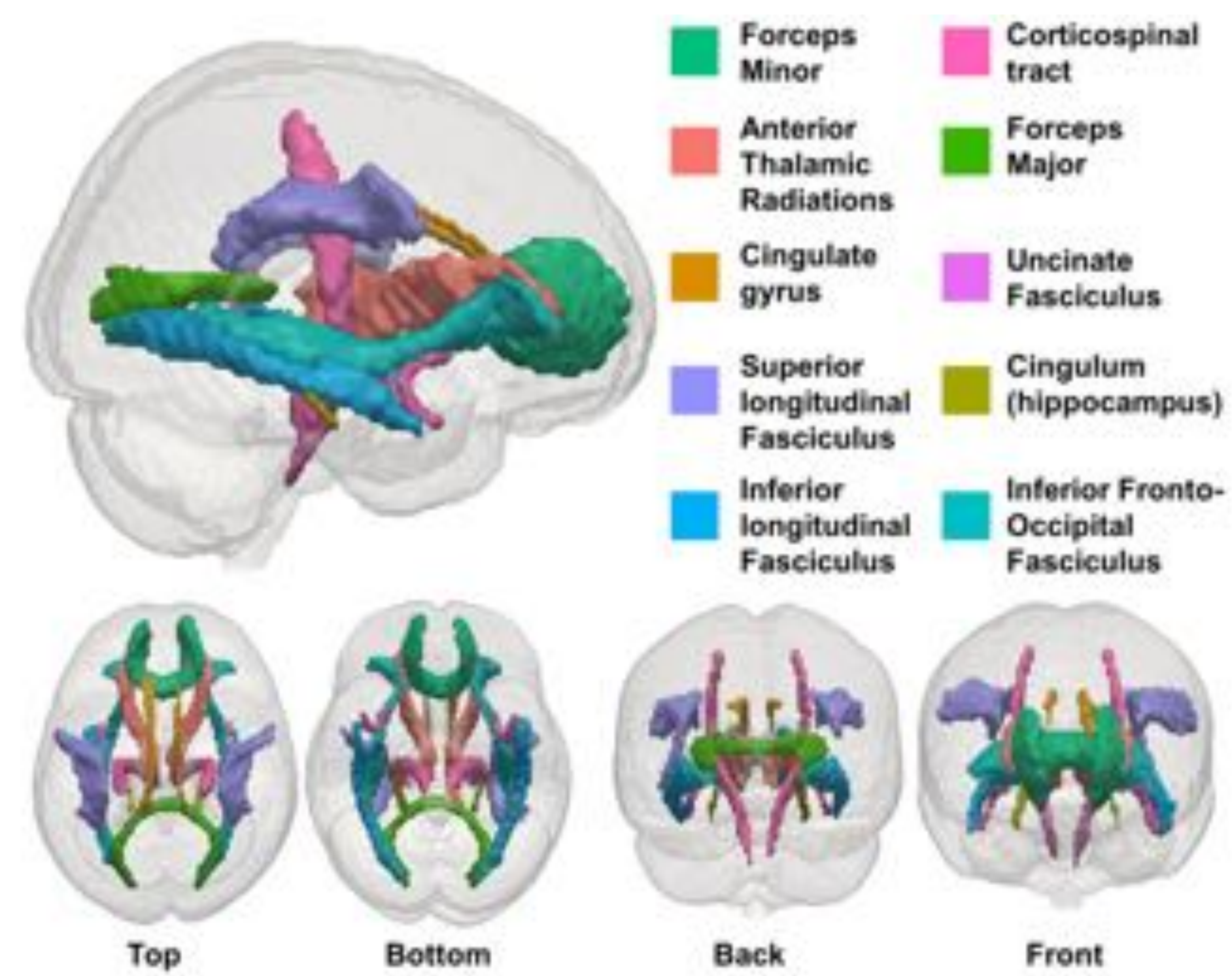
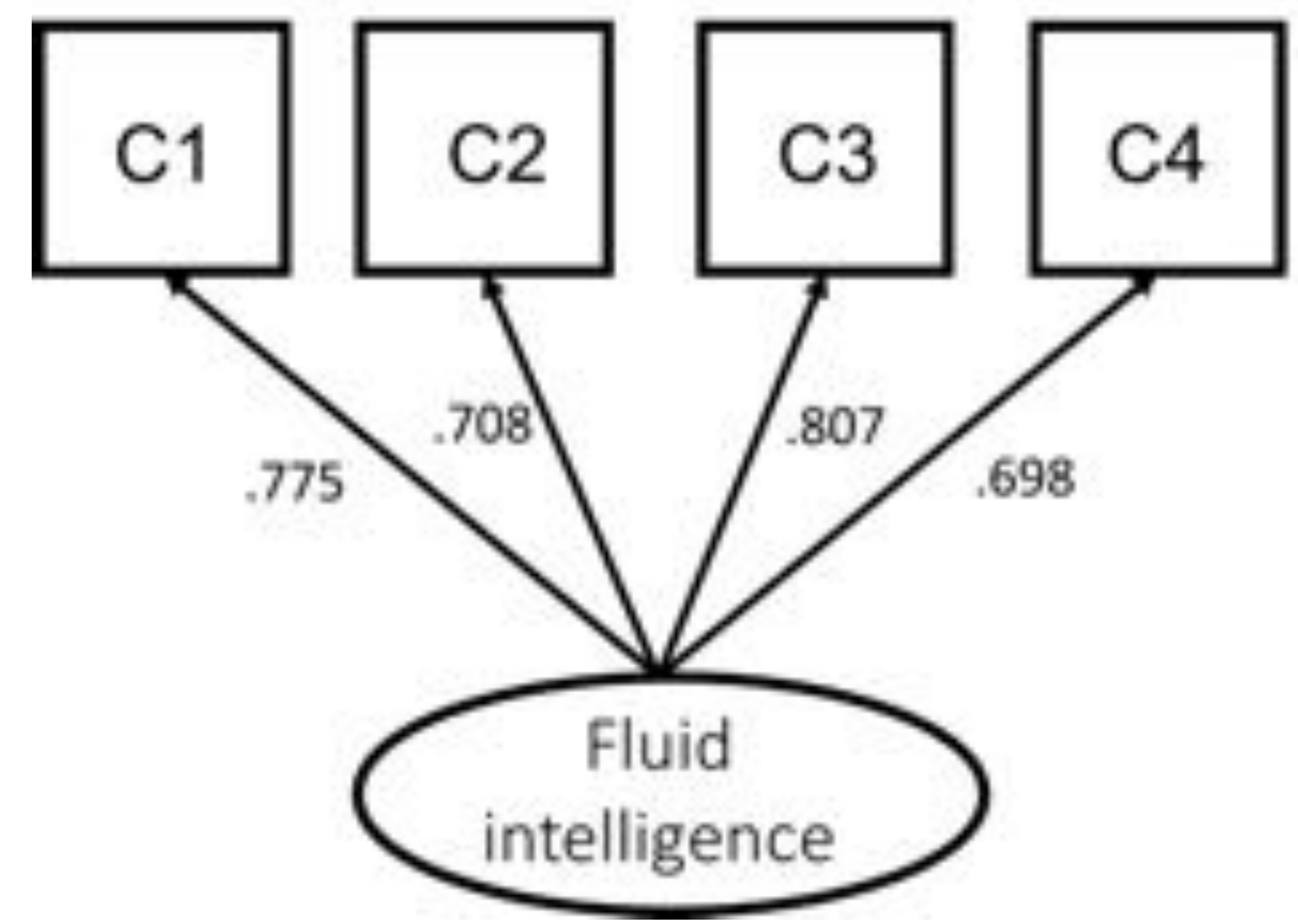


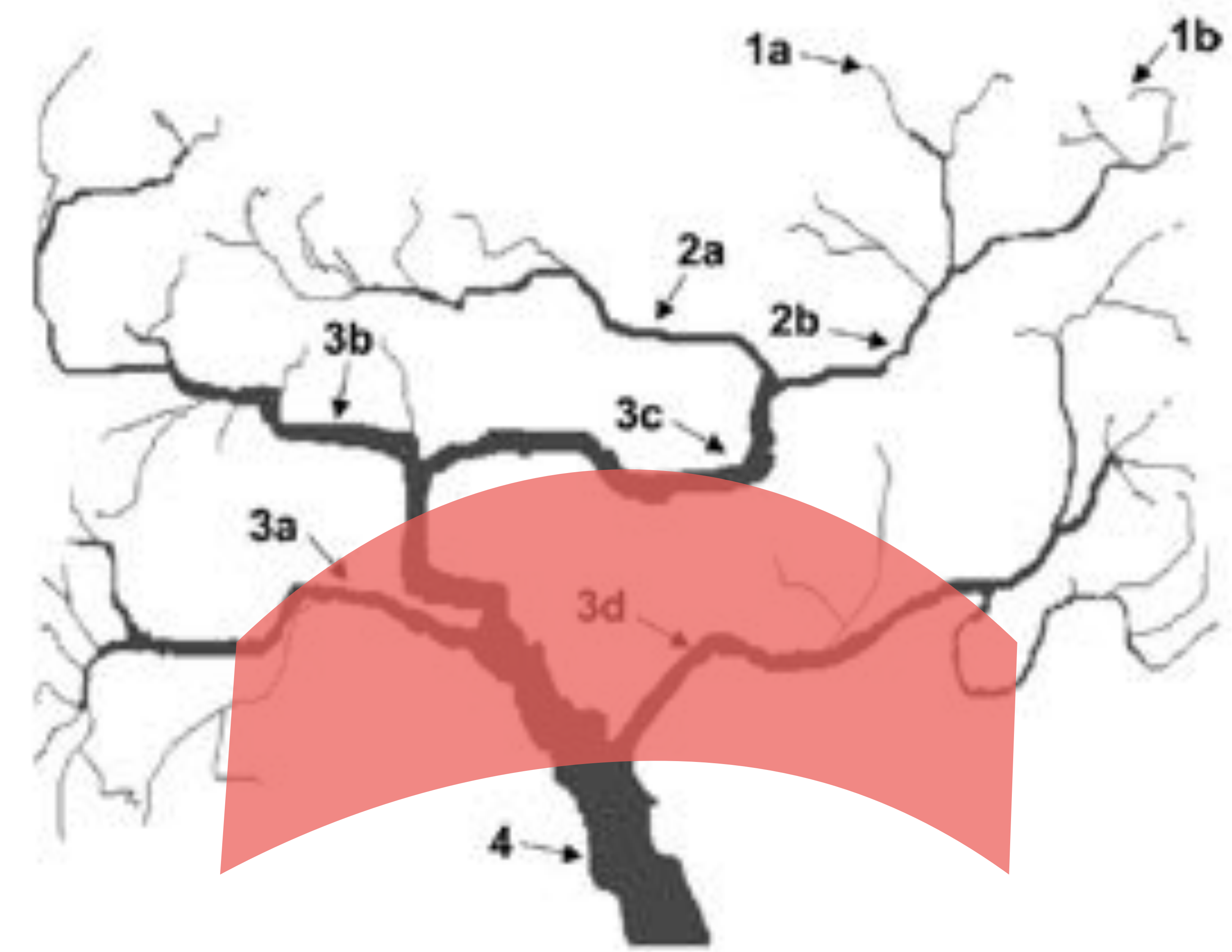
Fluid intelligence

- Fluid intelligence: fits a 1 factor model

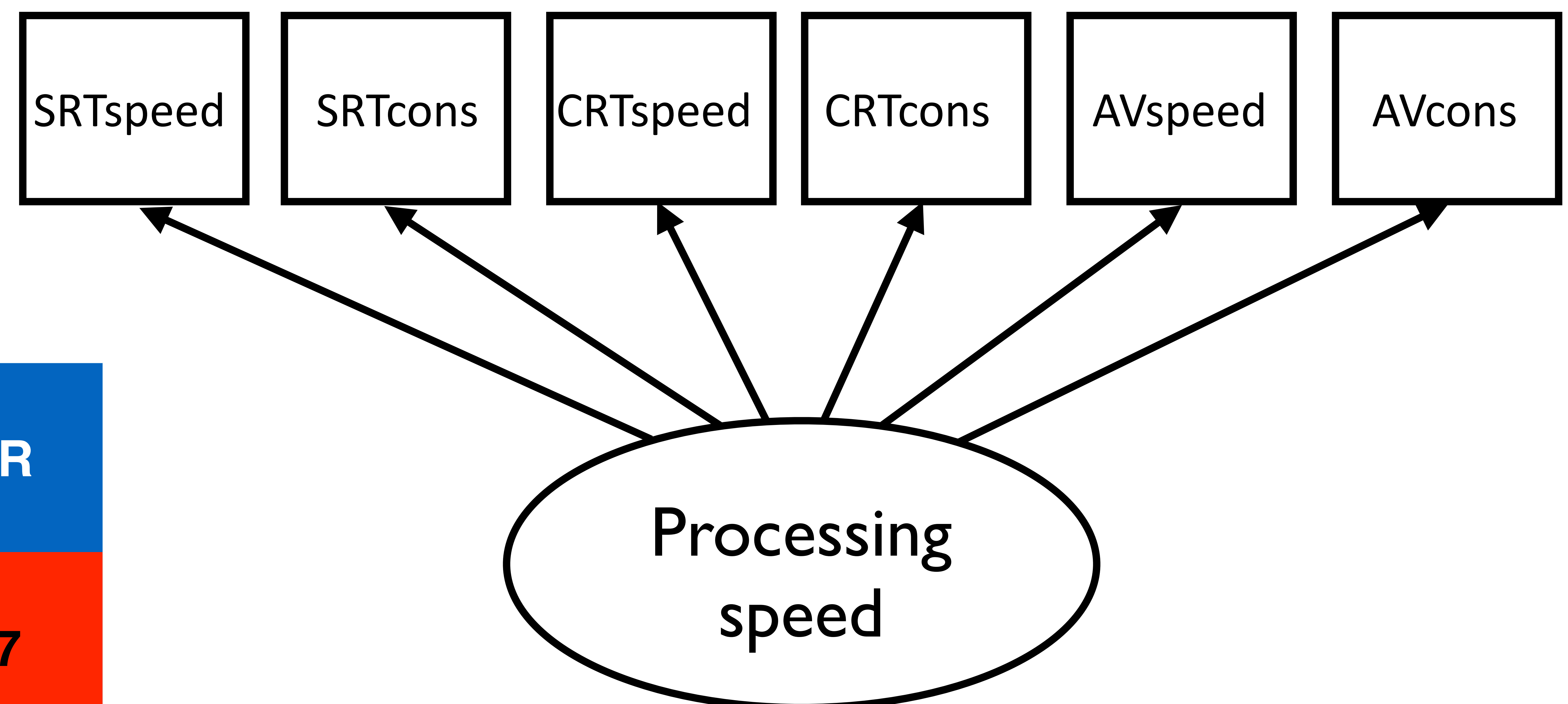
Model fit	RMSEA	CFI	SRMR
Fluid intelligence	**0.047**	**0.996**	**0.011**



Processing speed



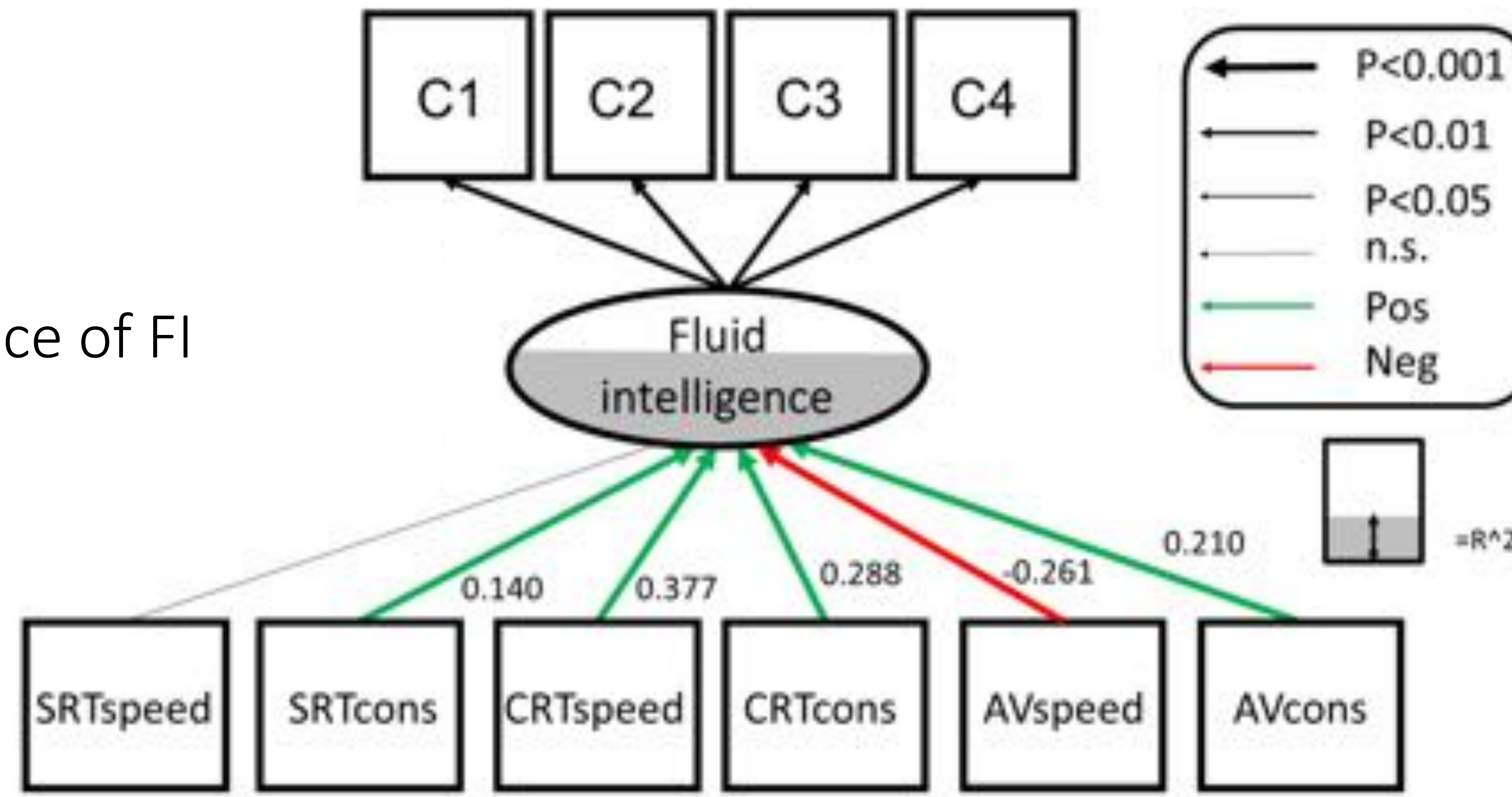
- Dimensionality increase?
- Processing speed: does not fit a single factor model
  - Nor do plausible alternatives



Model fit	RMSEA	CFI	SRMR
Processing speed	**0.348**	**0.57**	**0.157**

FI and PS

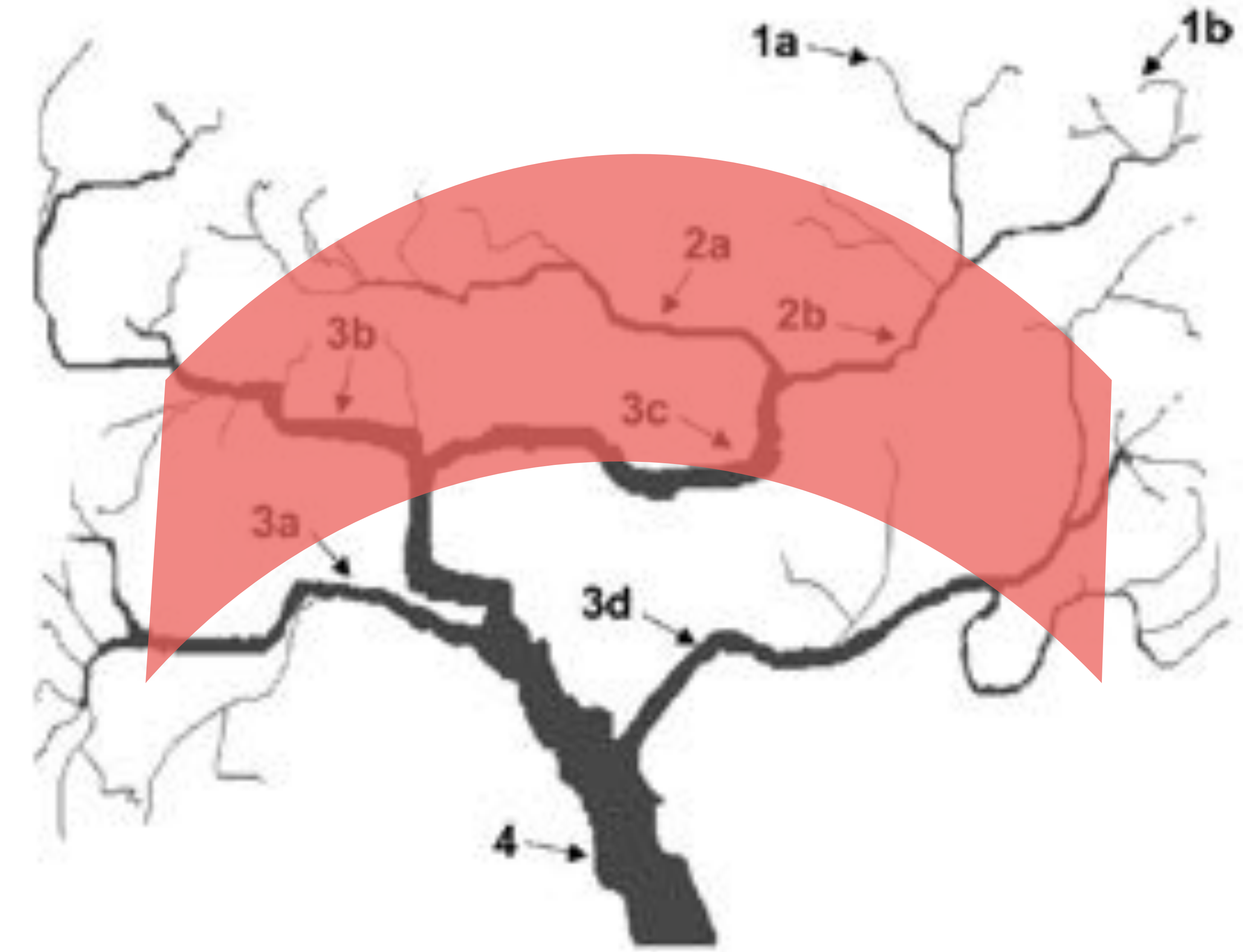
- A MIMIC model (Multiple Indicators, Multiple Causes)
- Processing speed has:
  - Multiple
  - Partially independent
  - Hierarchical
- ..influences on fluid intelligence
- Together explains 58.7% (!) of the variance of FI

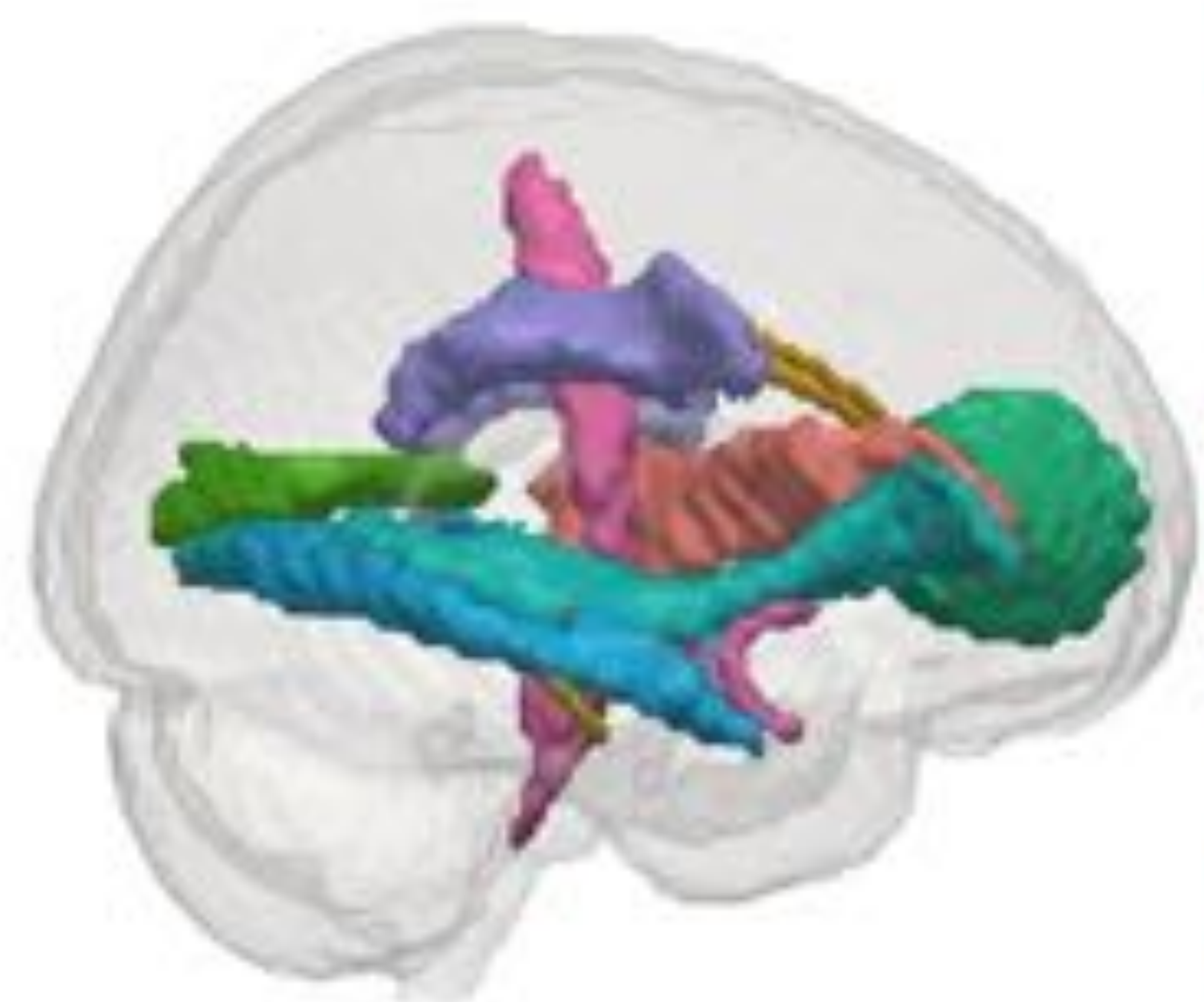


Model fit	RMSEA	CFI	SRMR
Fluid intelligence	0.000	1	0.01

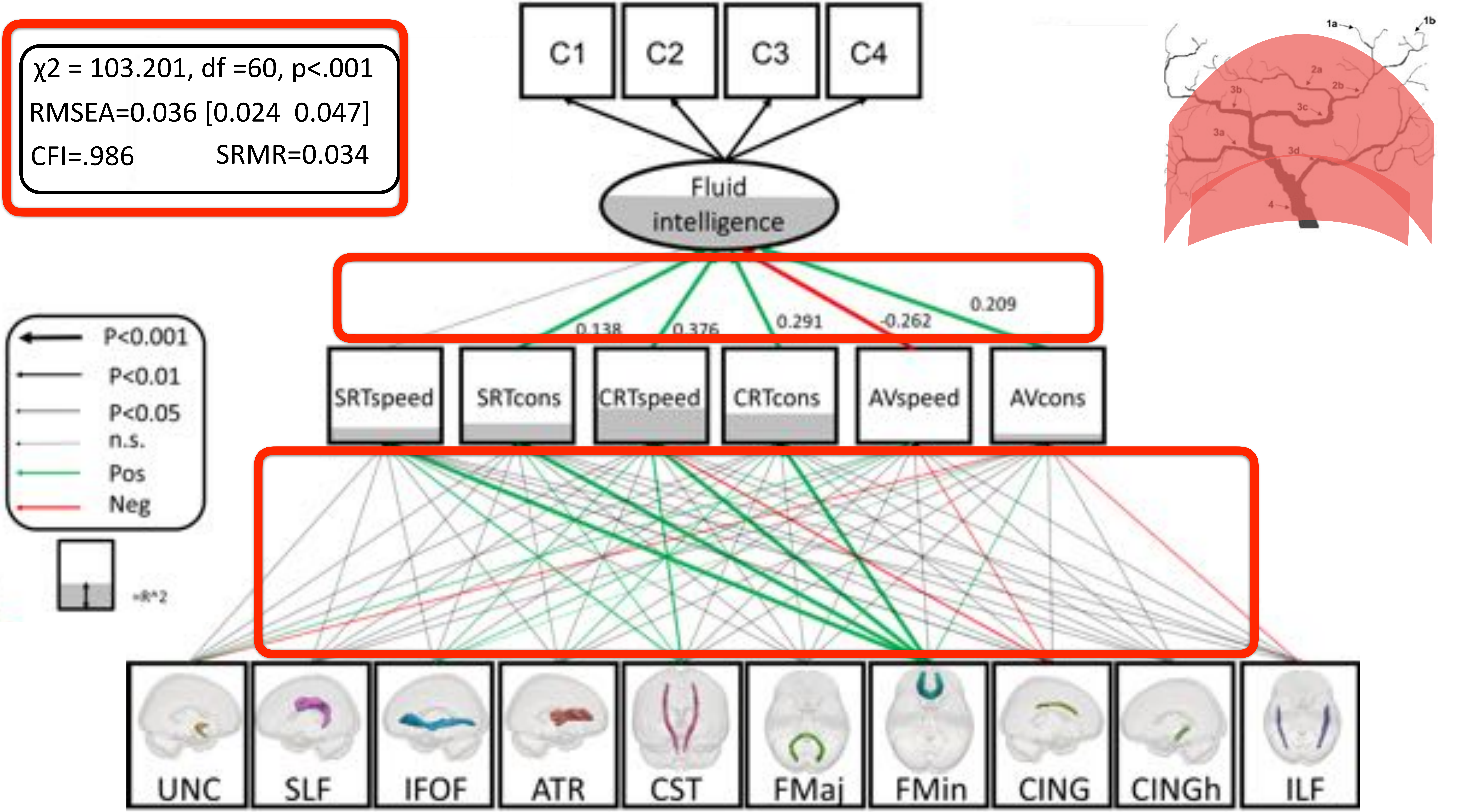
White matter integrity

- White matter single factor model
- Interim summary
  - Fluid intelligence fits a single factor model
  - Processing speed multidimensional
  - Predicts fluid intelligence in a many-to-one fashion
  - White matter multidimensional





Model fit	RMSEA	CFI	SRMR
White matter	0.141	0.82	0.069



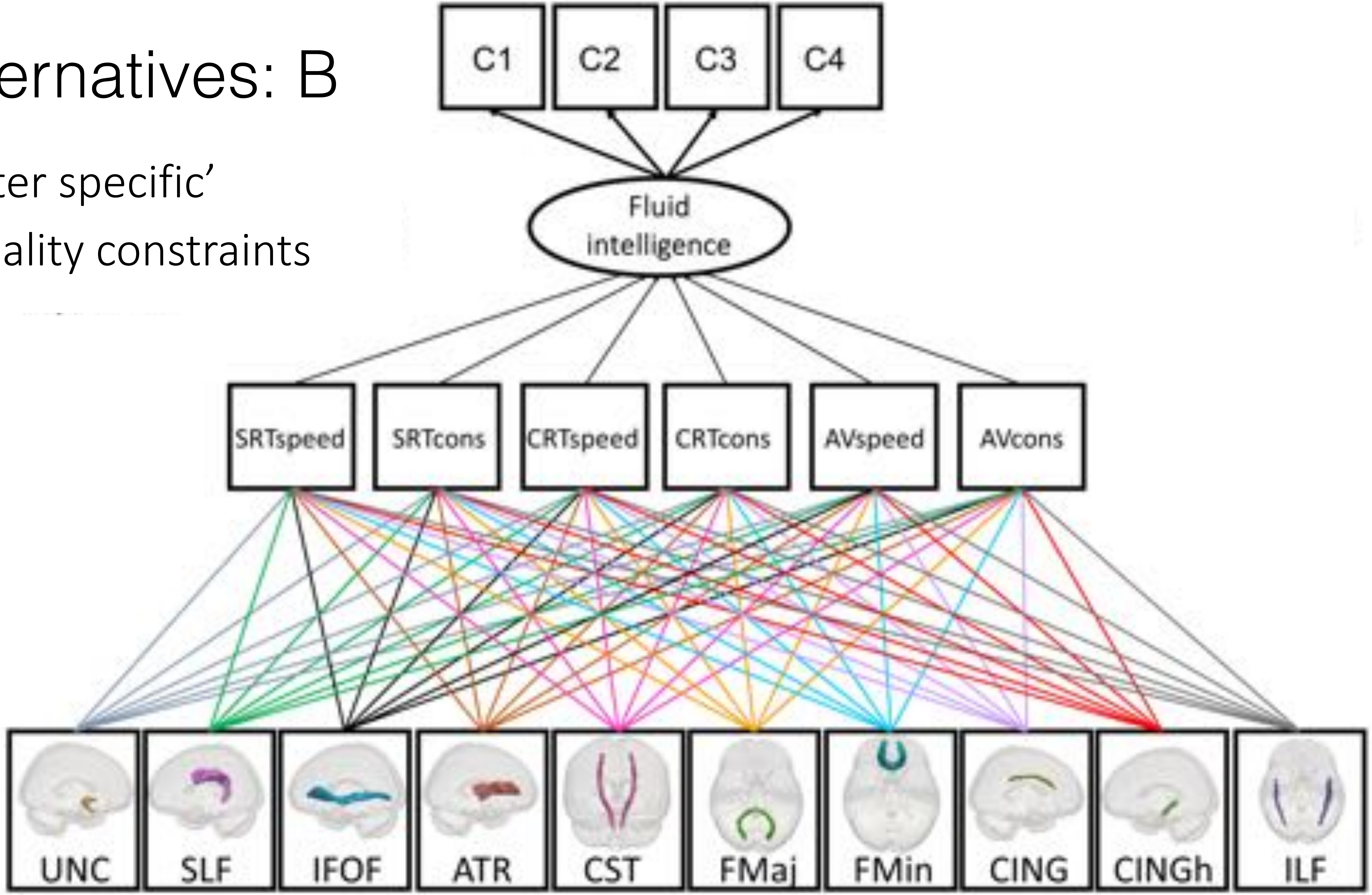
χ2 = 103.201, df =60, p<.001
RMSEA=0.036 [0.024 0.047]
CFI=.986 SRMR=0.034
C1
C2
C3
C4
Fluid intelligence
0.138
0.376
0.291
-0.262
0.209
SRTspeed
SRTcons
CRTspeed
CRTcons
AVspeed
AVcons
P<0.001
P<0.01
P<0.05
n.s.
Pos
Neg
UNC
SLF
IFOF
ATR
CST
FMaj
FMin
CING
CINGh
ILF

Model alternatives: A

- Invert ‘layers’
- Model fits more poorly (AIC_{diff}=225.383)
- Alternative explanation: number of variables (6 vs 10)
- Compare all 210 combinations
- Watershed ‘wins’ 210/210 comparisons

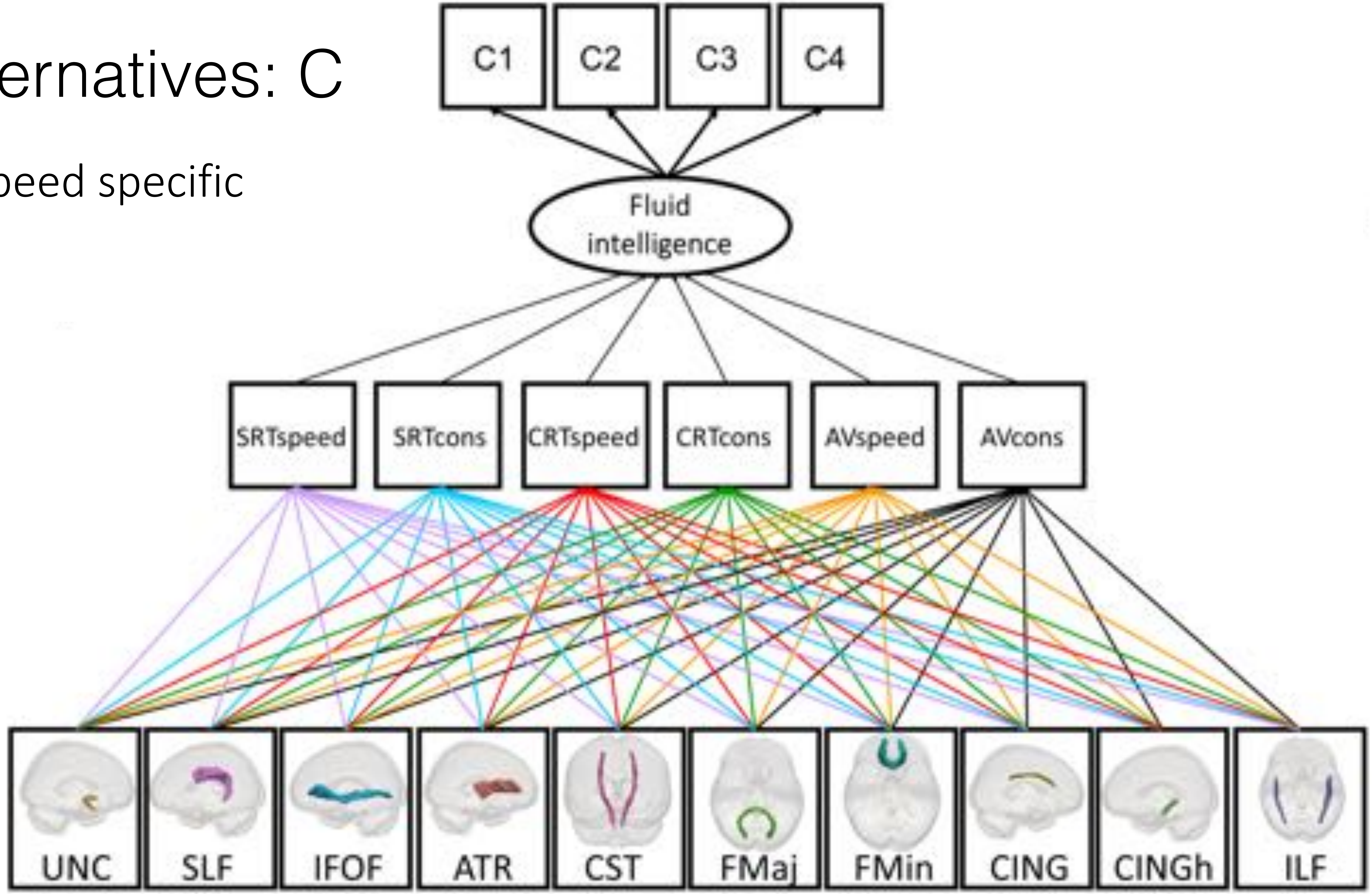
Model alternatives: B

- ‘White matter specific’
- Impose equality constraints



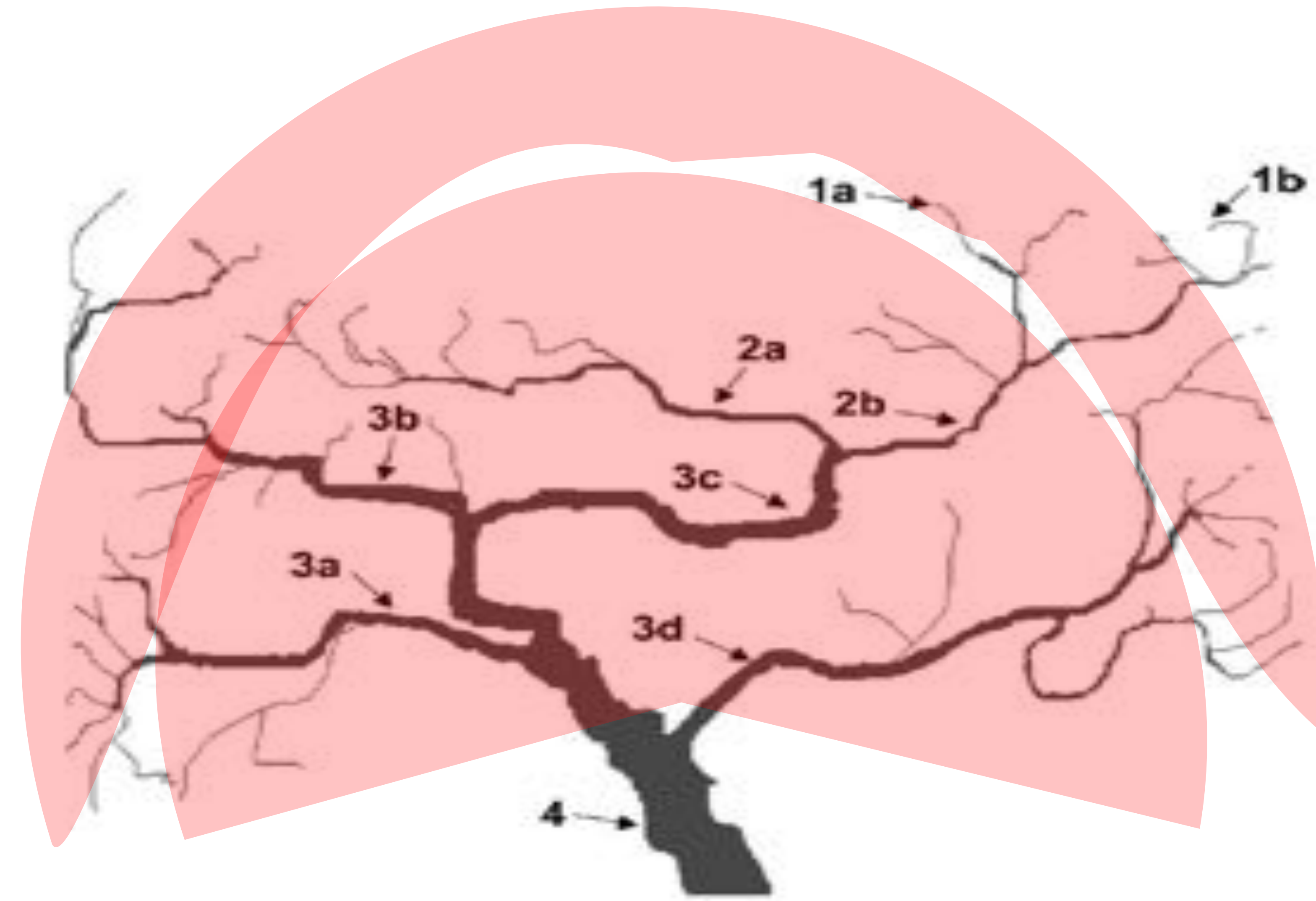
Model alternatives: C

Processing speed specific

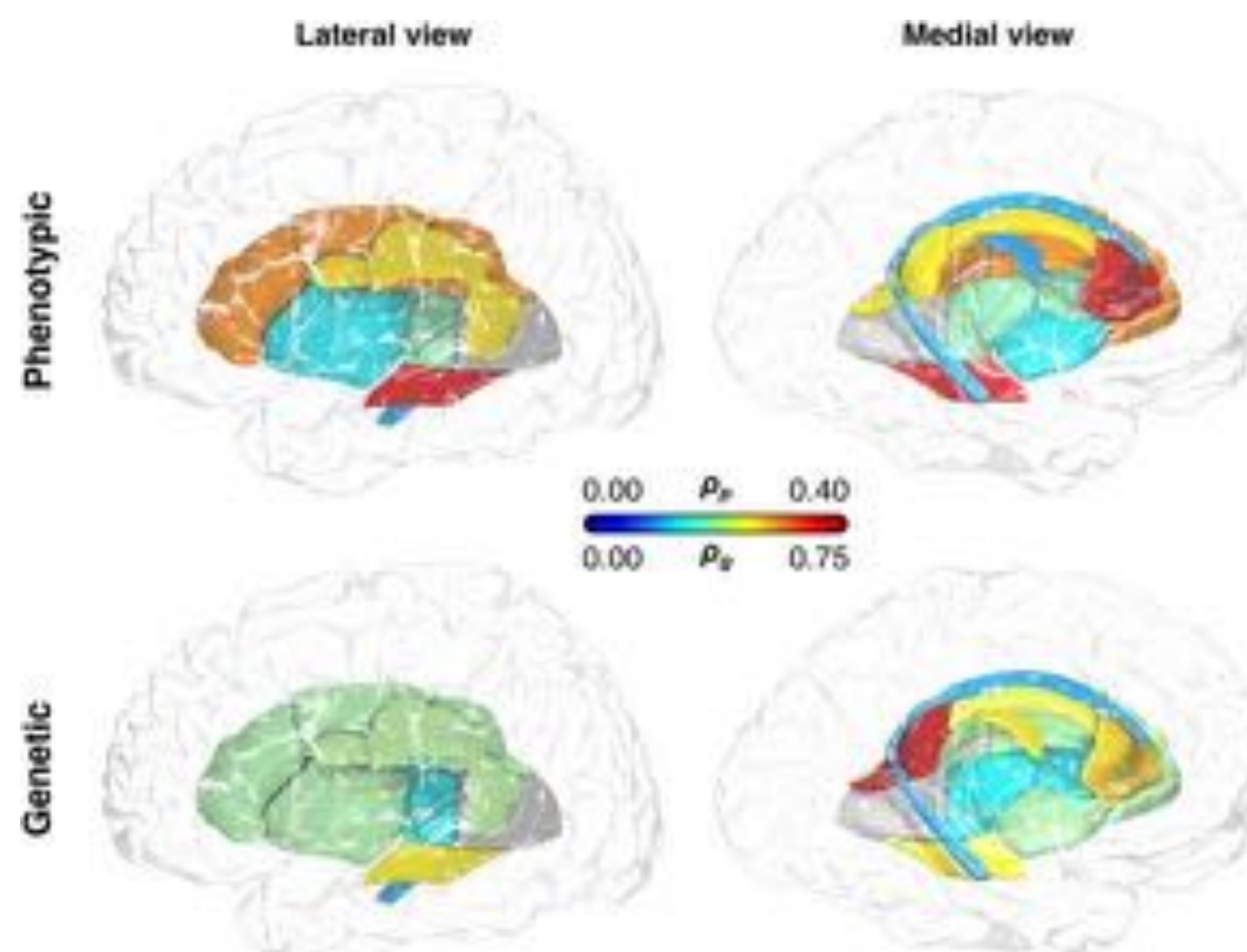


Watershed extended: Genetics

- Watershed predicts shared genetic antecedents for WM and PS



- *'Quantitative genetic analysis demonstrated **a significant degree to which common genes influenced joint variation in FA and brain processing speed.'***



Kochunov, P., Thompson, P. M., Winkler, A., Morrissey, M., Fu, M., Coyle, T. R., ... & Sampath, H. (2016). The common genetic influence over processing speed and white matter microstructure: Evidence from the Old Order Amish and Human Connectome Projects. *NeuroImage*, *125*, 189-197.

Summary

- Data compatible with watershed model
  - RT and WMI not unidimensional
  - Many-to-one mapping of PS and FI & WM and PS
  - Inverted model fits significantly worse
  - Preliminary evidence for genetic predictions
- Plausible account of inter-individual differences
- Possible explanation of coupled age-related declines (but see Bender et al., 2016)

Interim summary

- Psychometric techniques powerful tools to test theoretical frameworks for neurocognitive theories
- So far: cross-sectional
- Inherent limitations

Only Time Will Tell: Cross-Sectional Studies Offer No Solution to the Age–Brain–Cognition Triangle: Comment on Salthouse (2011)

Naftali Raz
Wayne State University

Ulman Lindenberger
Max Planck Institute for Human Development

- Longitudinal SEM
  - Latent change score models
  - Latent growth models

'As a cross-sectional study on a sample with a broad age range, this study is irrelevant to the questions of cognitive aging'

How and why do higher cognitive abilities develop (rapidly) during adolescence?

- Positive manifold: most robust finding in all of psychology
- Famously: g factor

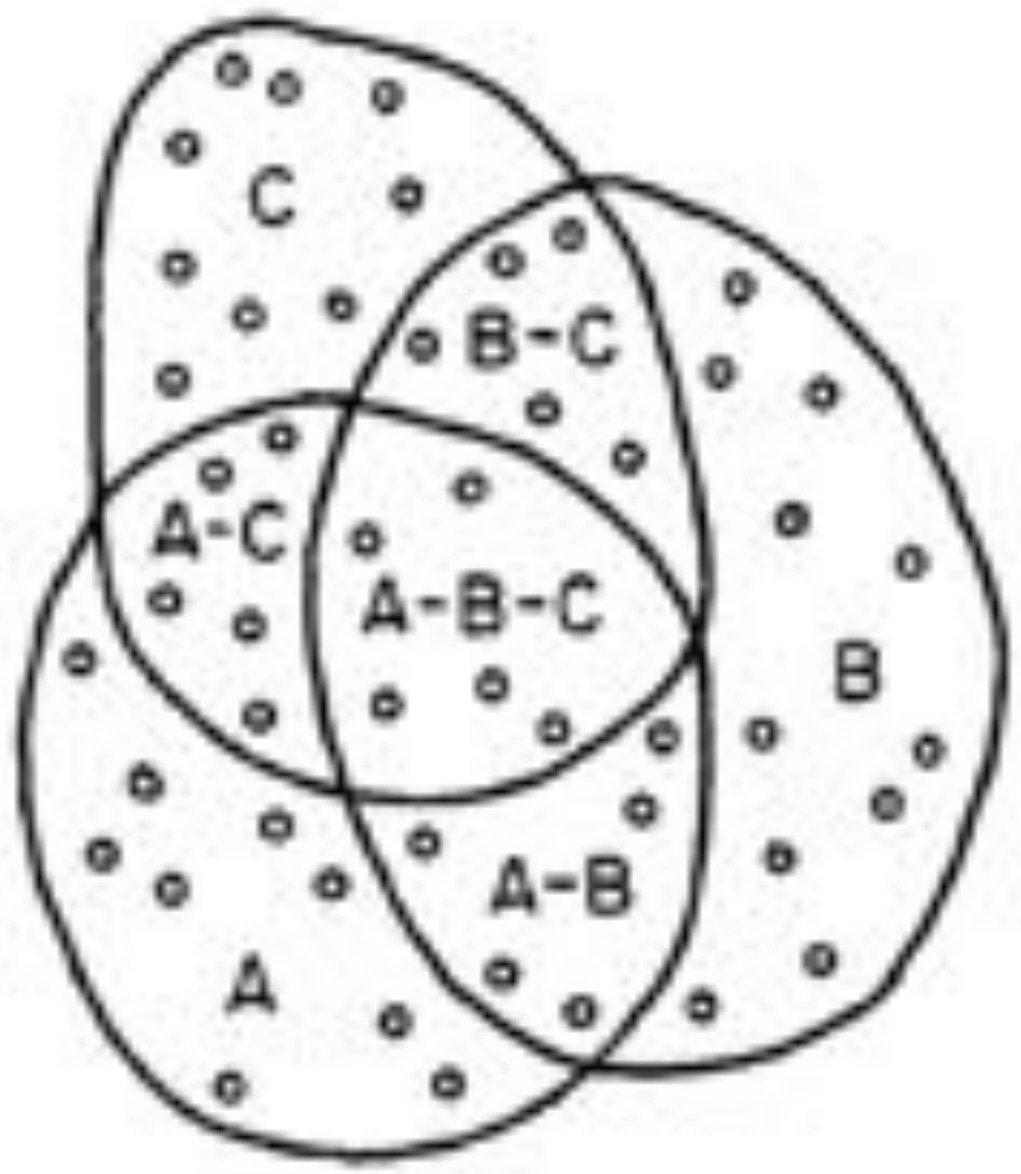
Table 1.4: Pearsonian intercorrelation matrix, combined kindergarten to adult sample (decimals omitted). 29 variables from the Woodcock-Johnson psycho-educational battery — revised, $N = 1425$ (correlations corrected for age).

Variable:		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
Memory for Names	1	1000																												
Memory for Sentences	2	279	1000																											
Visual Matching	3	213	254	1000																										
Incomplete Words	4	167	255	191	1000																									
Visual Closure	5	148	103	178	176	1000																								
Picture Vocabulary	6	404	403	302	267	229	1000																							
Analysis-Synthesis	7	275	324	280	205	161	323	1000																						
Visual-Auditory Learning	8	342	343	287	192	205	382	376	1000																					
Memory for Words	9	208	559	221	245	046	225	215	246	1000																				
Cross Out	10	170	241	621	168	241	242	291	265	203	1000																			
Sound Blending	11	245	323	245	367	133	323	265	332	335	246	1000																		
Picture Recognition	12	293	216	212	123	234	256	233	299	135	257	212	1000																	
Oral Vocabulary	13	388	534	310	319	234	632	419	405	364	315	389	304	1000																
Concept Formation	14	306	382	306	236	206	325	484	376	227	305	275	269	458	1000															
Memory for Names (Delayed Recall)	15	721	236	155	168	129	383	269	460	173	123	242	234	359	284	1000														
Visual-Auditory Learning (Delayed Recall)	16	345	364	362	120	192	255	269	480	110	168	192	273	271	323	446	1000													
Numbers Reversed	17	259	416	384	227	129	255	368	321	401	309	316	206	396	354	225	182	1000												
Sound Patterns	18	233	257	204	221	109	269	271	259	243	229	294	168	331	299	222	214	282	1000											
Spatial Relations	19	280	266	278	158	265	317	389	369	189	343	225	288	388	404	240	289	311	294	1000										
Listening Comprehension	20	331	409	266	334	204	576	349	344	279	263	351	256	642	375	294	221	308	274	320	1000									
Verbal Analogies	21	379	454	334	228	242	522	455	445	310	344	355	321	639	496	377	330	403	304	465	526	1000								
Calculation	22	256	351	435	142	132	299	423	347	252	358	293	208	471	401	249	242	413	257	376	374	483	1000							
Applied Problems	23	337	416	419	206	175	439	470	388	312	388	360	271	603	489	313	268	438	315	486	524	631	655	1000						
Science	24	380	437	260	285	233	633	368	364	246	280	323	244	658	389	362	270	336	260	385	619	544	440	570	1000					
Social Studies	25	371	477	298	262	200	626	386	374	270	278	323	255	693	411	348	245	332	256	344	638	595	508	617	702	1000				
Humanities	26	390	447	308	281	252	622	343	414	297	284	355	281	663	359	368	283	326	262	340	372	598	427	536	633	672	1000			
Word Attack	27	281	370	356	263	119	316	303	366	322	255	484	202	468	329	269	228	398	316	312	326	415	422	450	346	354	398	1000		
Quantitative Concepts	28	342	427	408	305	162	497	437	436	309	361	320	244	613	413	337	280	433	299	440	513	624	656	728	602	637	576	471	1000	
Writing Fluency	29	225	350	494	195	123	260	309	347	266	410	358	196	398	335	197	194	365	229	276	285	394	420	426	293	336	409	488	434	1000

Kievit, R. A., Lindenberger, U. Goodyer, I.M., Jones, P. B., Fonagy, P., Bullmore, E. T., the NSPN Consortium & Dolan, R. J. (Submitted). Mutualistic coupling between vocabulary and reasoning supports cognitive development during late adolescence and early adulthood

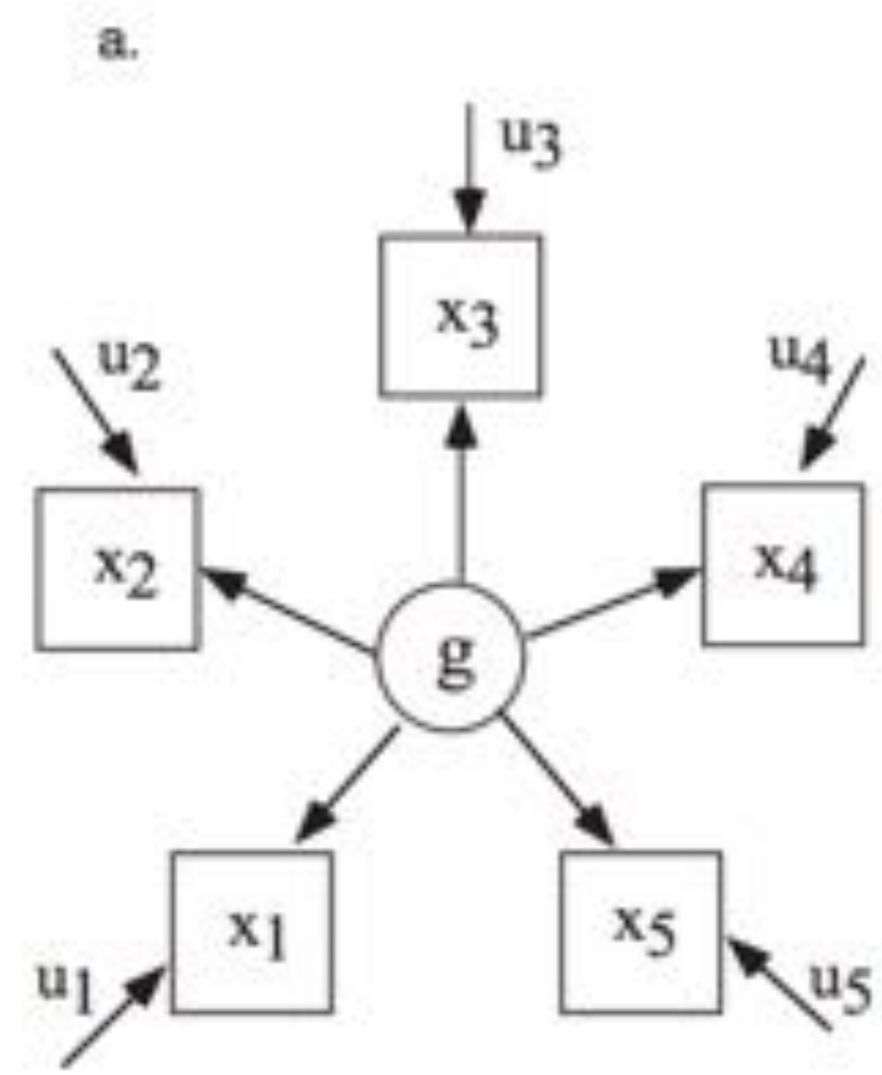
Identical (cross-sectional) covariance matrix

Thomson's *Bonds model*



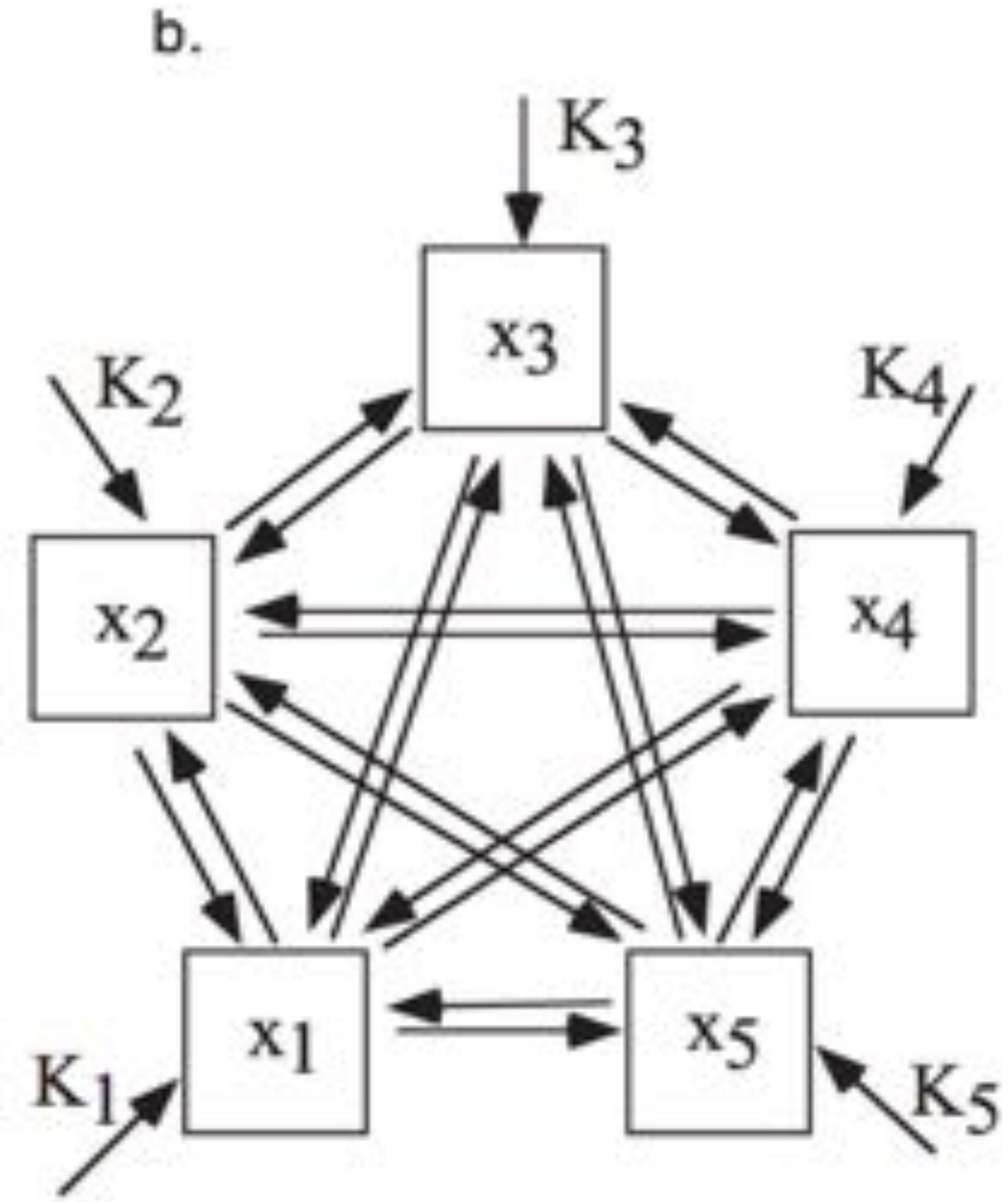
Thomson, G. (1916). A Hierarchy without a General Factor. British Journal of Psychology, 8, 271-281.

g factor



Spearman, C. (1927). The abilities of man. Oxford: Macmillan Publishers Limited.

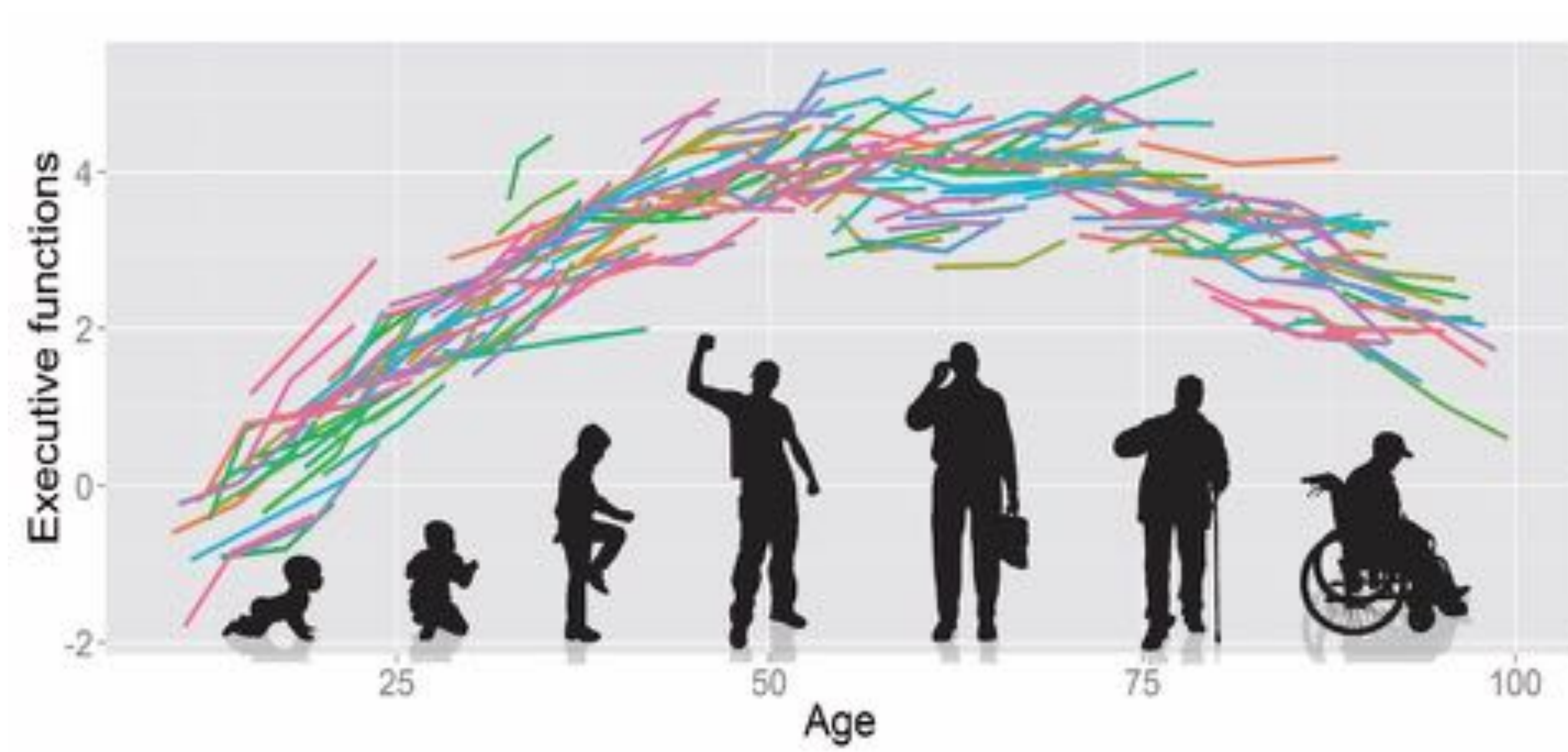
van der Maas, Mutualism



Van Der Maas, H. L., Dolan, C. V., Grasman, R. P., Wicherts, J. M., Huizenga, H. M., & Raijmakers, M. E. (2006). A dynamical model of general intelligence: the positive manifold of intelligence by mutualism. Psychological review, 113(4), 842.

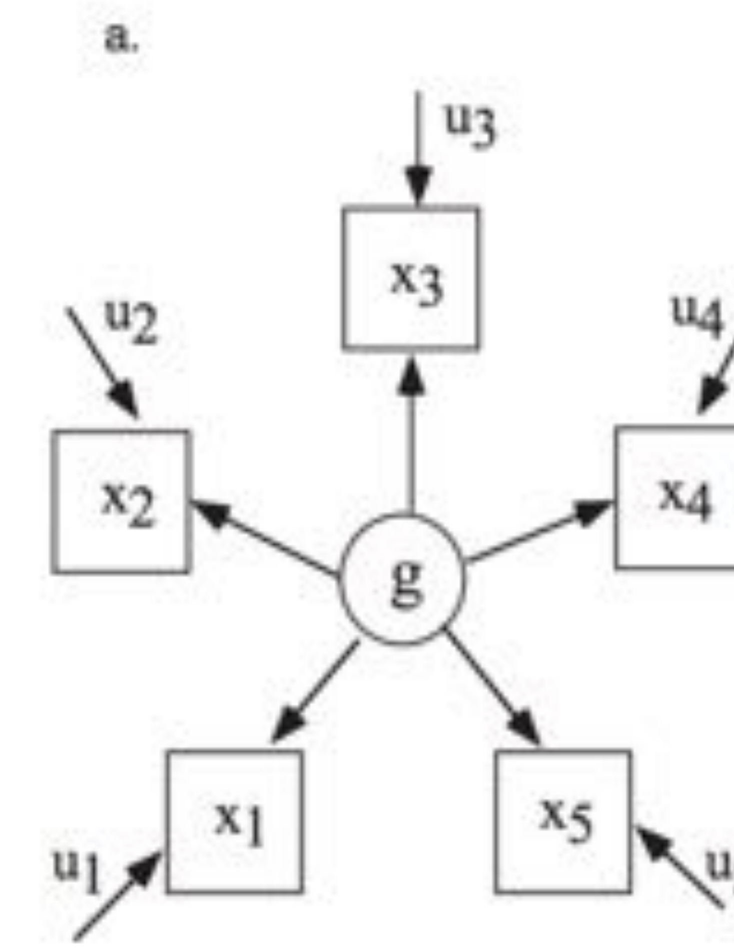
How to tease them apart?

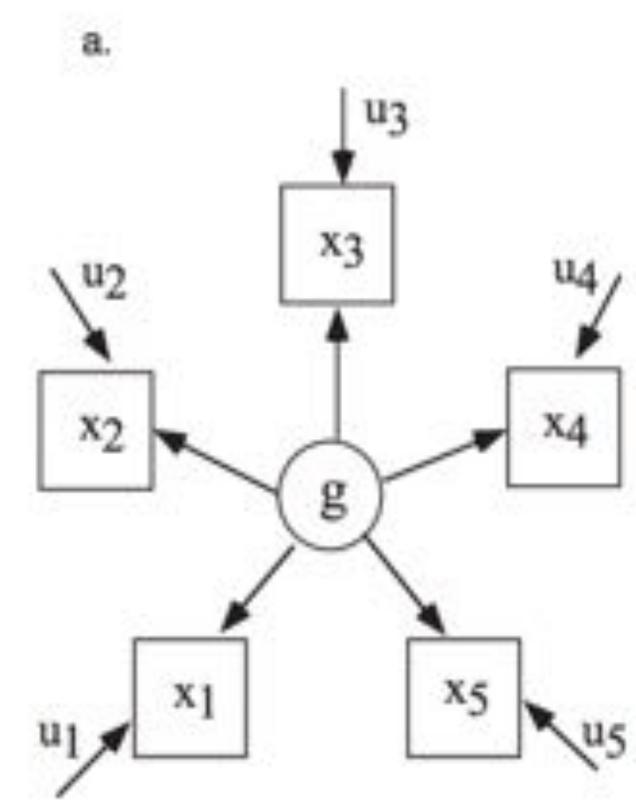
- Focus on development
- Two goals:
  - Better understand cross-sectional patterns
  - Improve possibility of appropriate interventions
- Directly compare three competing models



1) g factor model (Spearman, 1927)

- Posits a single underlying ability (either directly or at the top of a hierarchy)
- Developmental predictions unclear
- Not directly discussed in e.g. Jensen (1998), despite 800 pages
- ’g factor theory’: only g changes, affects/explains all other change

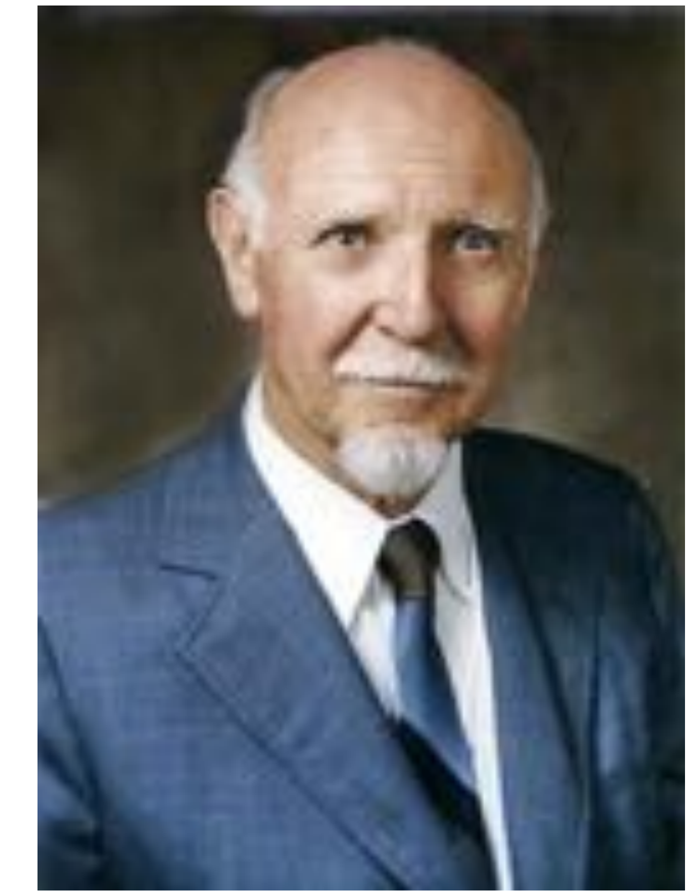


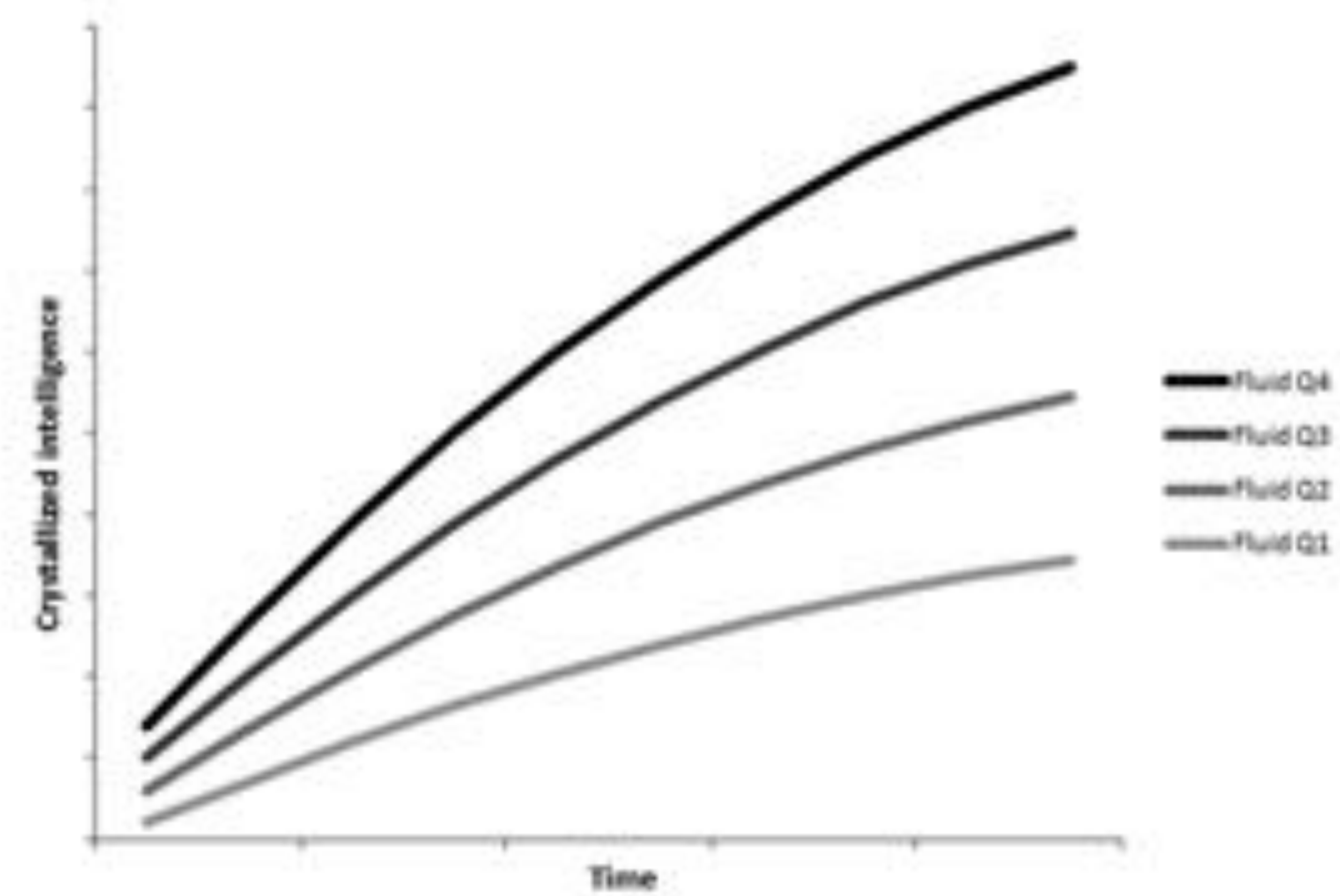


2) Investment theory

- Two kinds of abilities:
- Fluid:
  - Abstract, on the spot reasoning
- Crystallized:
  - Sum of knowledge across domains
  - Increases throughout life
- Investment theory:
  - You invest (use) fluid abilities to gain knowledge

“this year’s crystallized ability . . . is a cumulative function of several years’ operation levels of gf”

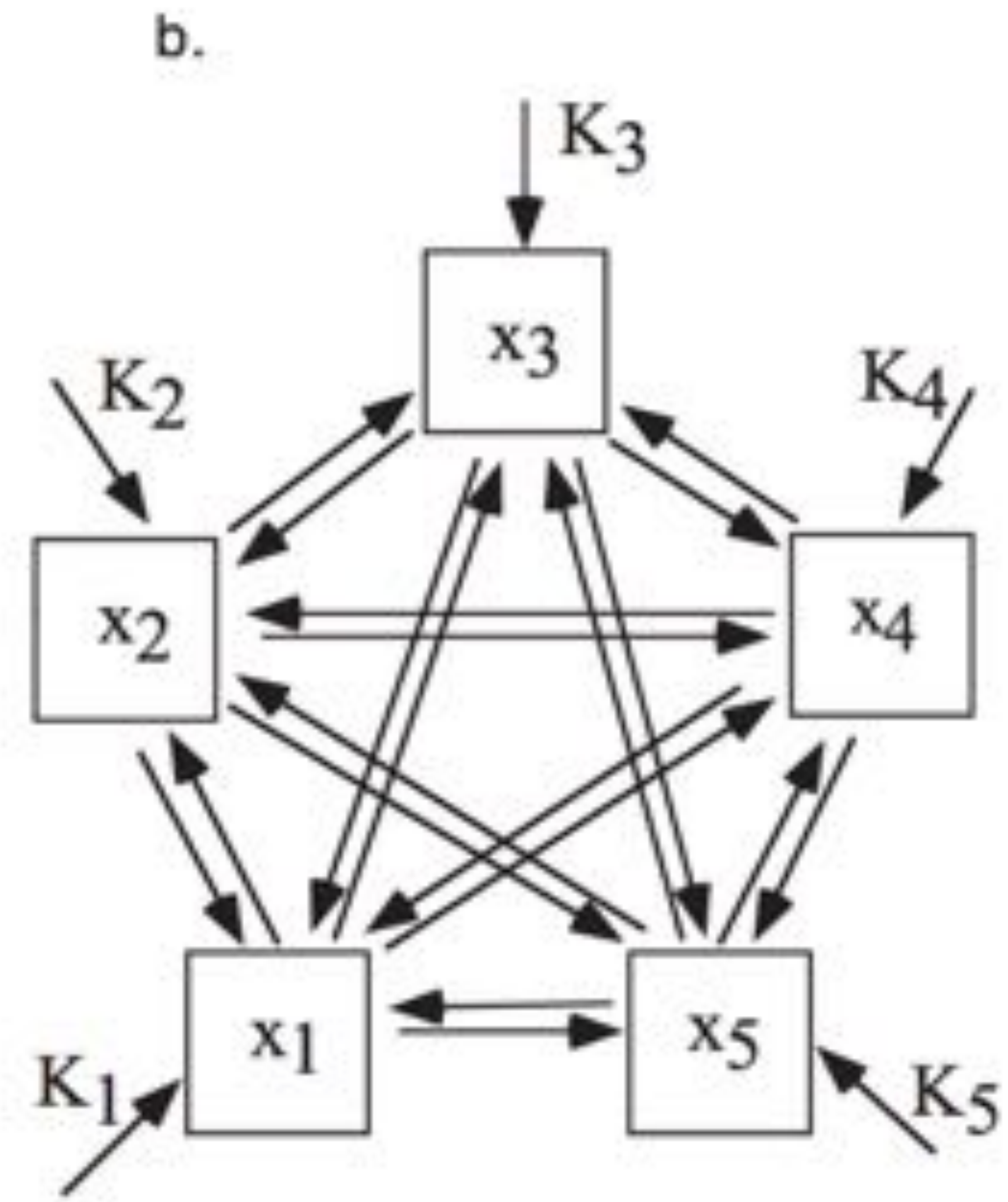


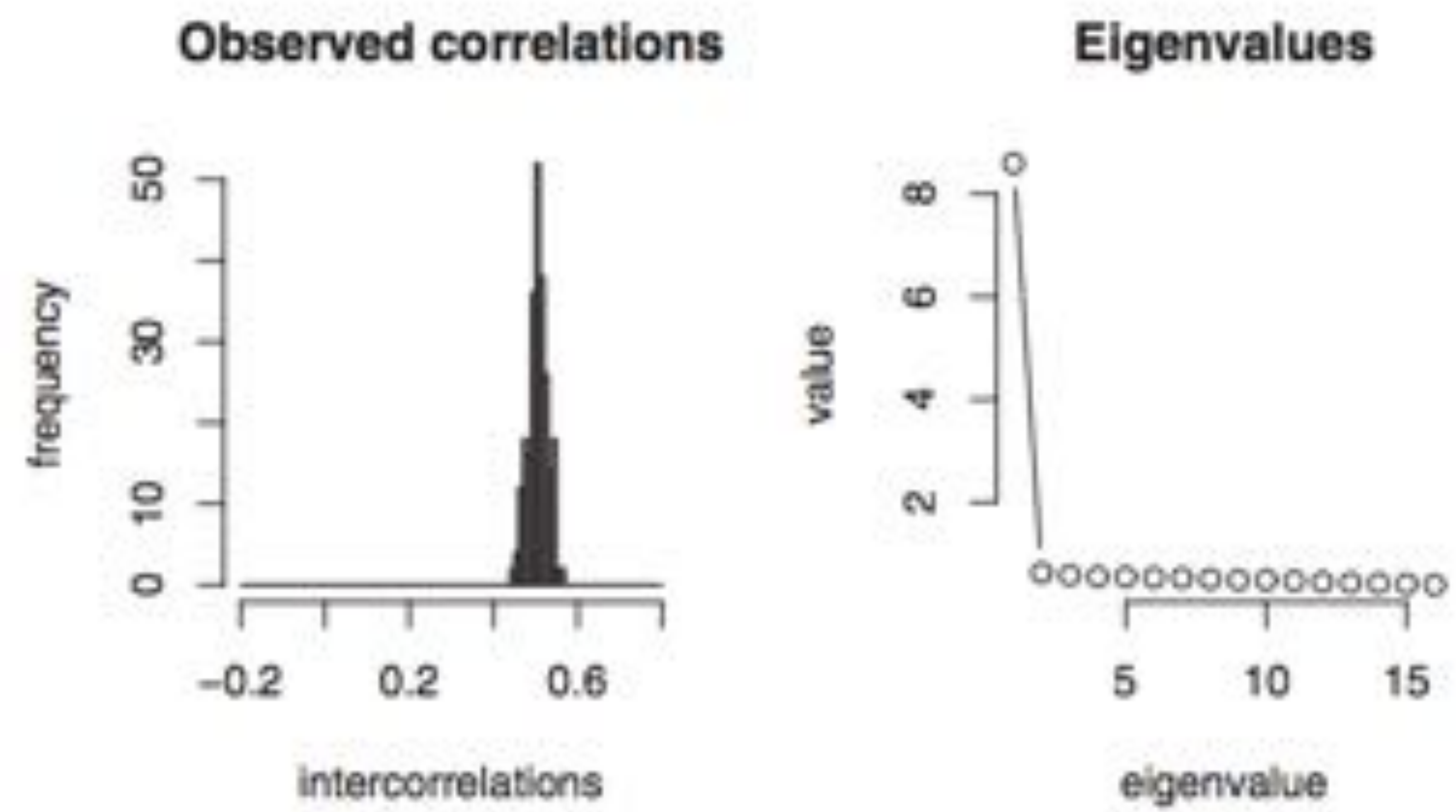


Cattell, R. B. (1987). Intelligence: Its structure, growth and action.

3) Mutualism model

- Positively interacting (partly) independent abilities during development
- Simulations yield identical positive manifold
- Summary measure may obscure dynamic systems

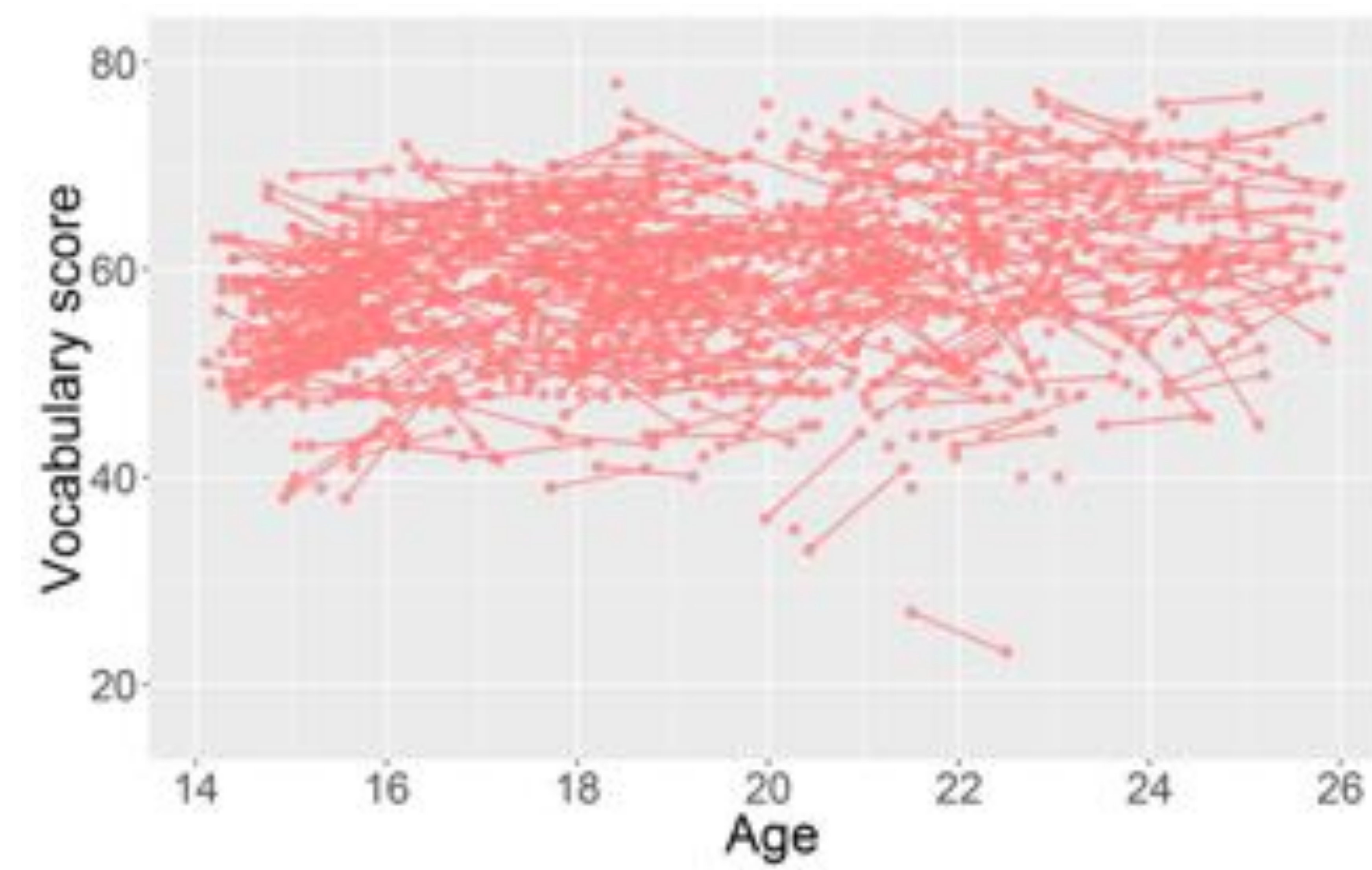


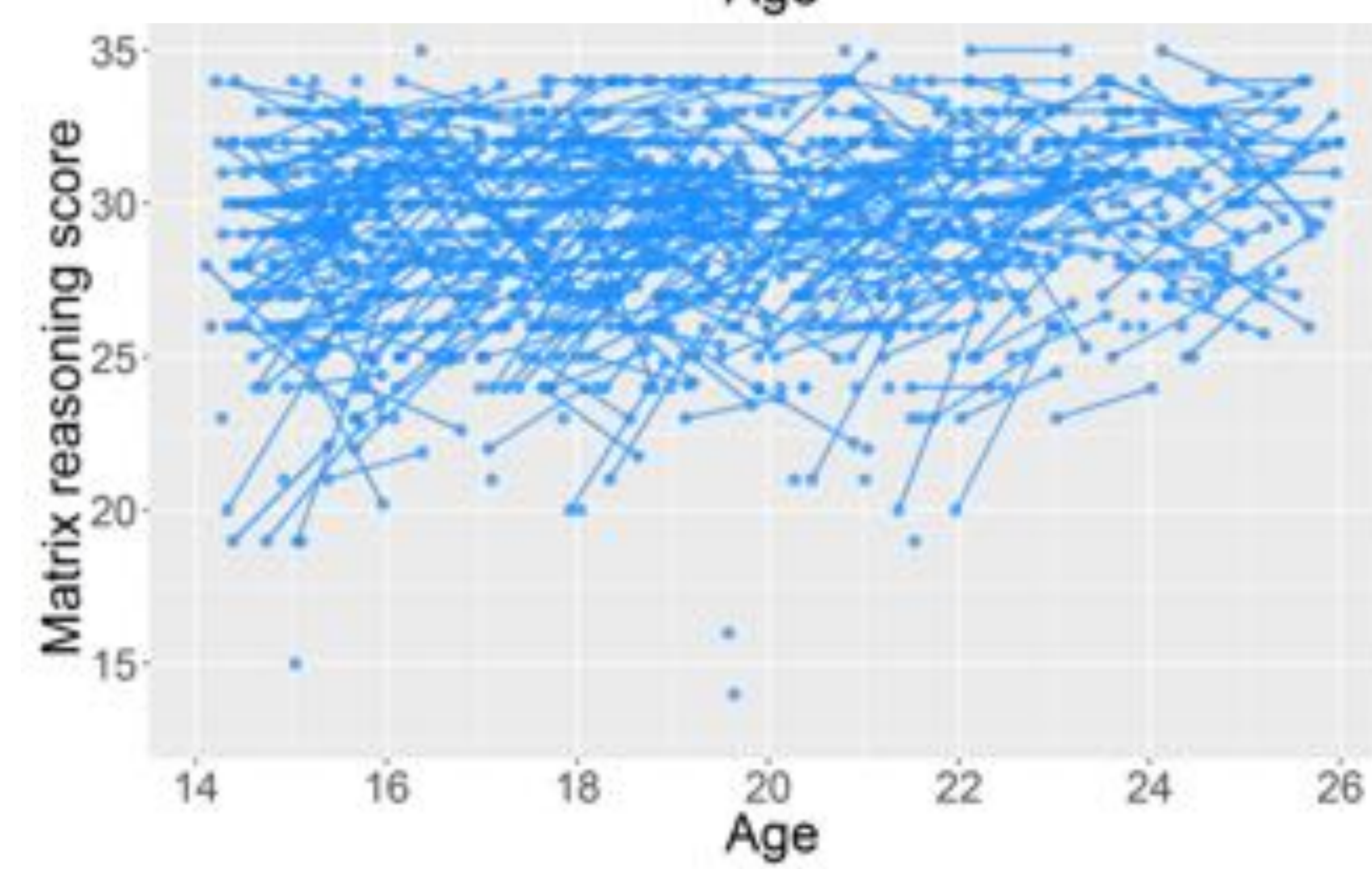


Data

- NSPN cohort
- N= 772 young adults (age 14.1-24.9, 393 female)
- N= 484 wave 2, mean interval 1.56 y
- WASI
- 1. Vocabulary (crystallised)
  - 'Name pictures displayed in a stimulus book'
  - 'Give definition of words'
- 2. Matrix reasoning (fluid)
- Good psychometric properties
  - E.g. reliability .87/.91

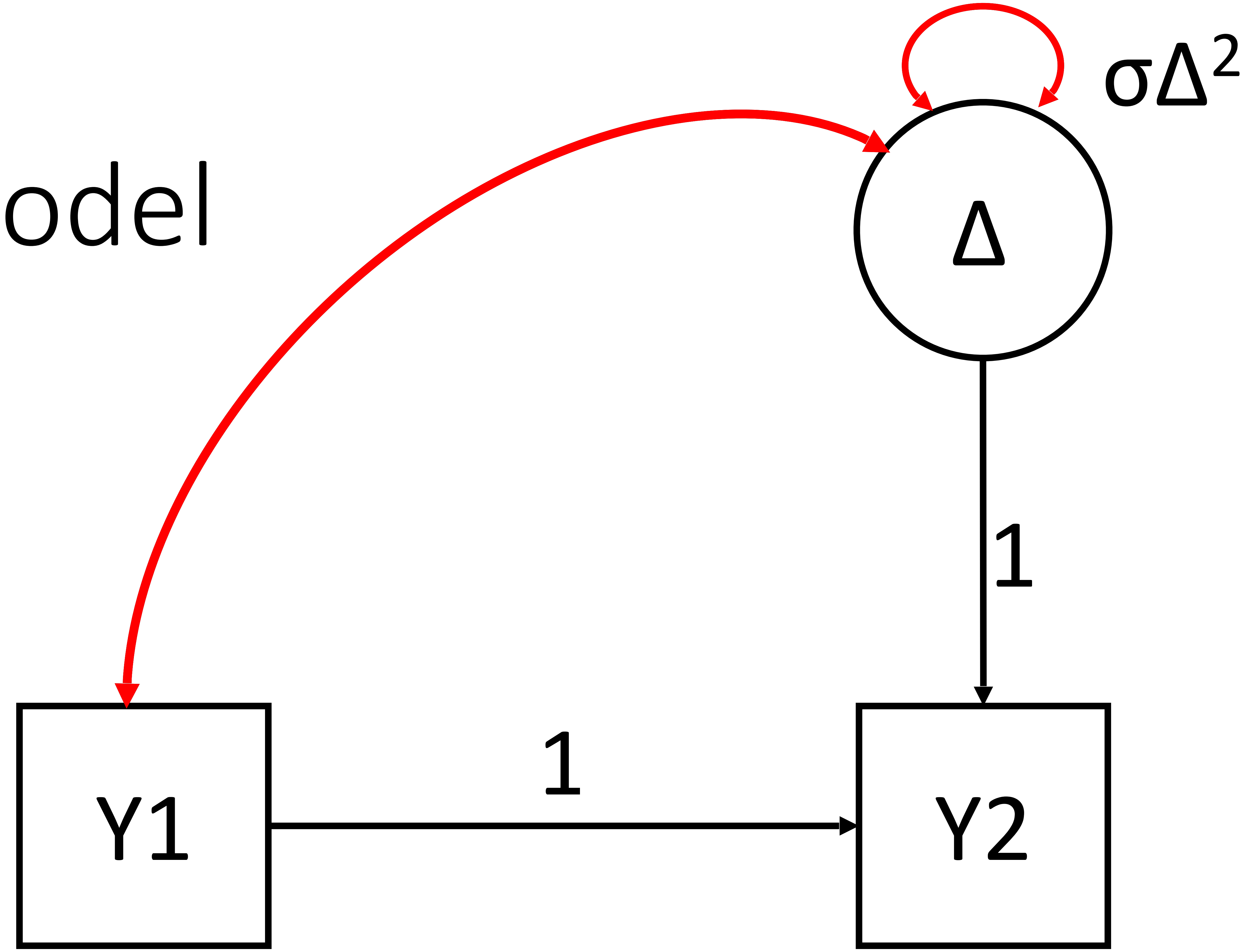
NSPN
NeuroScience in Psychiatry Network





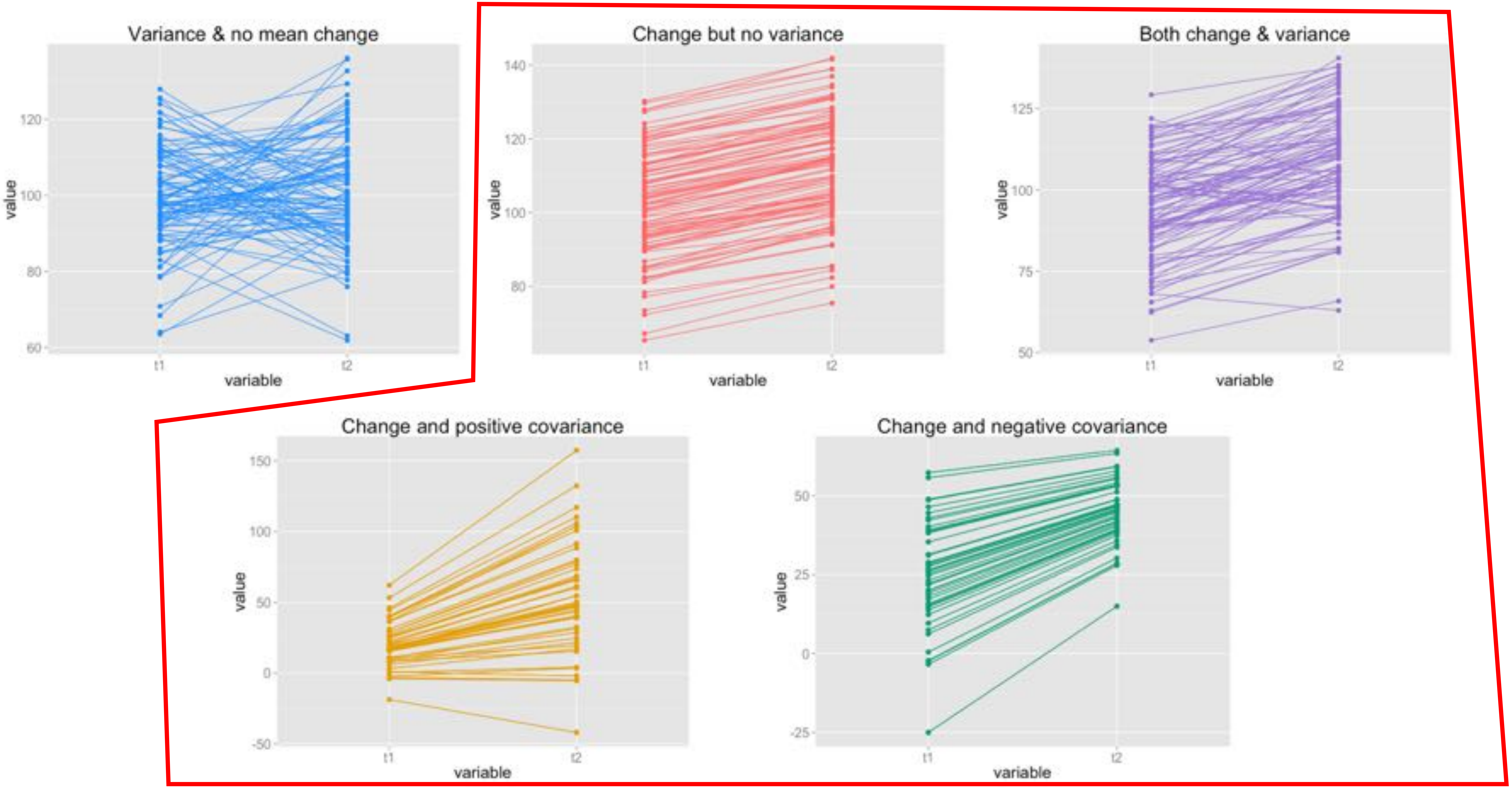
Latent Change Score model

- $y_{ti} = \beta_{t,t-1} y_{ti-1} + \Delta_{ti}$
- $y_{ti} = 1 * y_{ti-1} + \Delta_{ti}$
- $\Delta_{ti} = y_{ti} - y_{ti-1}$
- Mean Δ_{ti} = mean paired t-test
- But: Two extra parameters!
- Covariance/regression Δ_{ti}Y1
- Variance Δ_{ti}



McArdle, J. J., & Hamagami, F. (2001). Latent difference score structural models for linear dynamic analyses with incomplete longitudinal data.
McArdle, J. J. (2009). Latent variable modeling of differences and changes with longitudinal data. Annual review of psychology, 60, 577-605.

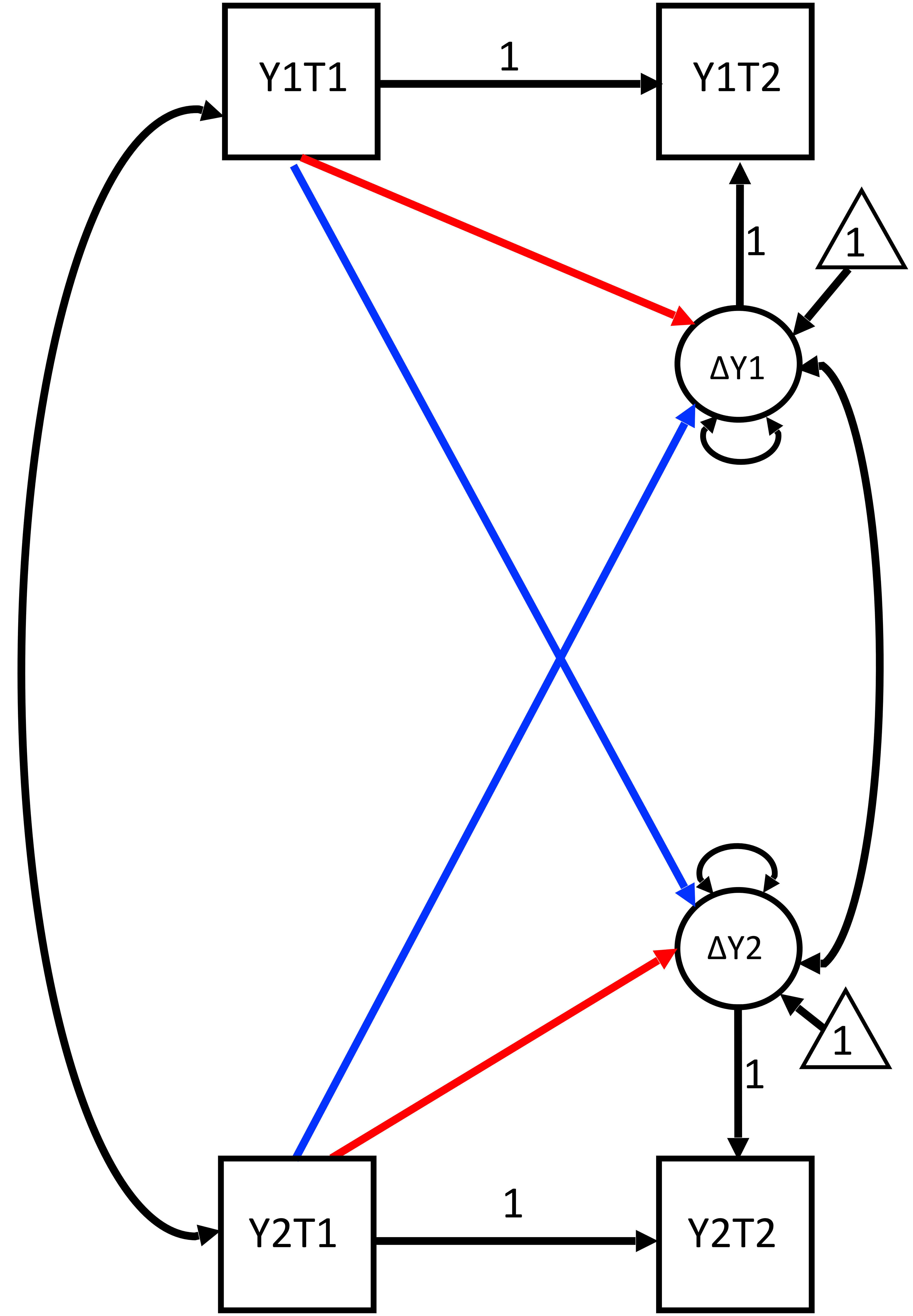
Powerful tool to distinguish various mechanisms

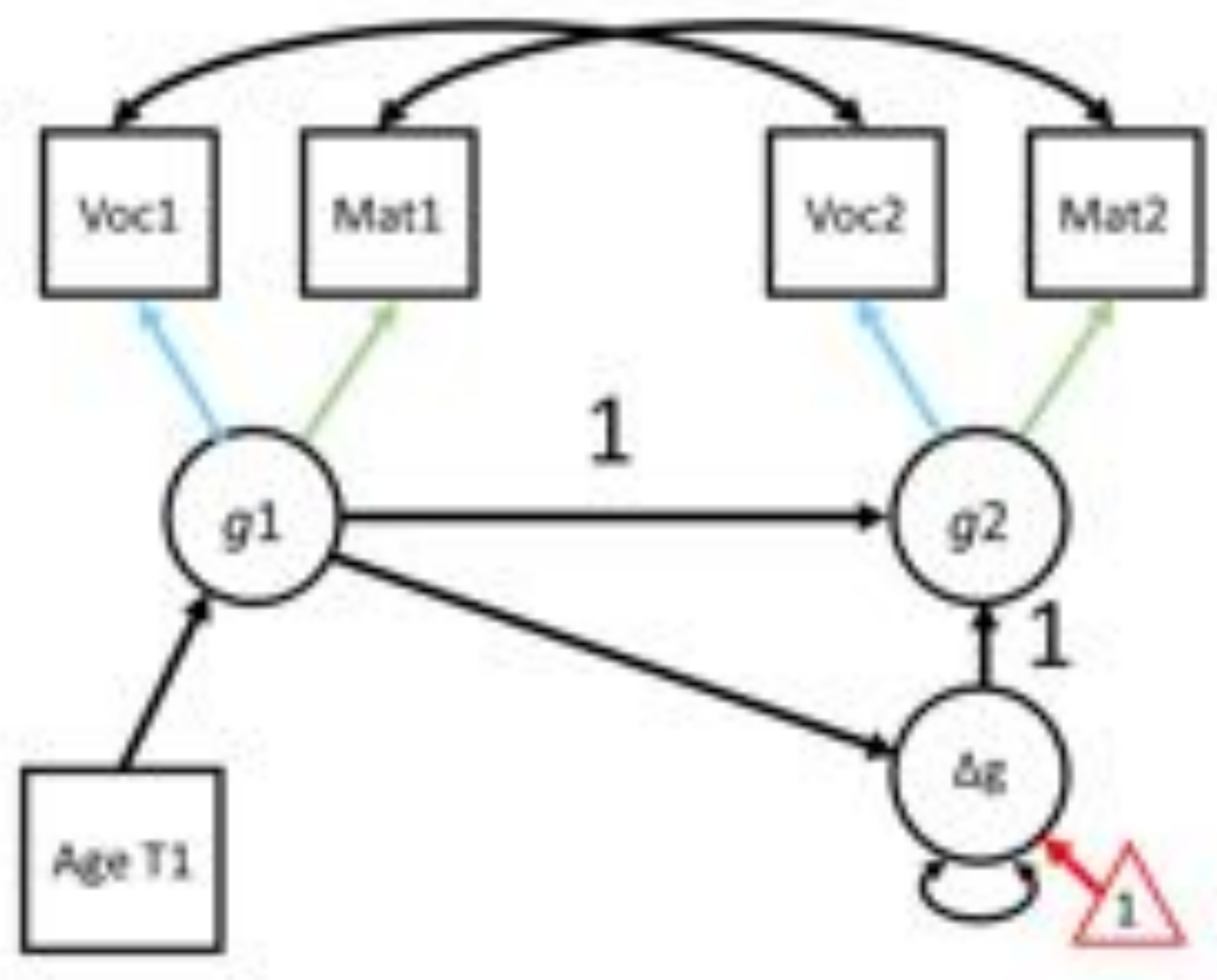


Bivariate latent change score model

- Simple extension
- Allows for investigation of
  - Self-feedback parameters
  - Coupling parameters

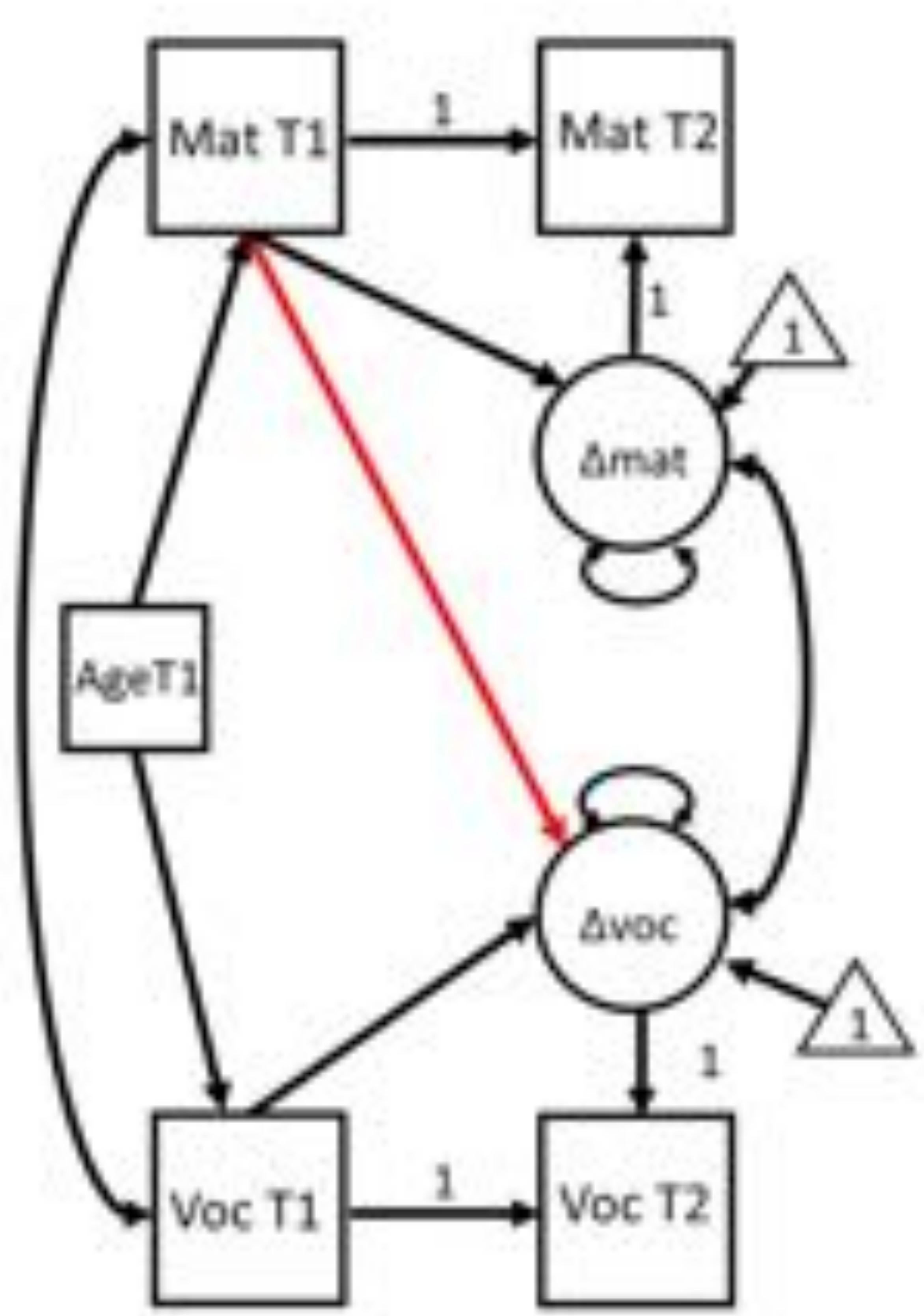
$$\Delta Y1_{ti} = \boxed{\beta 1} * Y1_{it-1} + \boxed{\gamma 12} * Y2_{it-1}$$





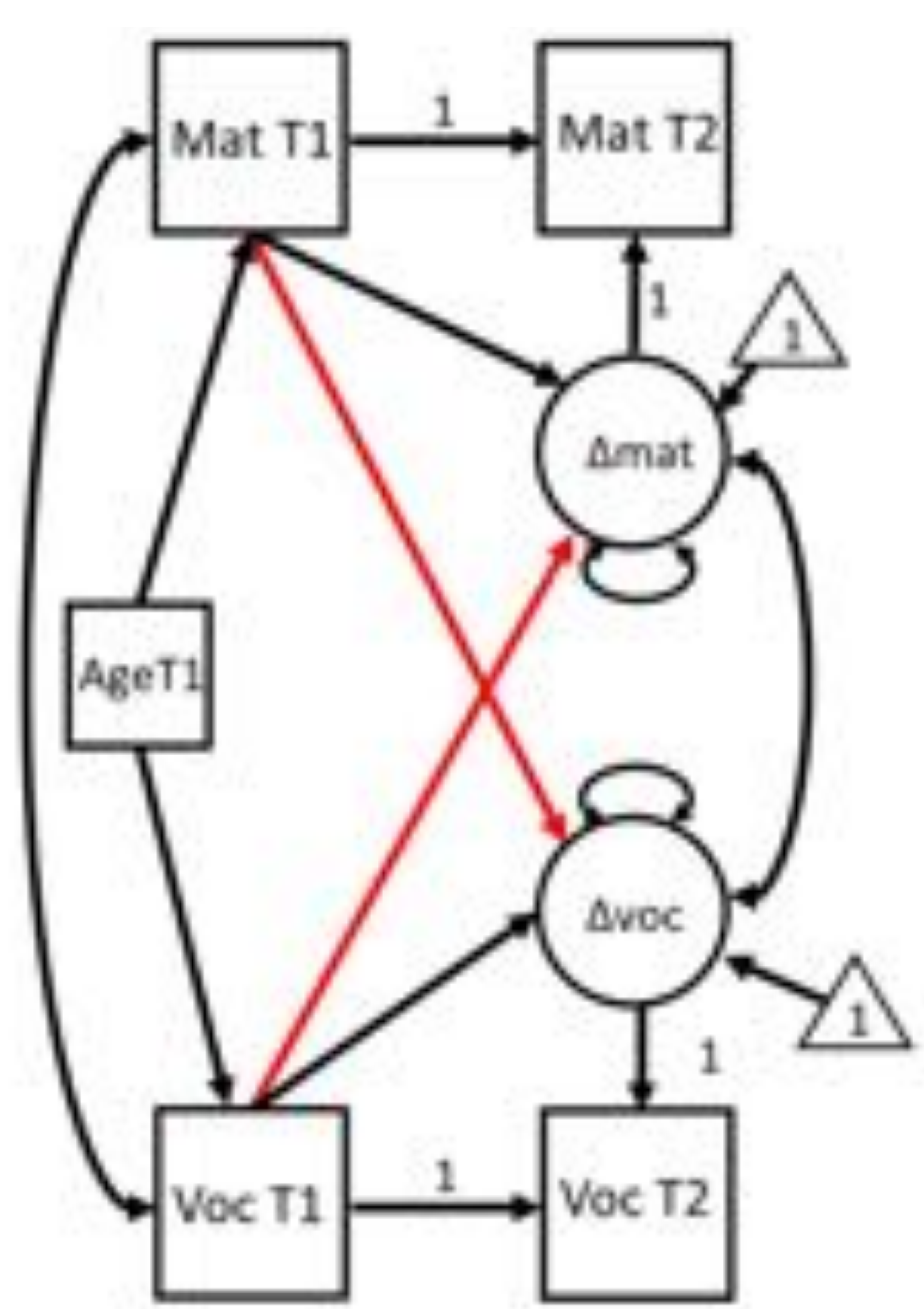
_g_ factor theory

only g changes, affects/explains all other change



Investment theory

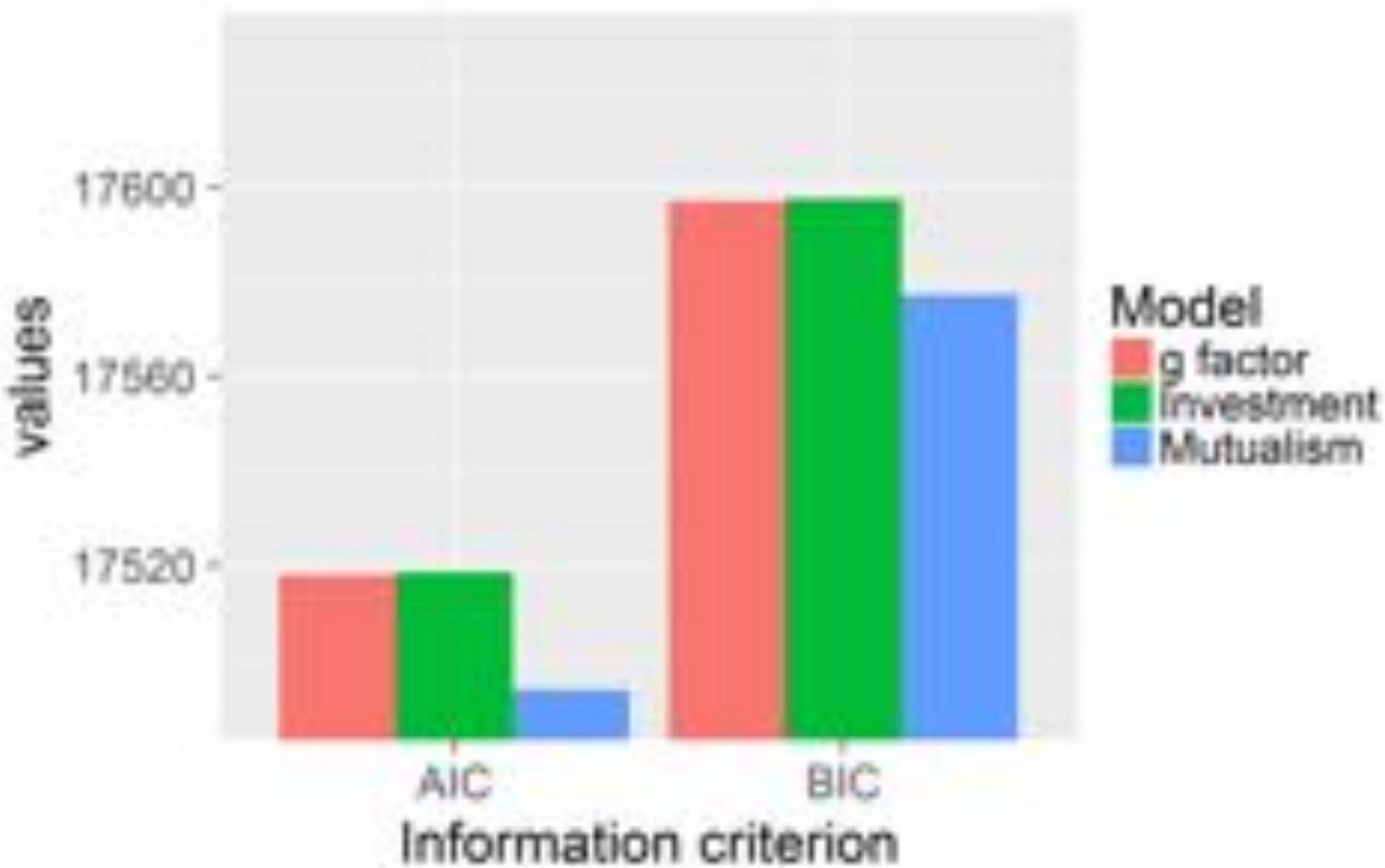
You **invest** (use) fluid abilities to gain knowledge

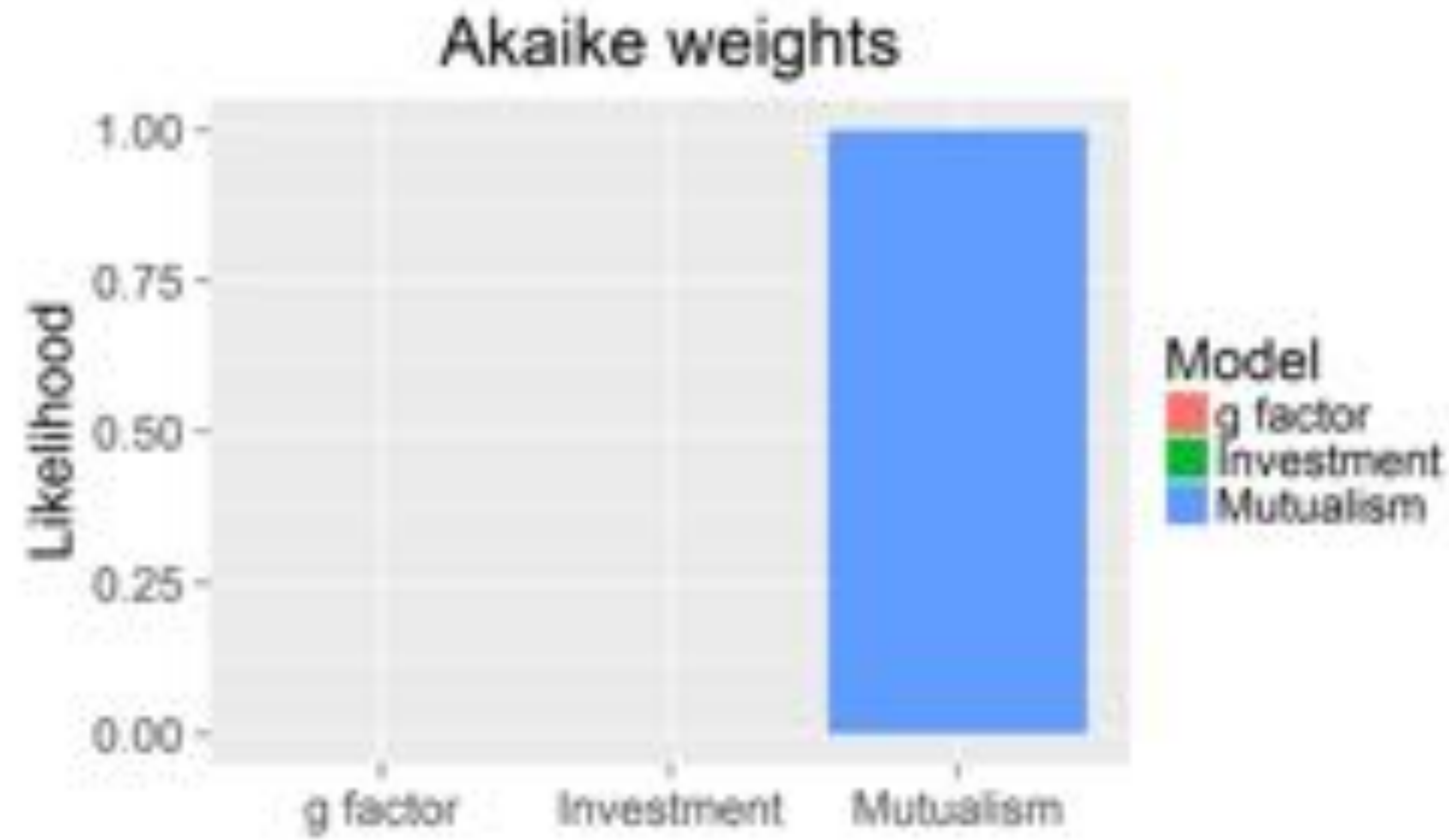


Mutualism theory

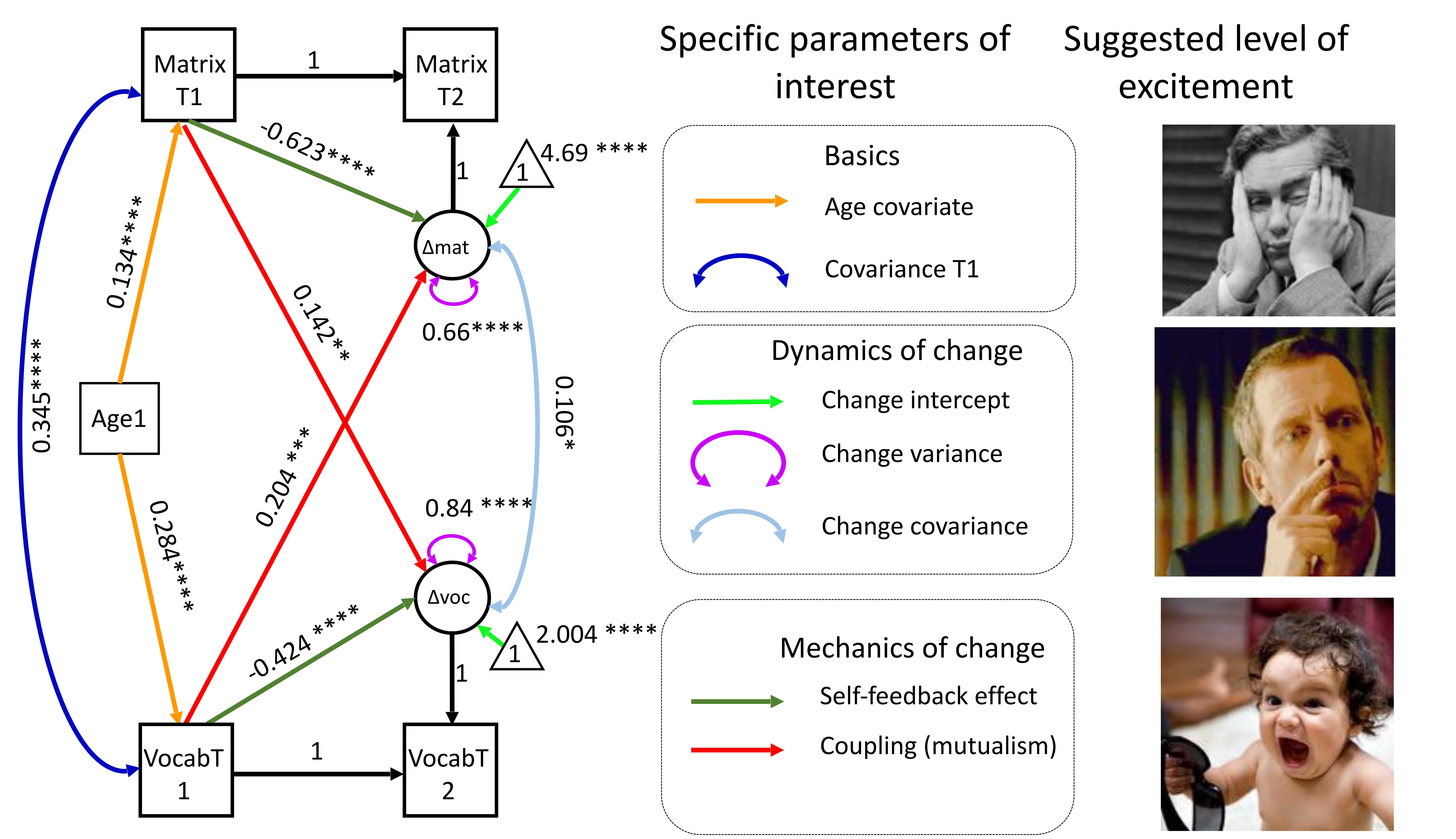
Cognitive abilities interact positively during development

Model comparison



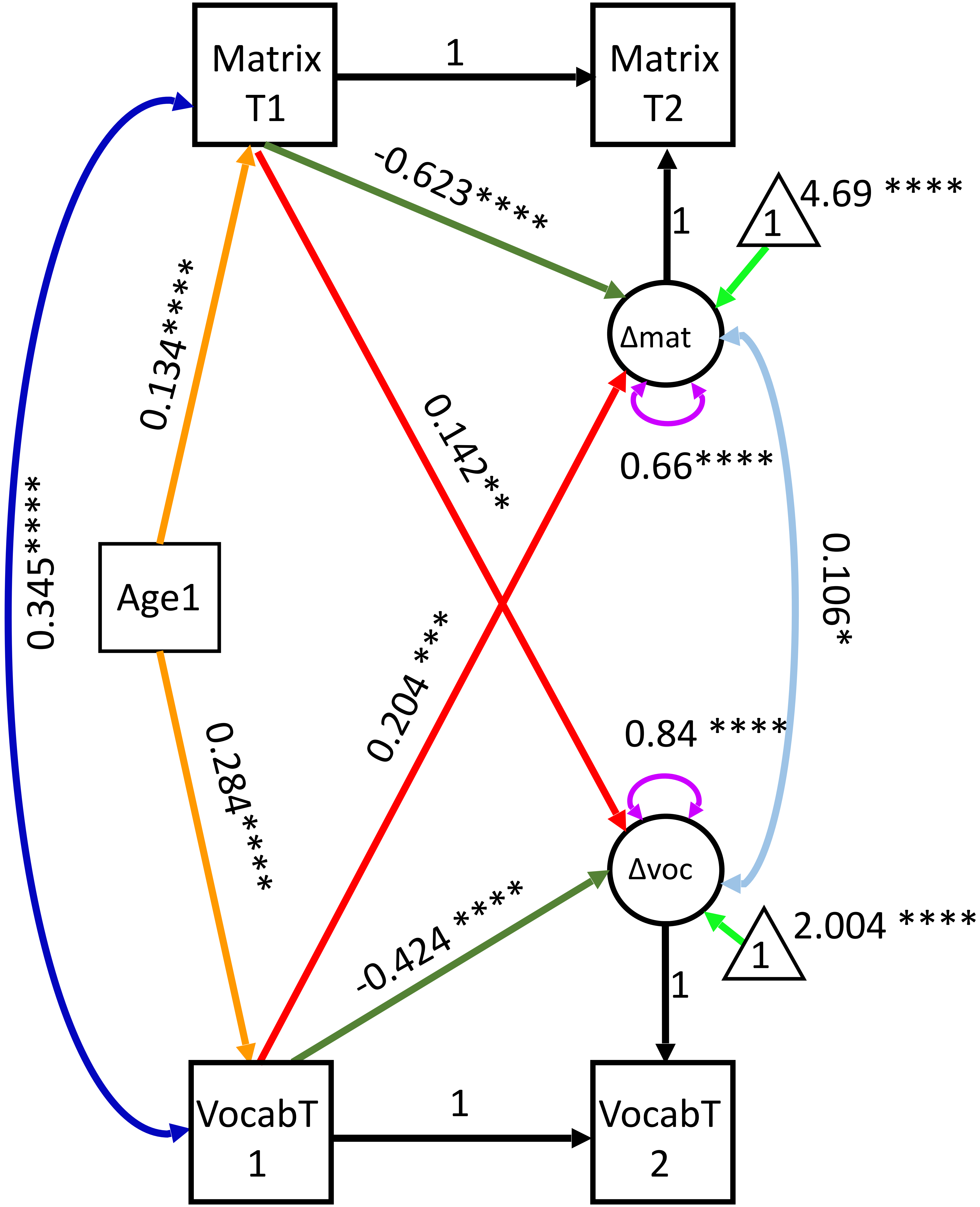


Model	**Chi-square**	**df**	**RMSEA**	**CFI**	**SRMR**
g factor	22.11	3	0.091 [0.060 0.125]	0.982	0.027
Investment	26.35	3	0.100 [0.068 0.137]	0.977	0.042
Mutualism	0.27	2	0.000 [0.000 0.038]	1	0.002



Matrix T1
Matrix T2
1
-0.623****
1
4.69 ****
1
Δmat
0.134****
0.142**
0.66****
0.345****
Age1
0.106*
0.204 ***
0.84 ****
0.284****
Δvoc
-0.424 ****
2.004 ****
1
1
VocabT 1
1
VocabT 2
Specific parameters of interest
Suggested level of excitement
Basics
Age covariate
Covariance T1
Dynamics of change
Change intercept
Change variance
Change covariance
Mechanics of change
Self-feedback effect
Coupling (mutualism)

Mutualism summary



- 1) Increase in matrix reasoning and vocabulary
- 2) Individual differences in growth
- 3) Correlated change
- 4) Higher starting values associated with lower rates of change within domains
- 5) Evidence for mutualism, or bivariate dynamic coupling: A higher starting score in one domain is associated with greater gains in the other

Mutualism model outperforms developmental accounts

- Mechanisms
  - Investment theory
  - Verbal decomposition of matrix rules
  - Vocabulary as an easy marker of intelligence
  - gene-environment interactions
- Limitations
  - Only two waves (more waves allow for more detailed investigation of dynamics, e.g. BDCS)
  - Only two measures (map sparseness of full coupling matrix)
  - Observed variables (measurement error)
  - Late adolescence (earlier in childhood, stronger effects?)

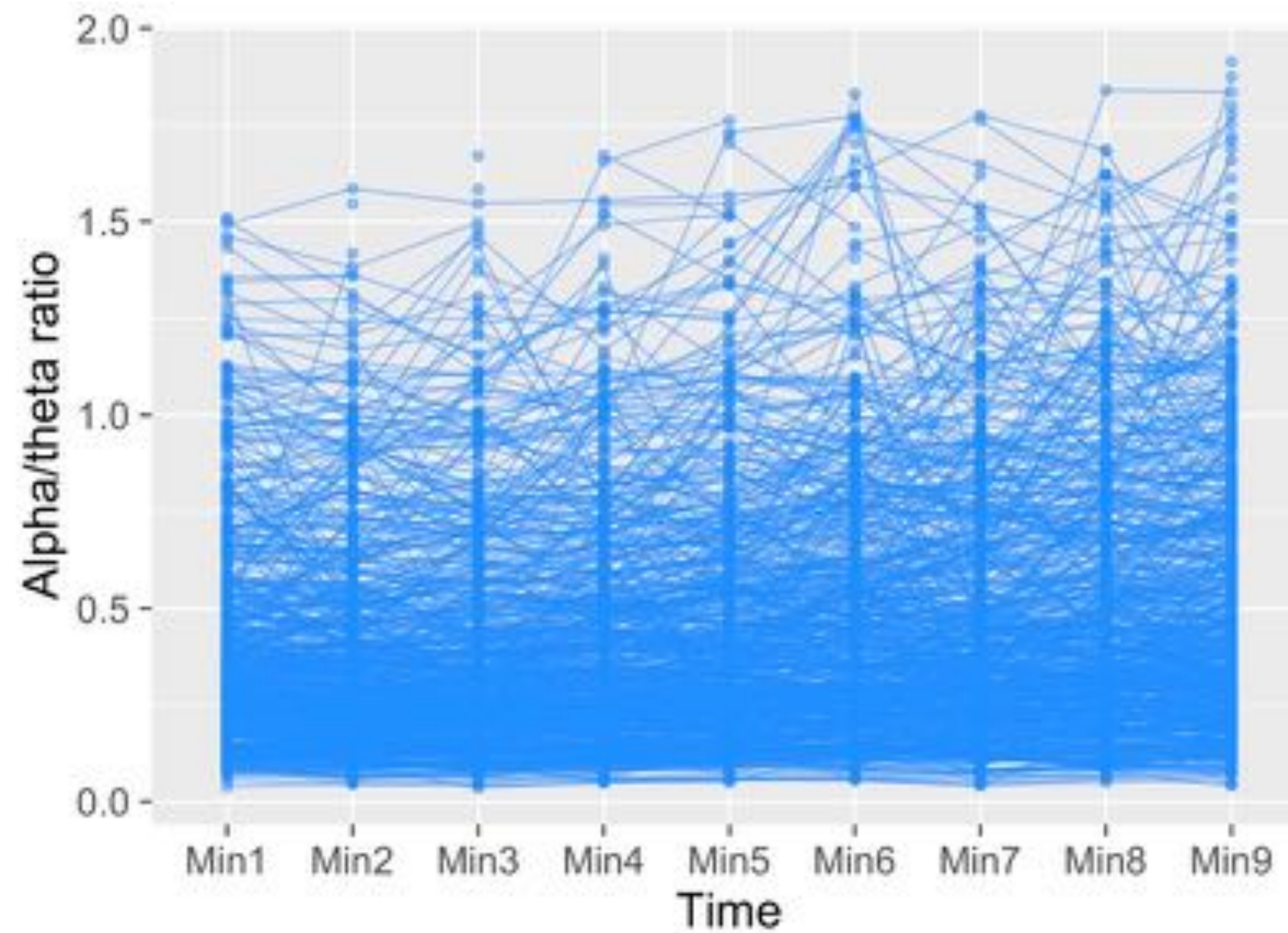
‘True’ longitudinal data

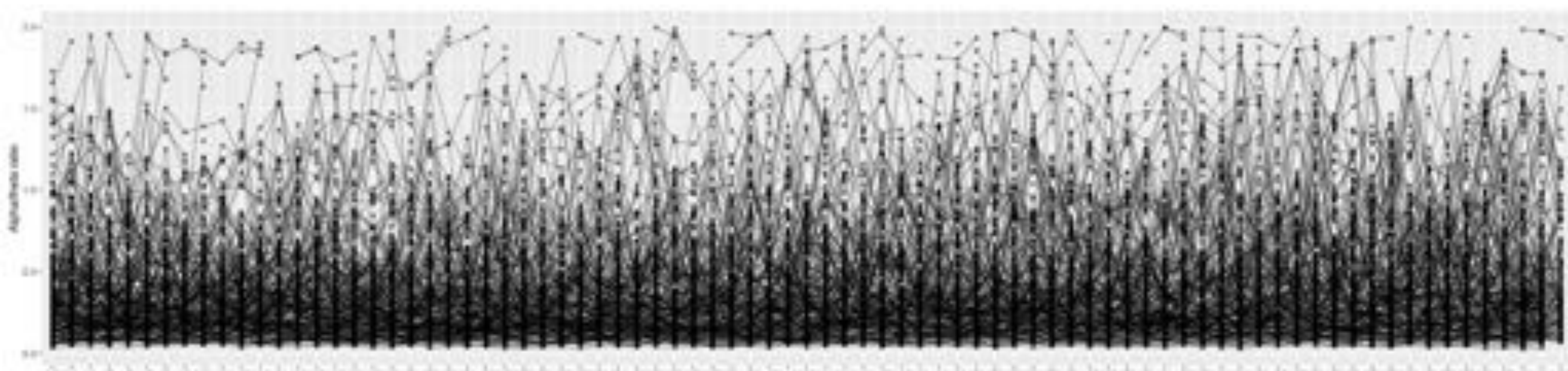
- Modeling drowsiness in MEG resting state
- Data:
  - MEG resting state
  - N=600 time 1 (9 minutes resting state)
  - N=220 time 2 (5 minutes resting state)
  - Variable: Alpha/theta ratio (power)
- Questions:
  - Do people increase in drowsiness during RSN?
  - Are properties trait-like or state-like?
  - What determines drowsiness?

Šušmáková, K., & Krakovská, A. (2007). Classification of waking, sleep onset and deep sleep by single measures. Meas Sci Rev, 7, 34-38.

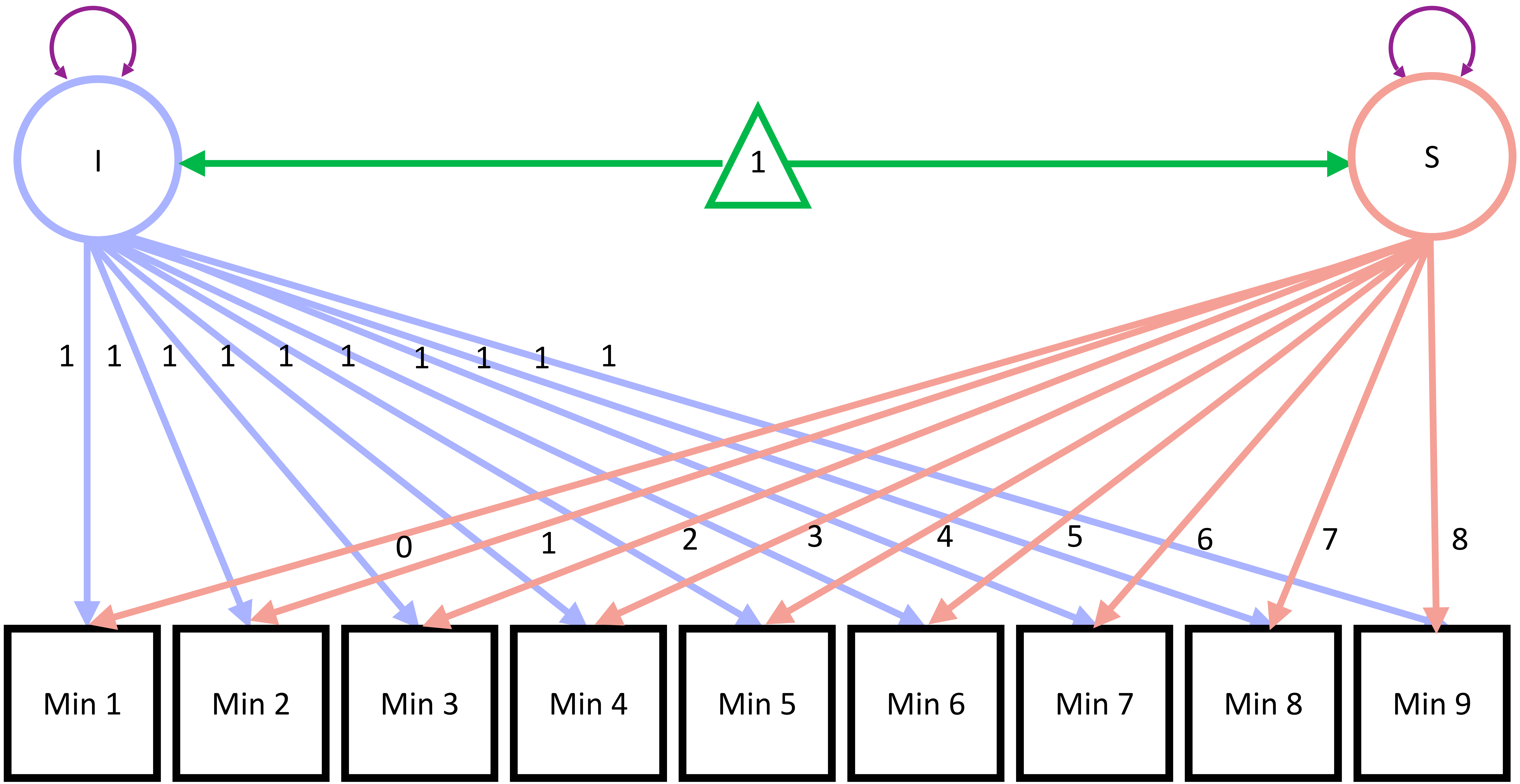
Raw data (saignant?)

- N=623, alpha/theta averaged 4 seconds
- ‘Time parcels’ (average per minute)





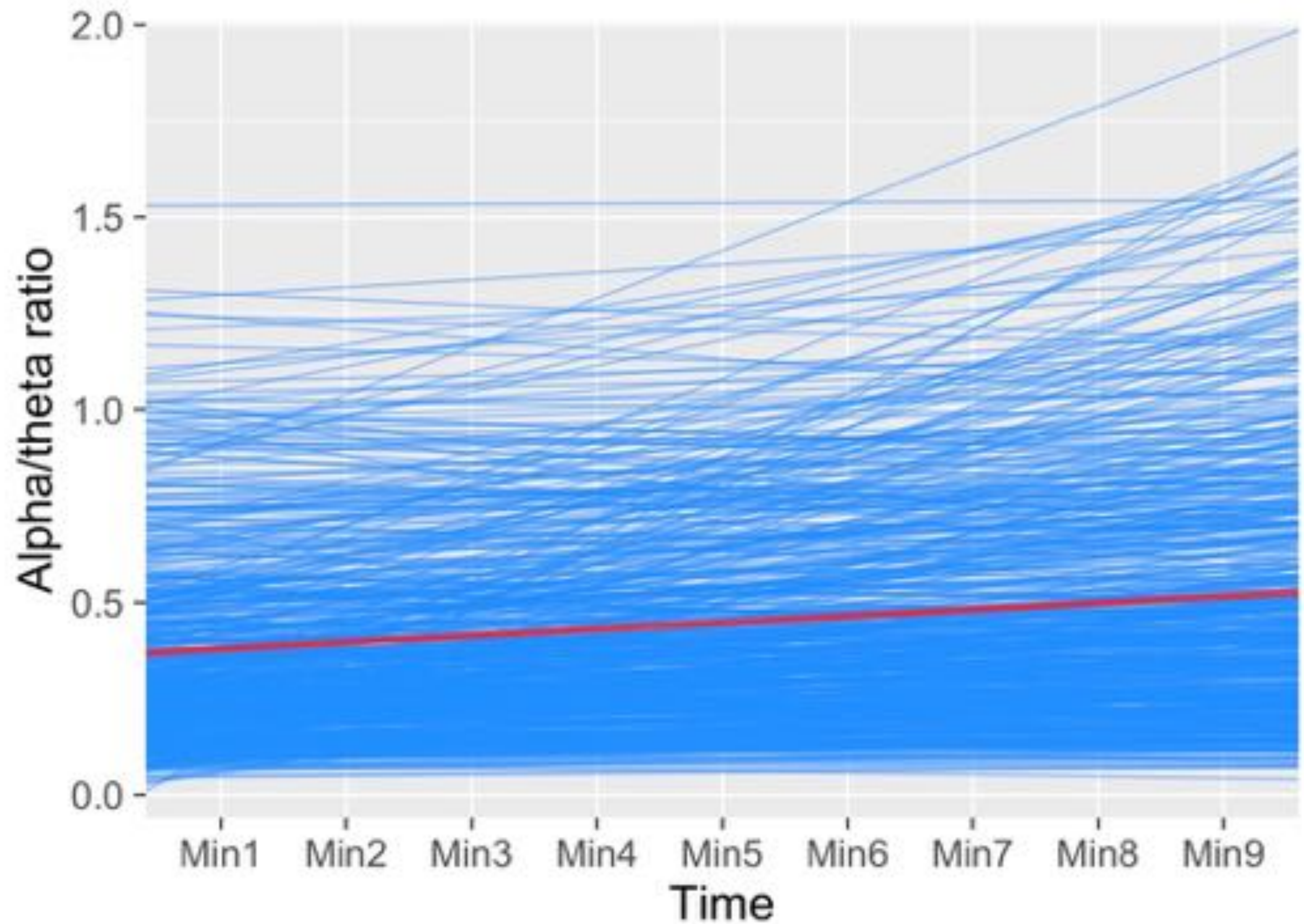
Linear latent growth model



Fit model

$\chi 2 = 169.024$, df =40, $p<.001$
RMSEA=0.074 [0.067 0.081]
CFI=.935 SRMR=0.030

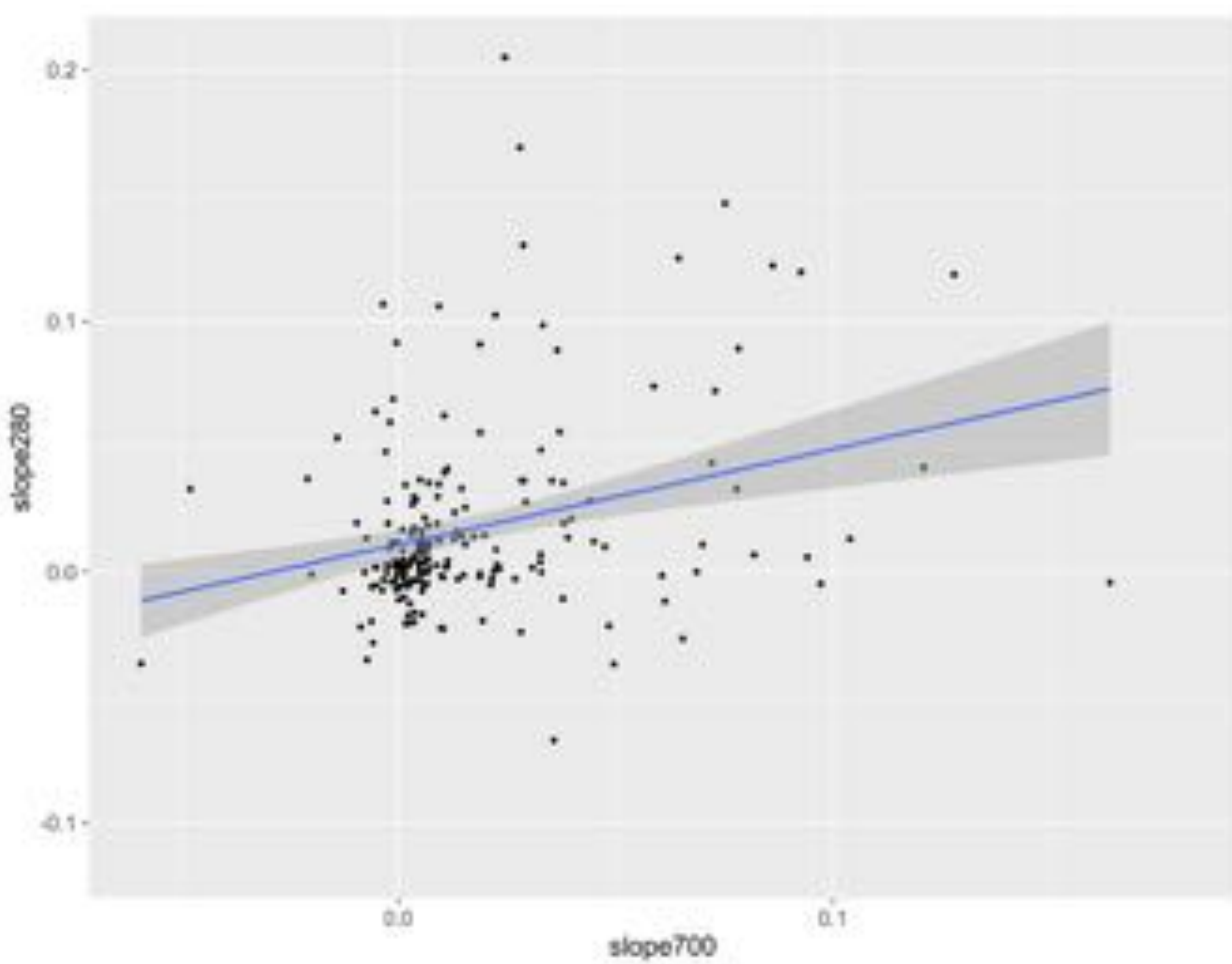
- Key findings:
- People differ in baseline alpha/theta
  - Intercept (0.07, z=12.42)
- People increase in alpha/theta (~drowsiness)
  - Slope (0.017, z=12.015)
- People differ in increase in drowsiness
  - Slope variance (0.001, z=7.946)



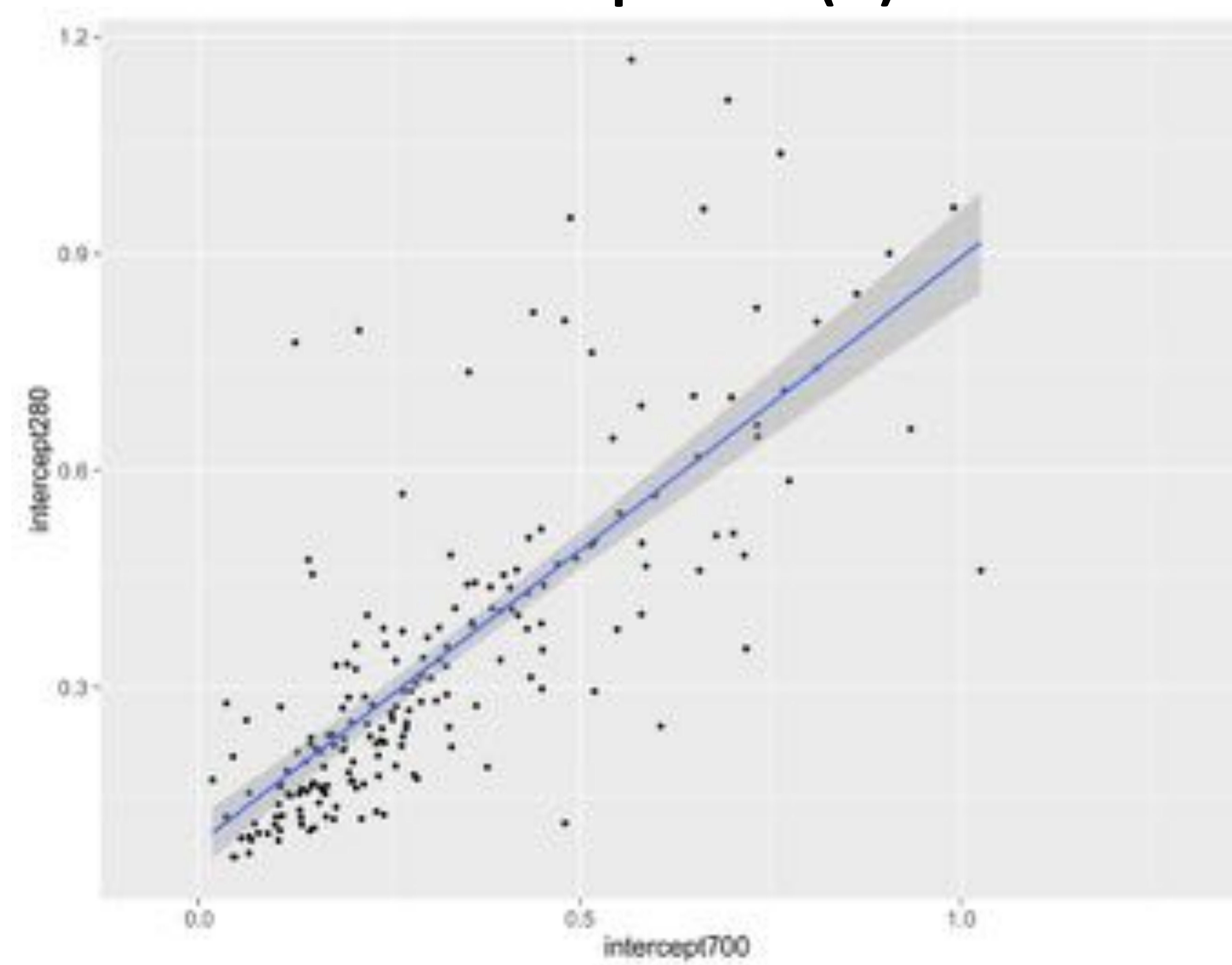
Is alpha/theta trait-like or state-like?

- Resting state repeated
- Time 1: N=650 (RSN=9 minutes)
- Time 2: subset, N=230 (RSN=5 minutes)
- Mean interval 1.36 years
- Fit LGM on two occasions (unconstrained)
- Estimate intercepts/slopes

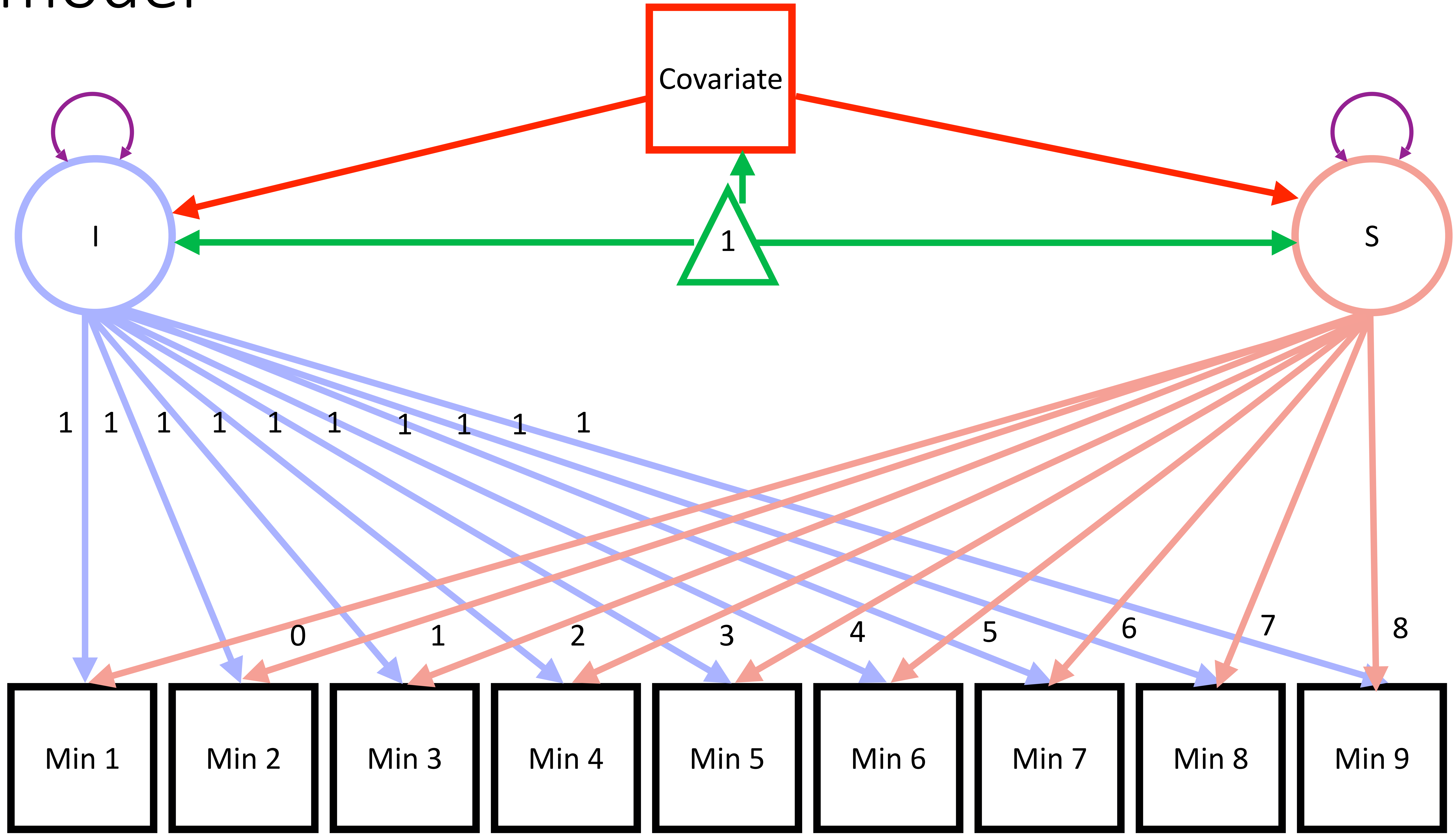
Slope: r=.25 (P<0.001)



Intercept: r=.8 (!!)

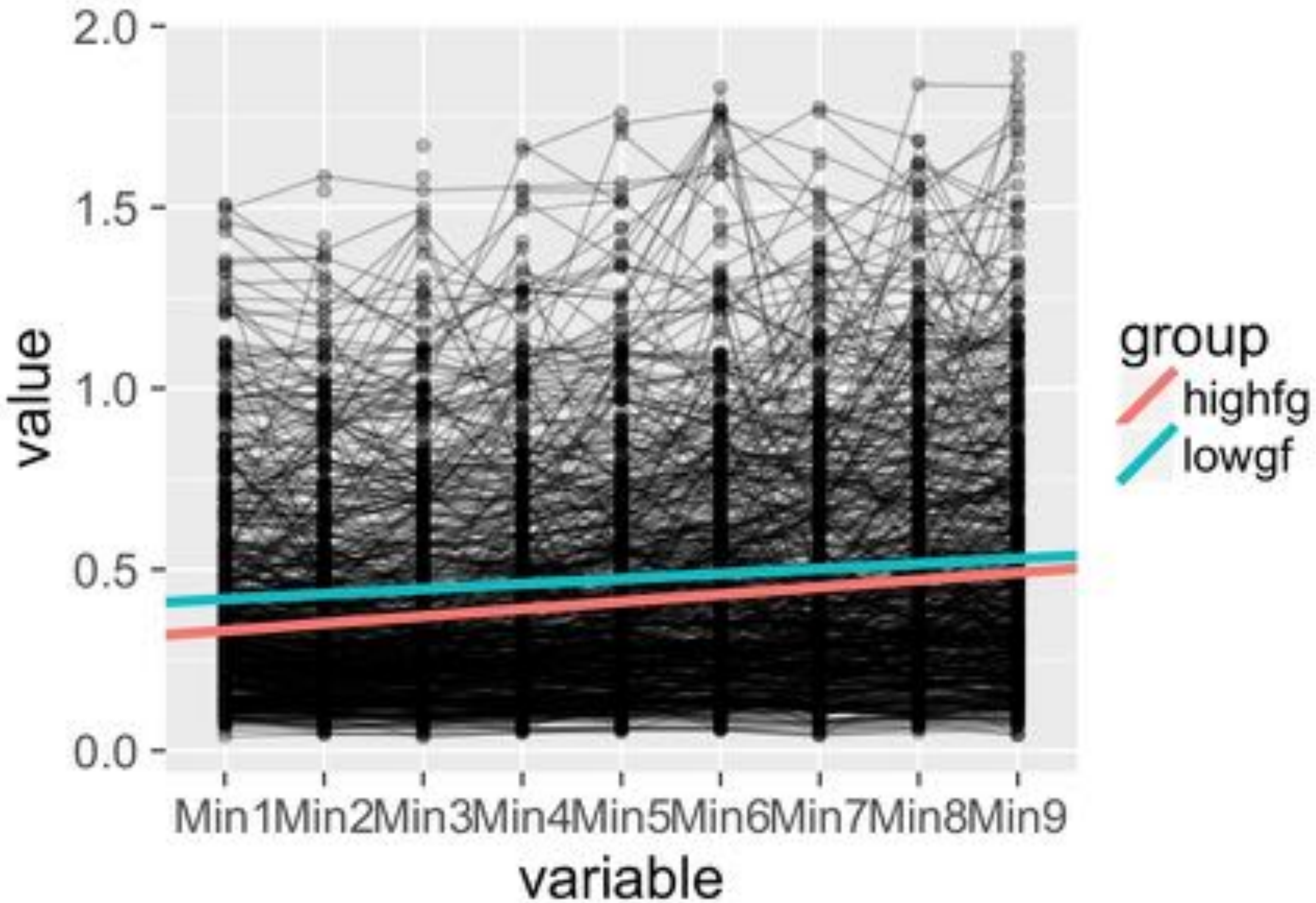


Relating mind and brain: Conditional growth model



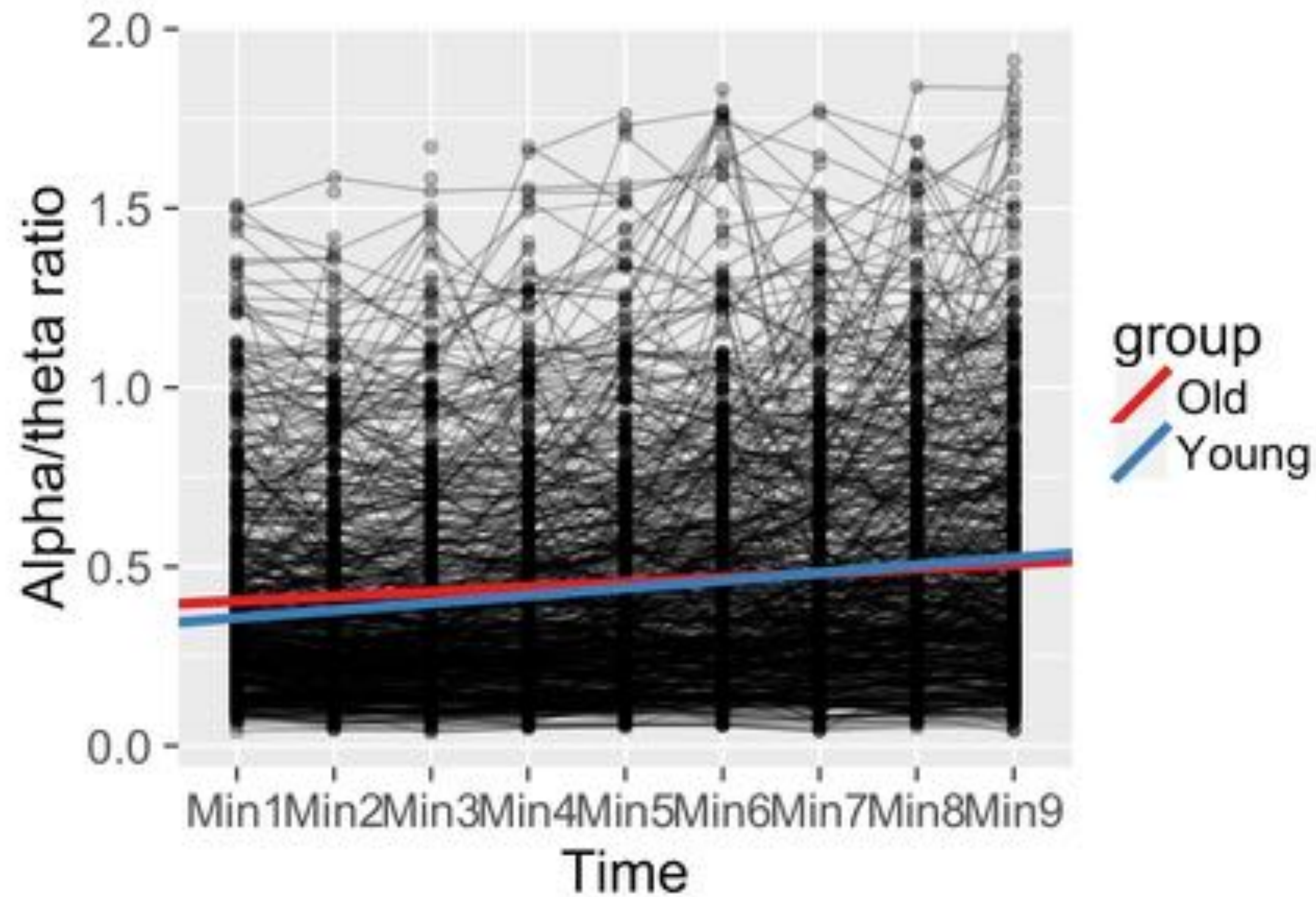
High fluid intelligence

Lower intercept (-0.162, $p<0.001$)
Steeper slope (0.141, $p<0.001$)



Older age

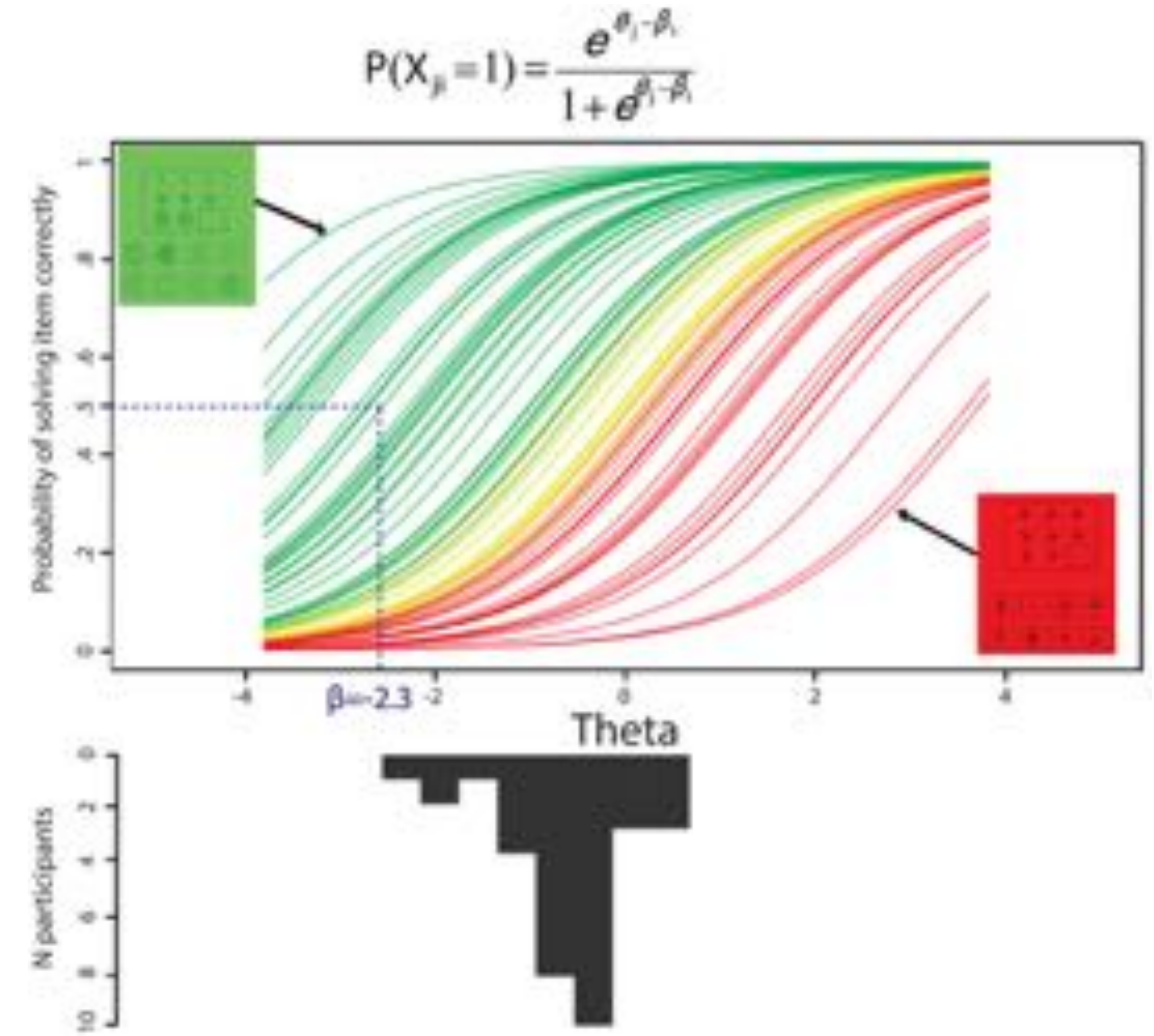
Higher intercept (0.115, $p=0.004$)
Shallower slope (-0.170, $p<0.001$)



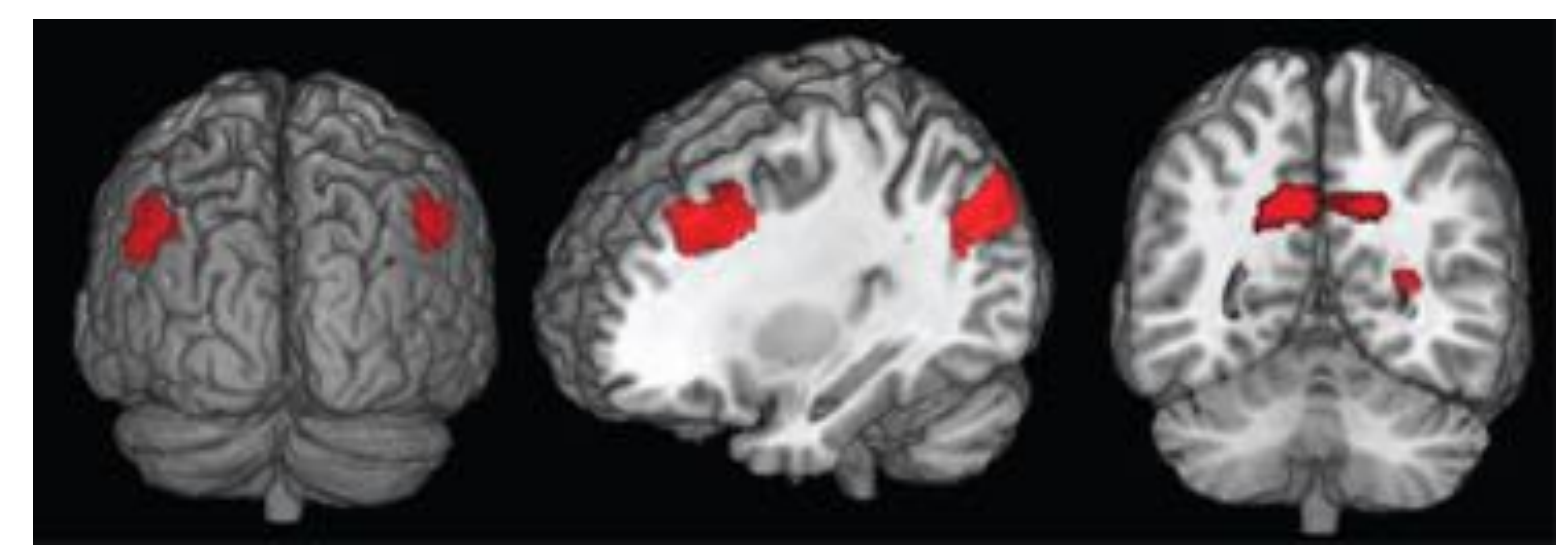
4) Summary and open questions

Open question 1: Neuroscience and the idiographic filter

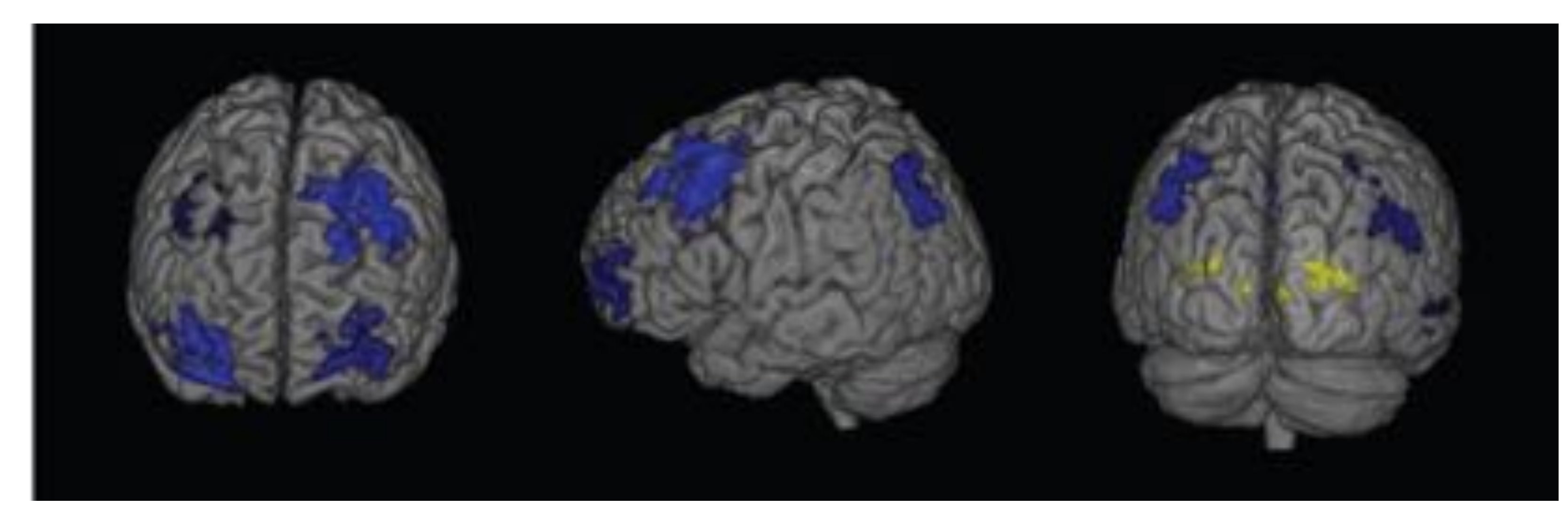
- How to combine inter-and intra individual differences?
- Neural ‘idiographic filter’ (Nesselroade et al., 2007)
- e.g. model individually specific signature of wakefulness



Difficulty (beta)



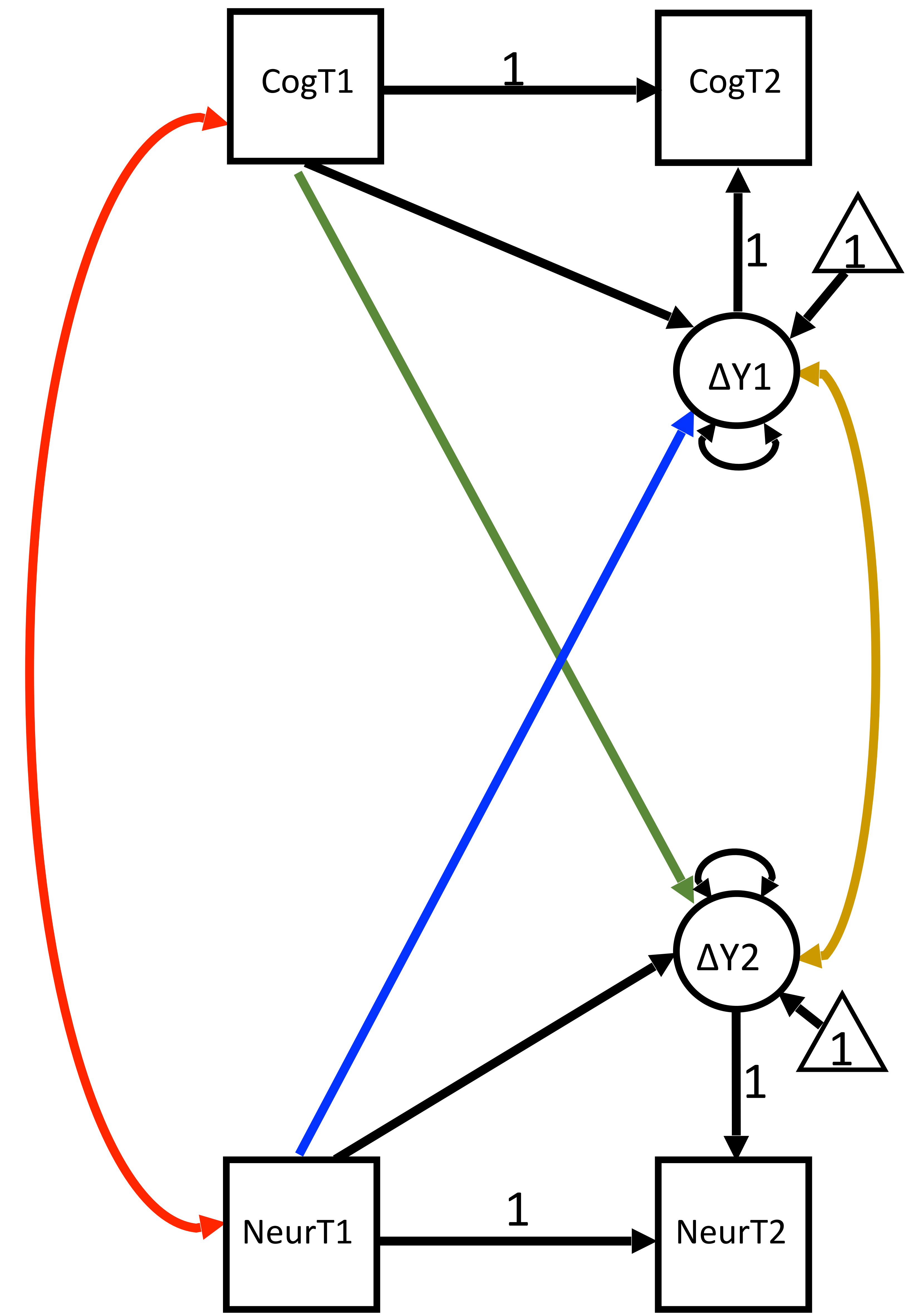
Ability (theta)



Kievit, R. A. Scholte, Waldorp & Borsboom. (under review). Inter- and intra-individual differences in fluid reasoning show distinct cortical responses

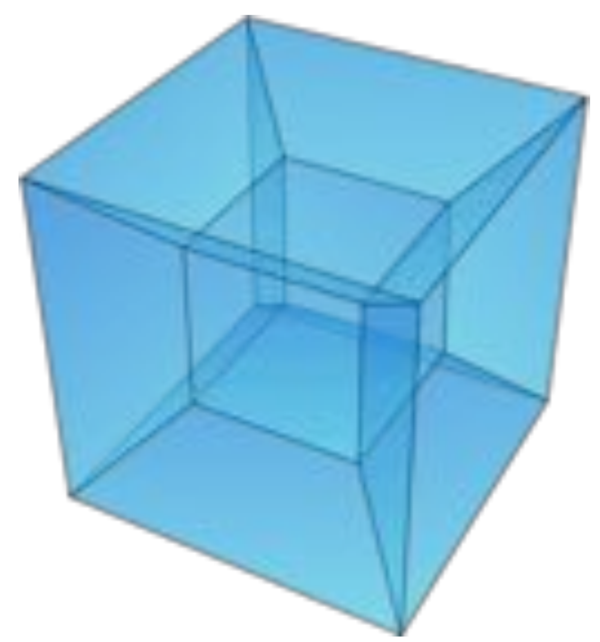
Open question 2: Towards a causal taxonomy of brain-behavior relationships

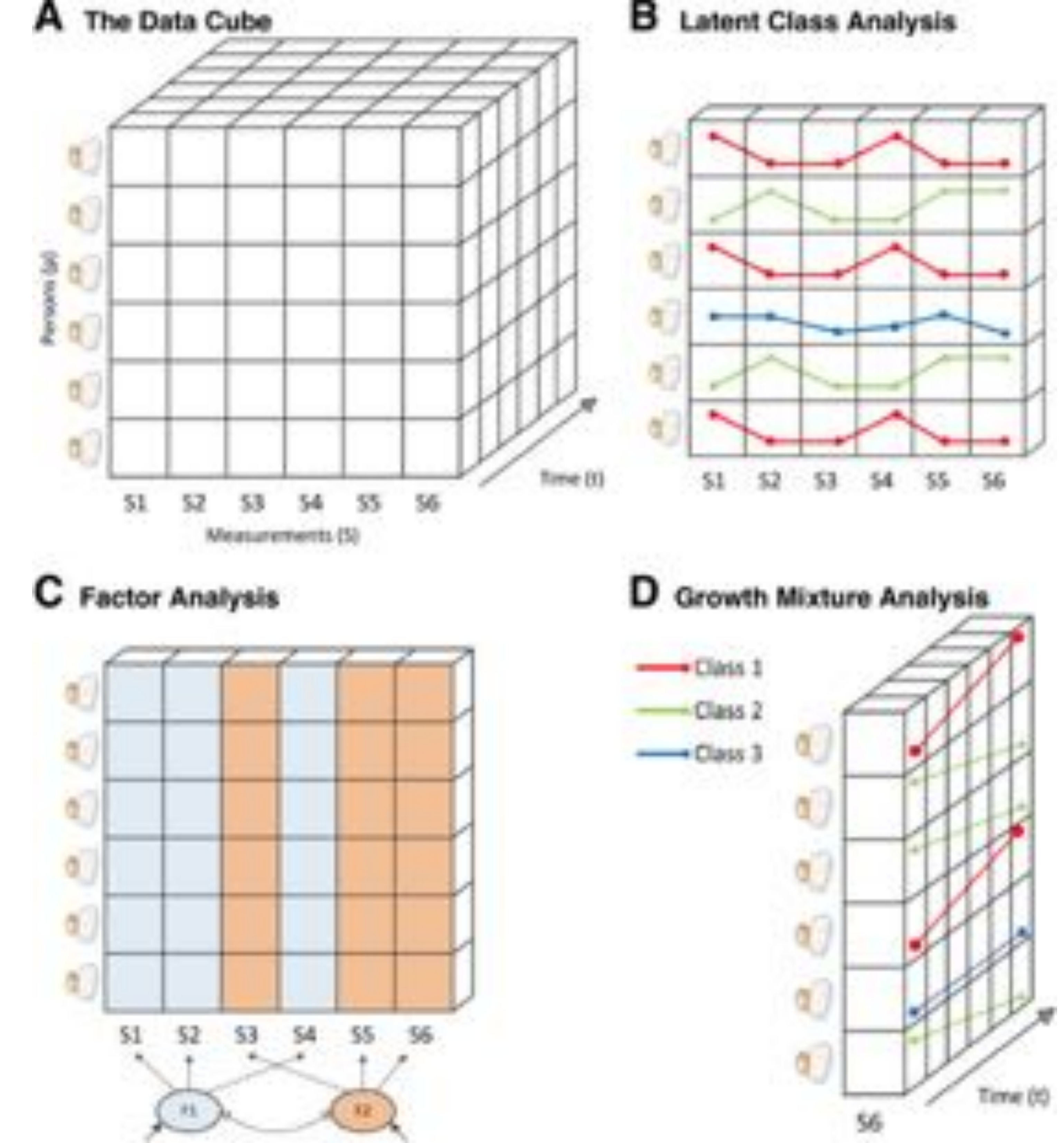
- Simplest case: 2 waves, only observed measurements
- Brain-behavior covariance (>99% of all papers)
- Brain structure as cause
- Brain structure as consequence (Plasticity)
- Correlated change (Unknown cause)

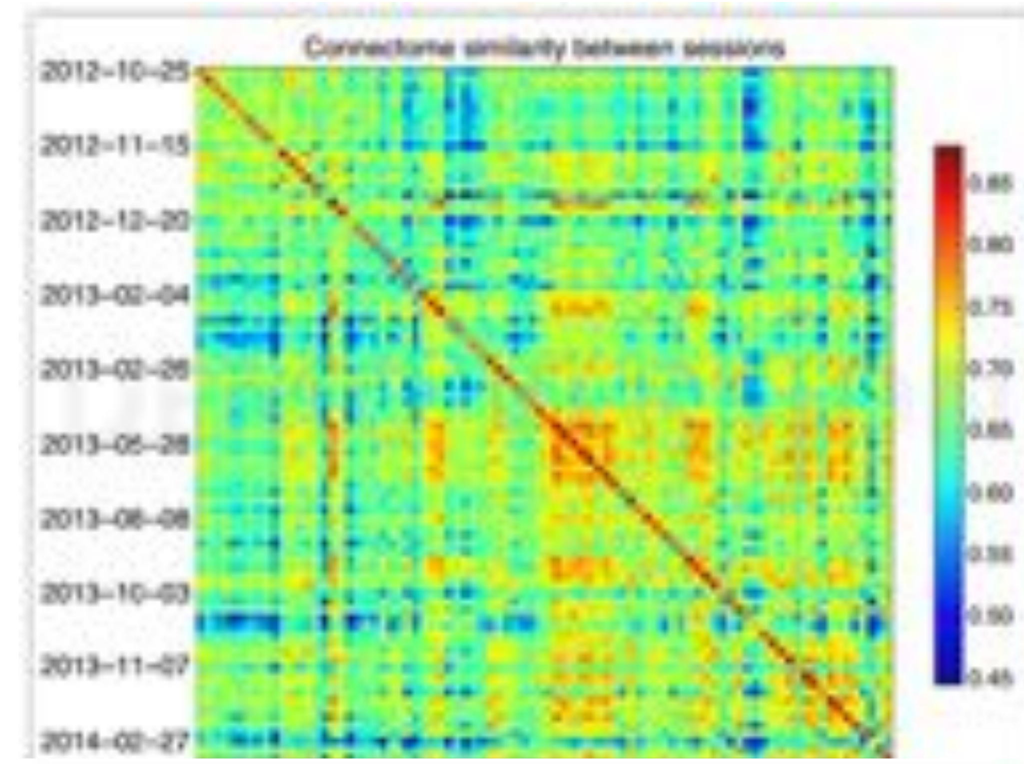


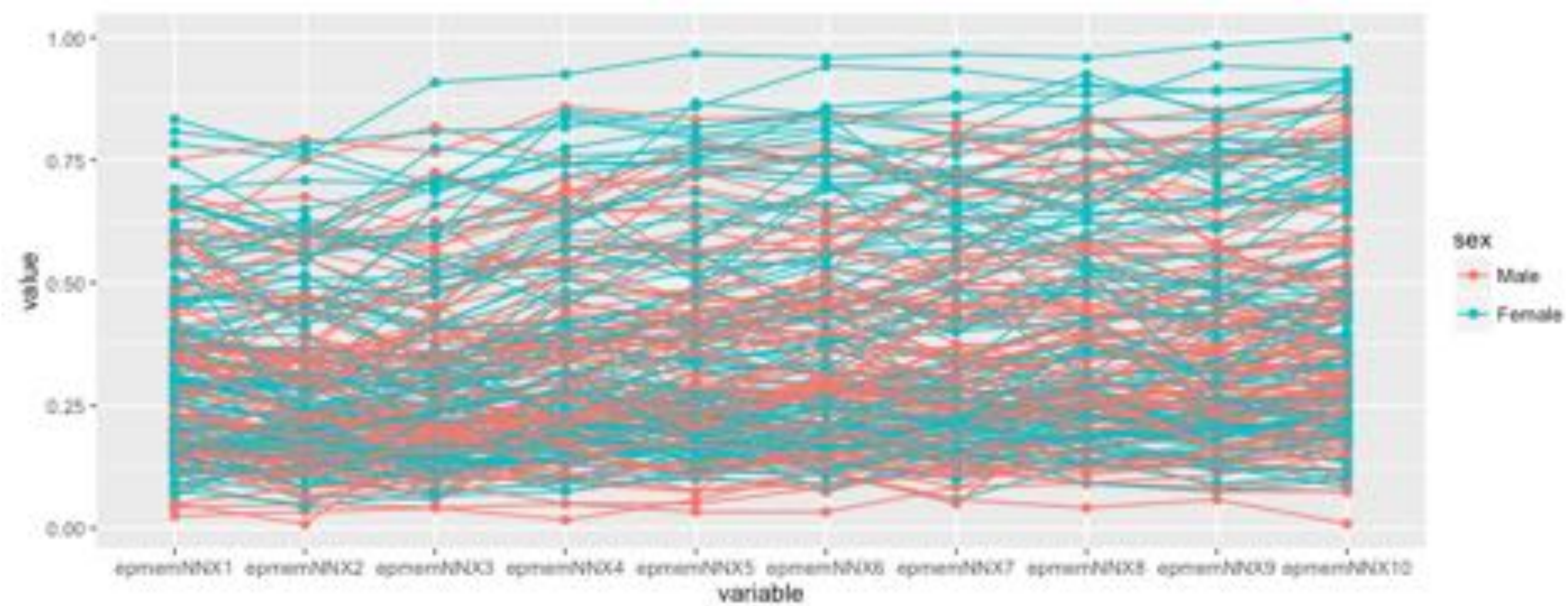
Future: Towards Cattell's hypercube

- Cattell's data cube
  - Persons
  - Measurements
  - Occasions
- The Cattell Hypercube
  - All three dimensions
  - Addition: neural measures
    - Longitudinal neural data
    - Multiple measures
    - Of multiple people









Hundred days of cognitive training enhance broad cognitive abilities in adulthood: findings from the COGITO study

Florian Schmiedek[1,2]*, Martin Lövdén[1,3] and Ulman Lindenberger[1]

Thanks to funders, collaborators & mascots

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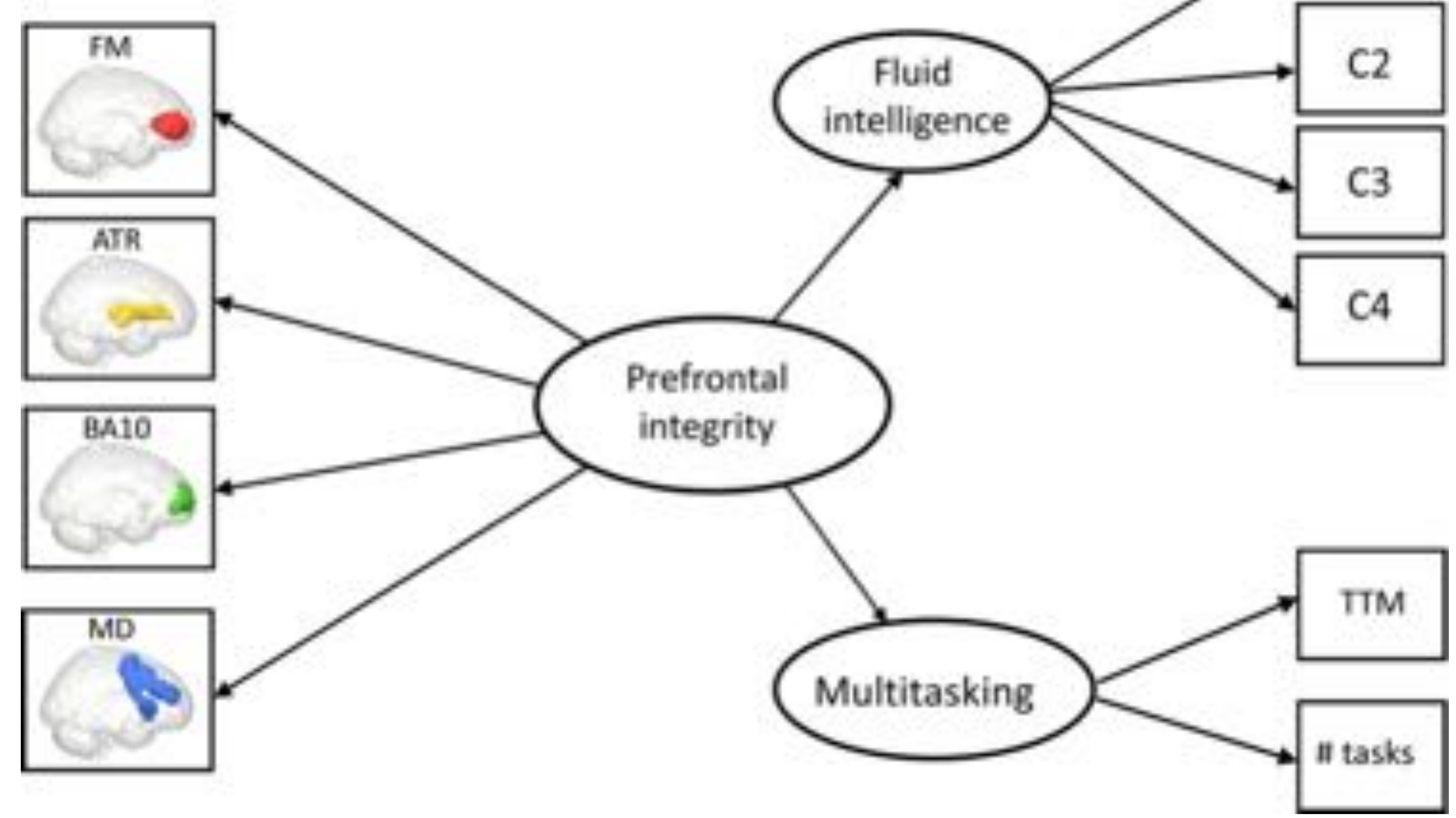
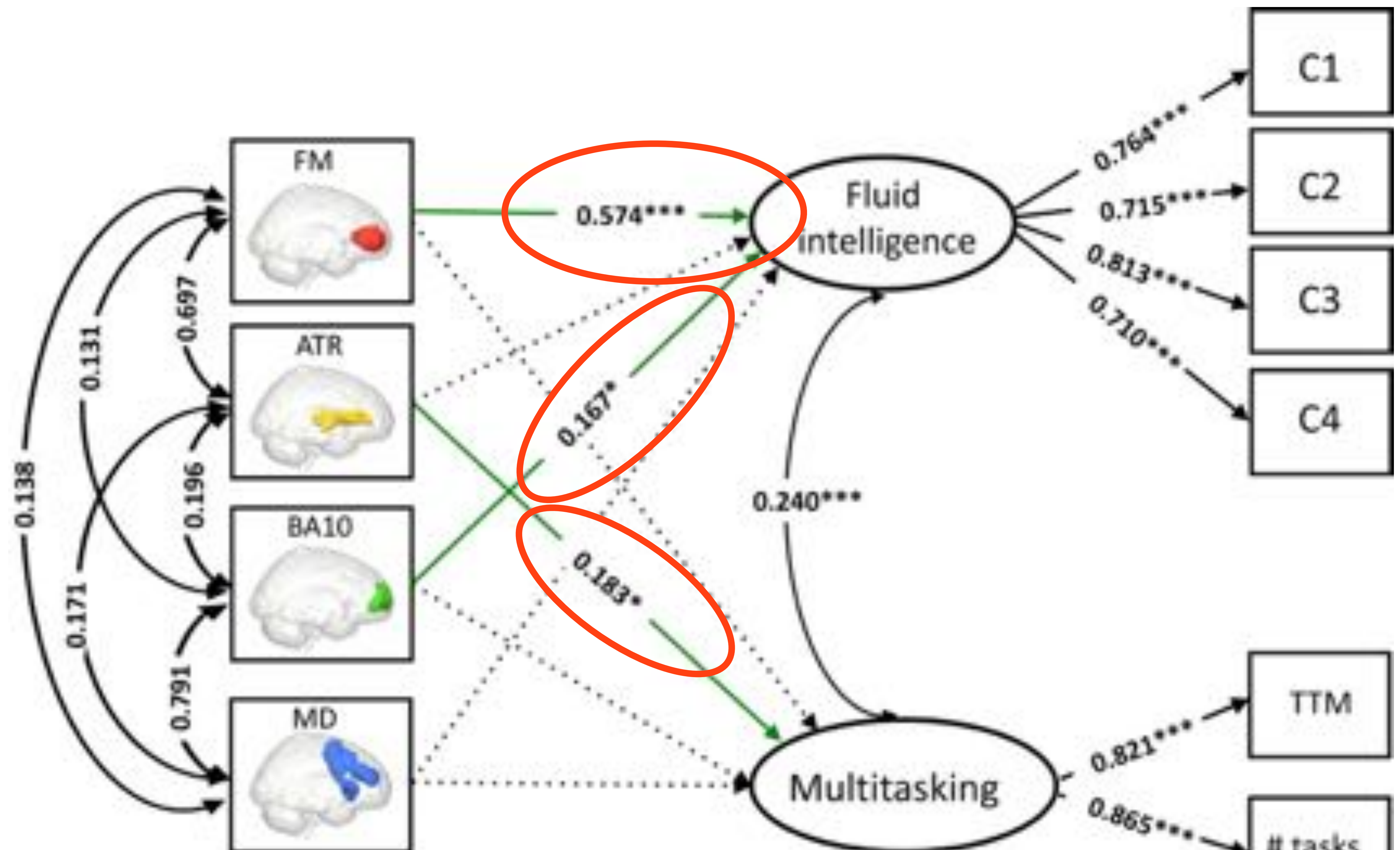
Testing the frontal lobe hypothesis

- Executive functions not unitary
- Frontal (neural) integrity not unidimensional
- Unique brain-behaviour mappings
- Grey and white matter: complementary roles
- Evidence against (simplistic versions of) frontal lobe hypothesis

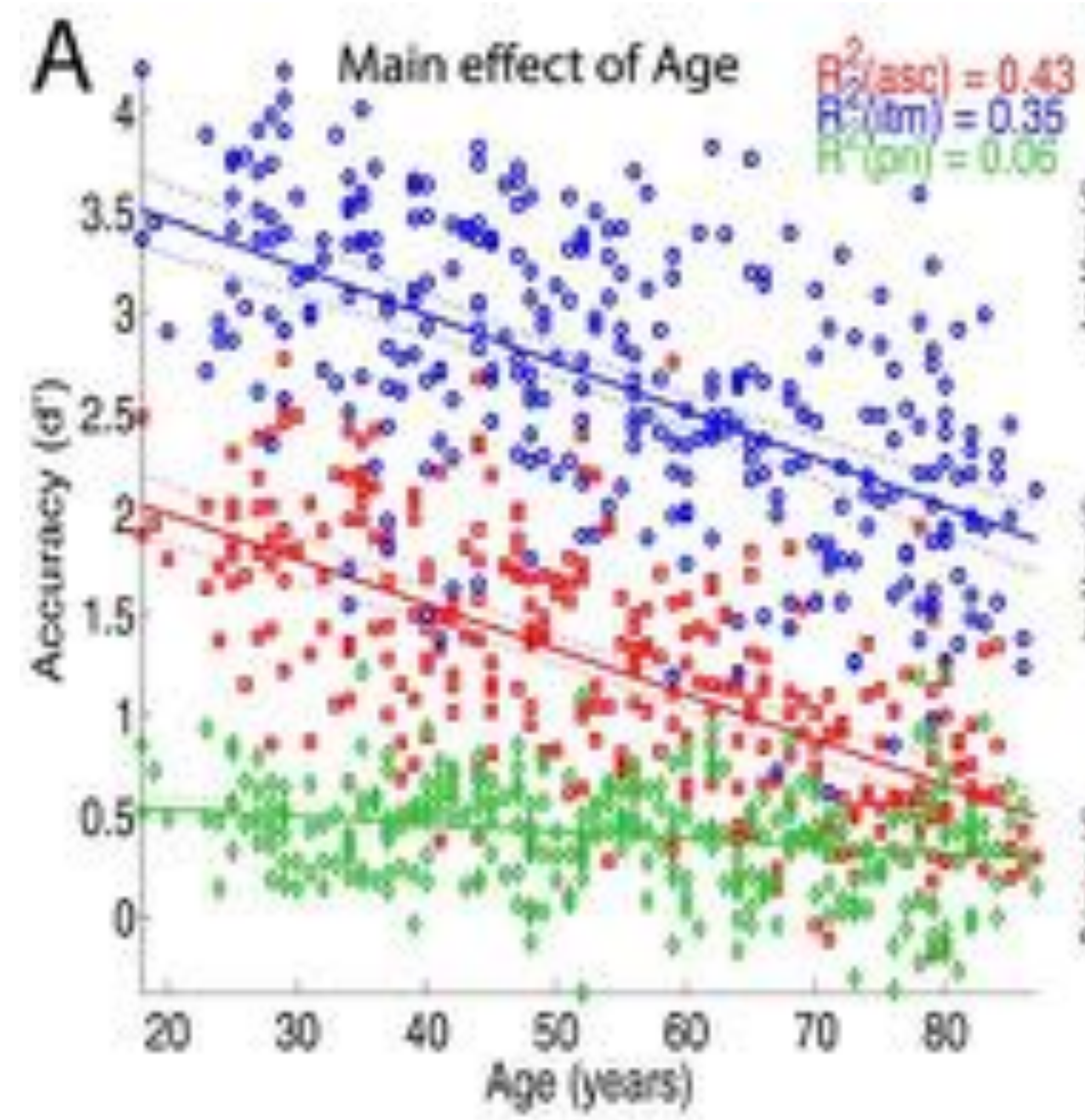


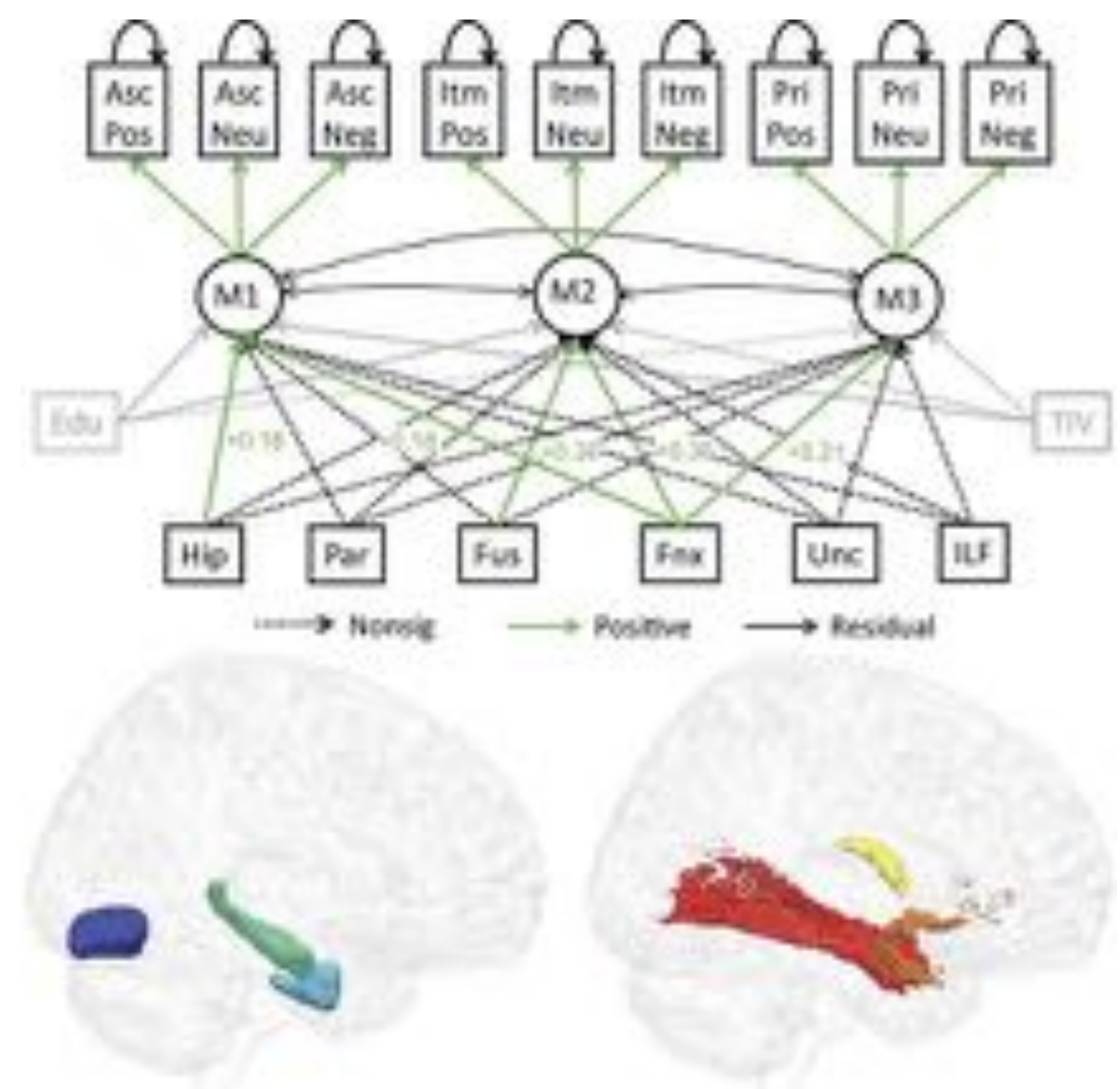


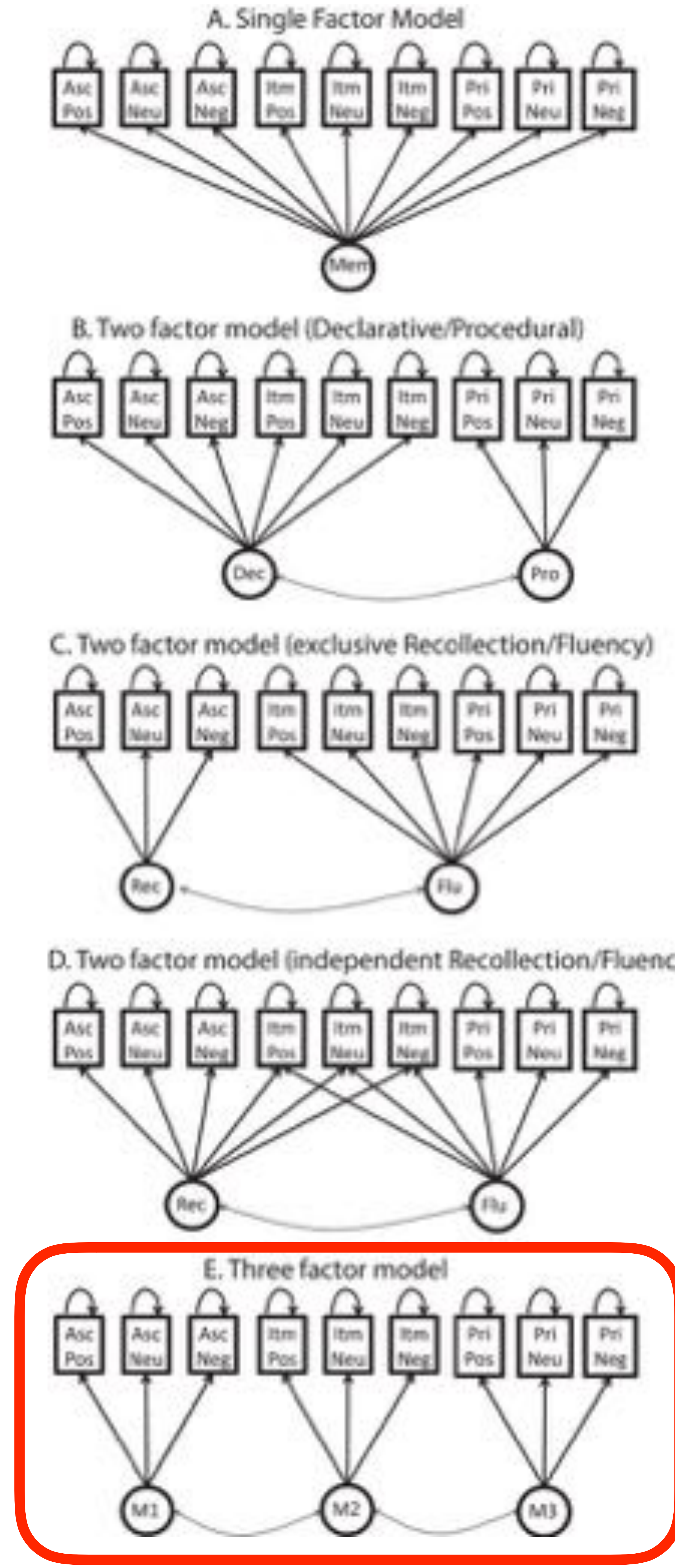
Kievit, R. A., Davis, S. W., Mitchell, D. J., Taylor, J. R., Duncan, J., Henson, R. N., & Cam-CAN Research team. (2014). Distinct aspects of frontal lobe structure mediate age-related differences in fluid intelligence and multitasking. *Nature Communications, 5,* 5658.

Understanding age-related changes in memory

- Directly comparing (mostly ‘word based’) memory models
- Yonelinas three factor model best
  - Associative memory
  - Recollection
  - Priming
- Differential age sensitivity
- Unique brain-behavior mapping for each factor

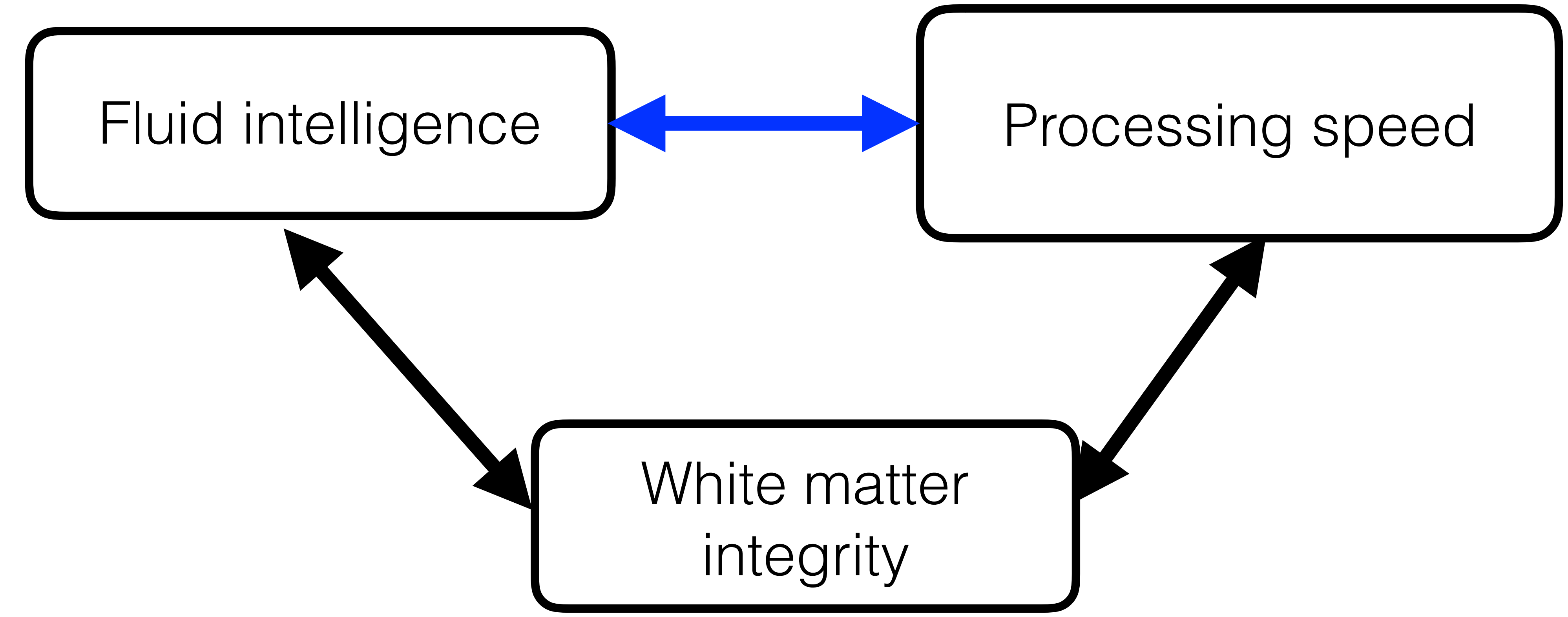




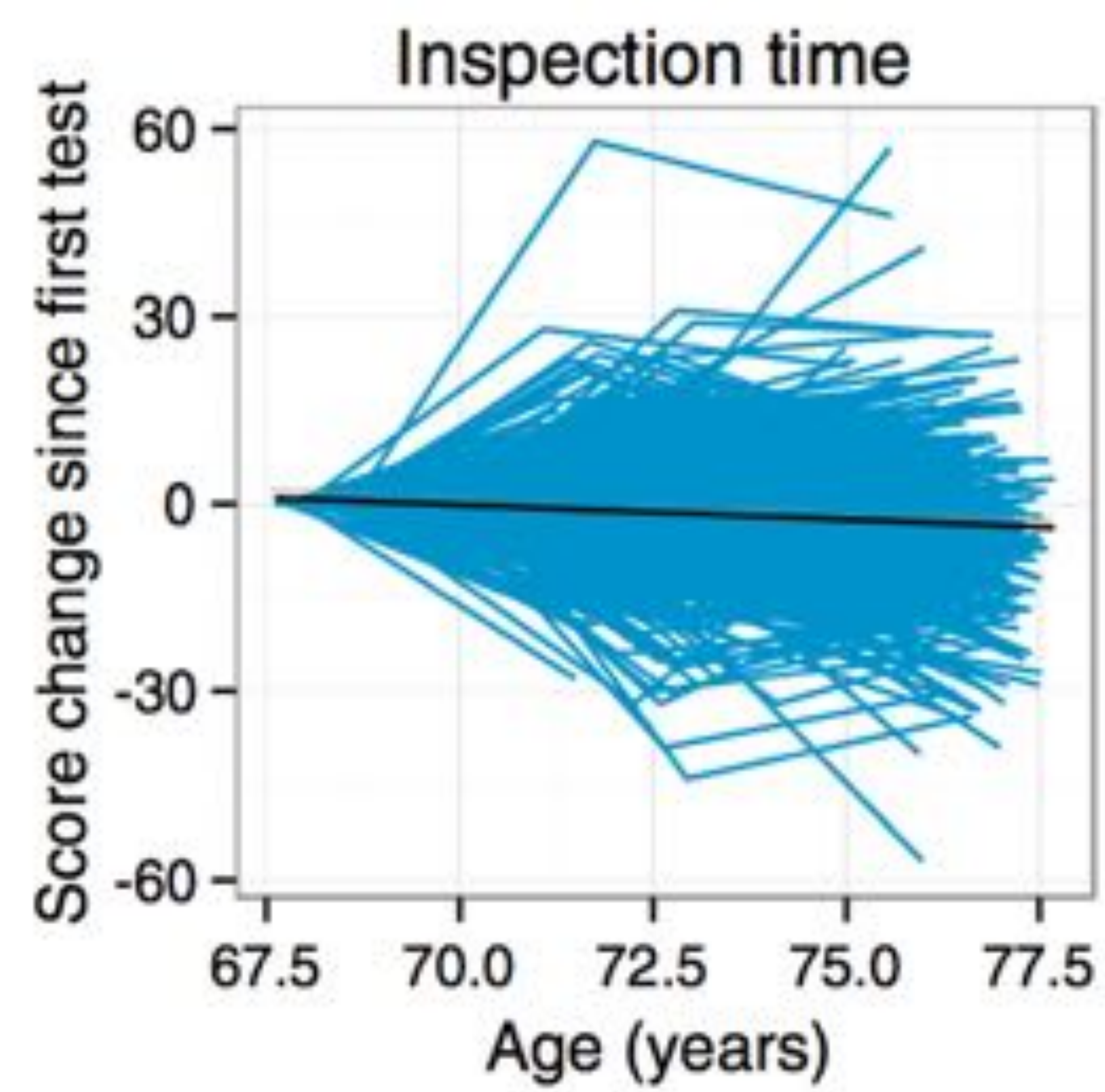


Henson, R. N. A., Campbell, K. L., Davis, S. W., Taylor, J. R., Emery, T., Erzinclioglu , S. Cam-CAN, & Kievit, R. A. (2016). Multiple determinants of ageing memories. Scientific Reports 6, 32527.

FI <-> PS



- Processing speed determines reasoning ability
- Salthouse (simultaneity, limited time) (1996)
- *Change* in inspection time and *change* in intelligence from 70 to 76 (r = 0.779) (Ritchie et al., 2013)
- Two thirds of the age-based changes in fluid and intelligence, perceptual speed shared (Ghisletta et al., 2012)



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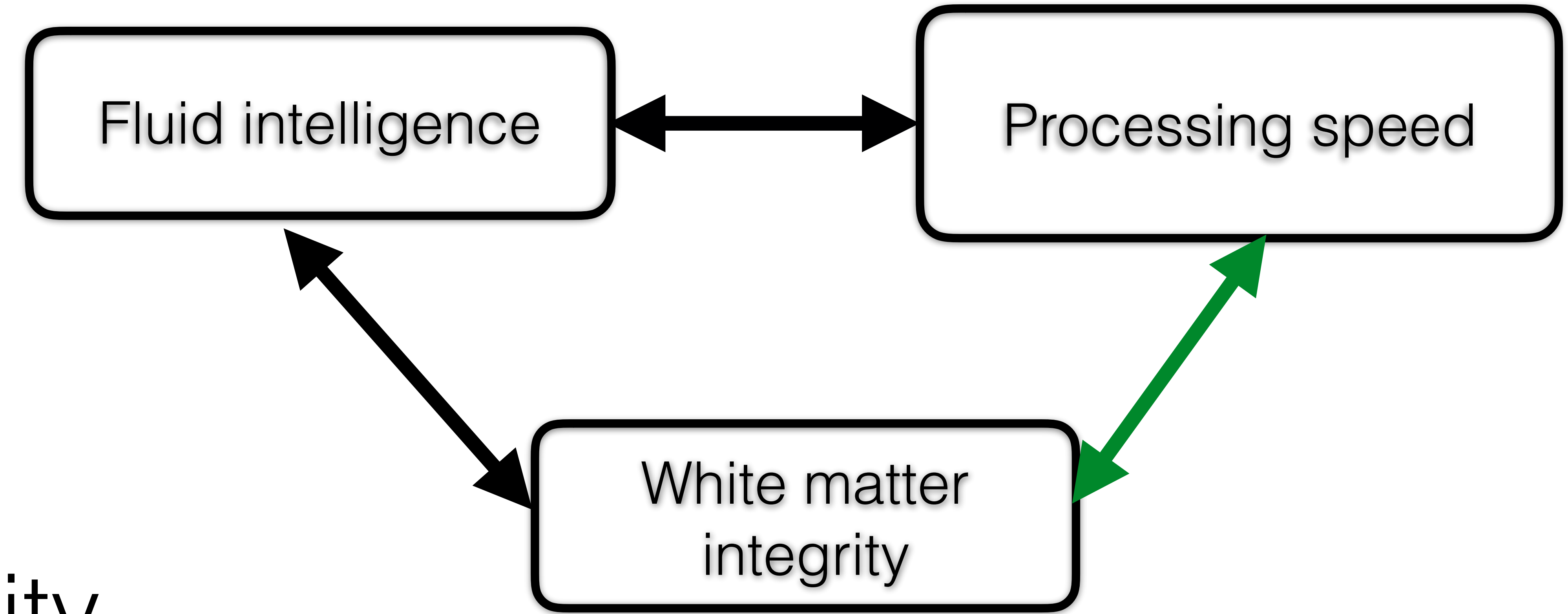
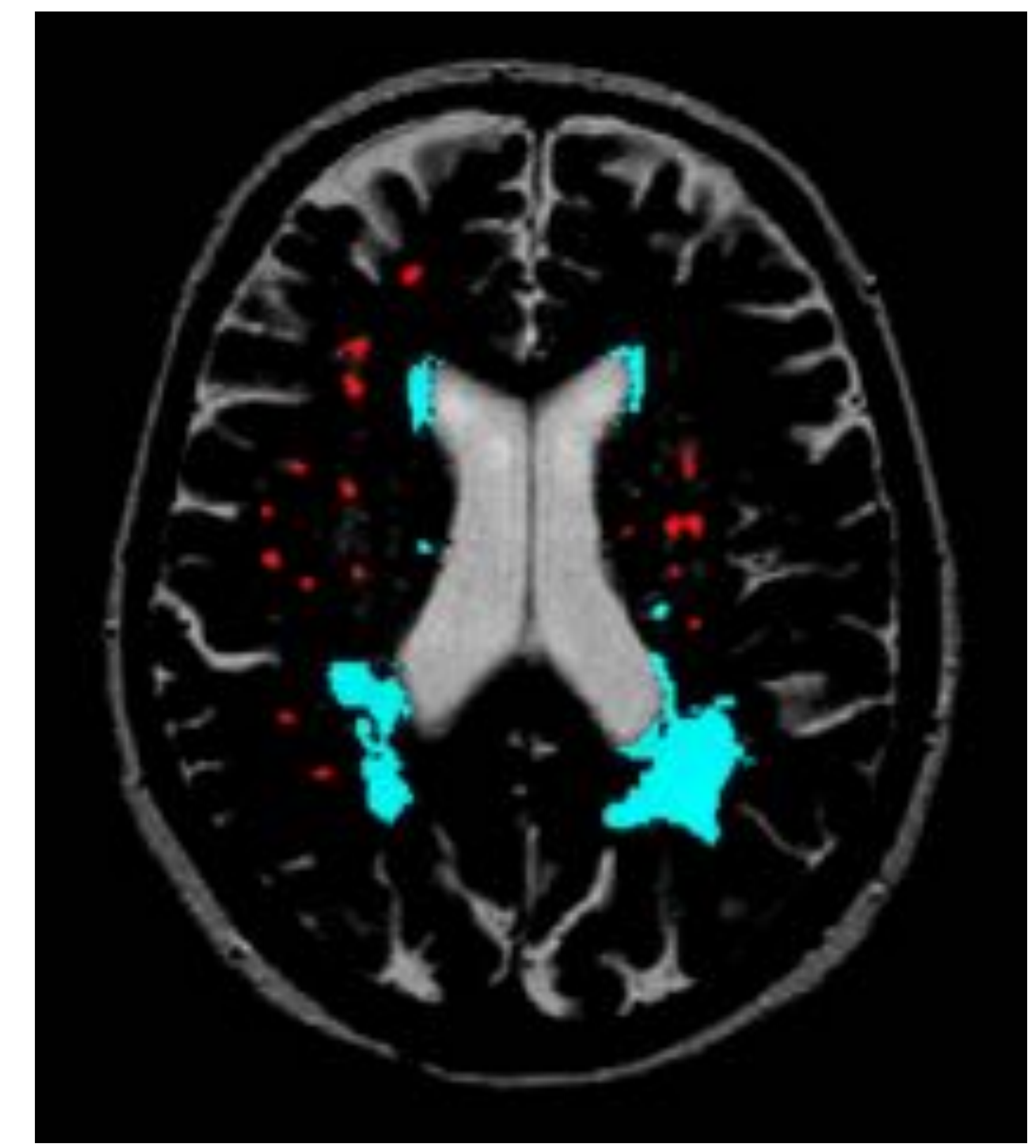


- A general factor of brain white matter integrity predicts information processing speed in healthy older people (Penke et al., 2010)
- Hyperintensities associated with slower response time (Papp et al., 2013)
- Mechanisms:
  - Faster nerve transduction speed
  - Lower gaussian noise



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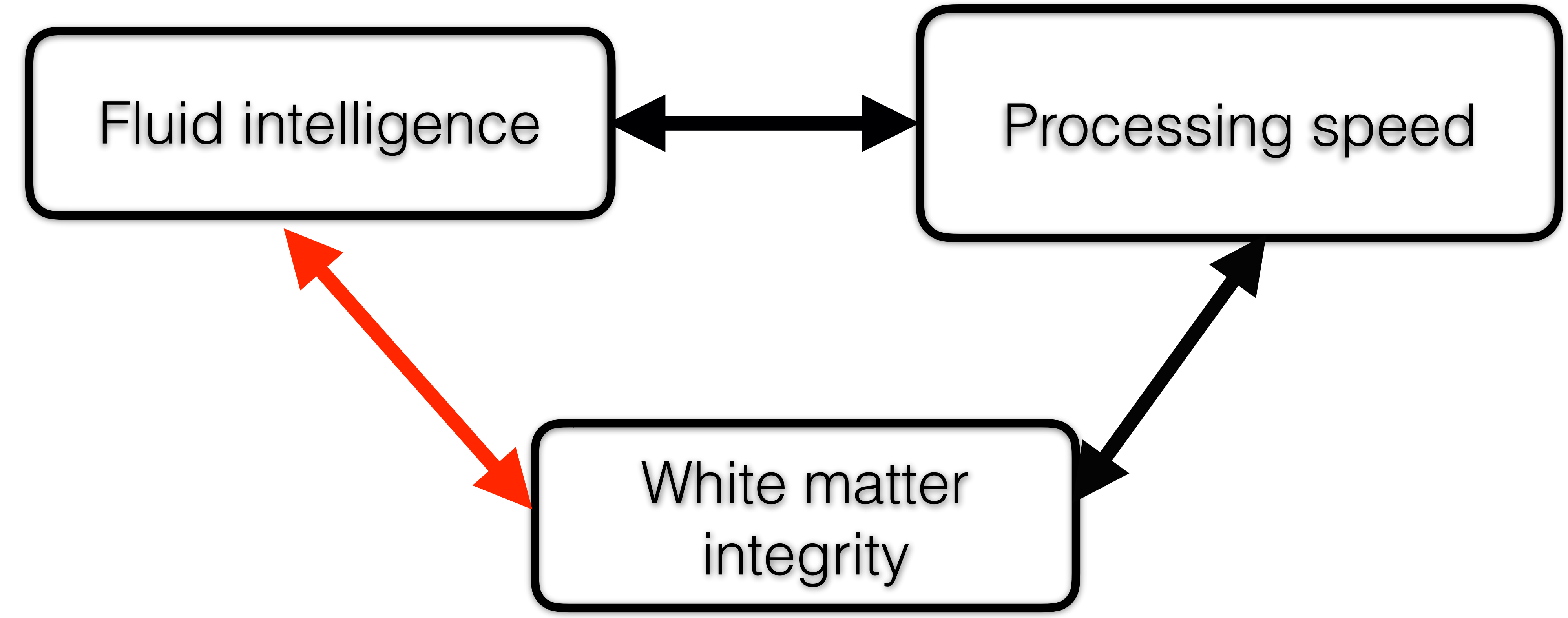

- White matter integrity predicts fluid intelligence in old age (e.g. Kievit et al., 2014)
- General white matter health predicts intelligence (Penke et al., 2012)
- Longitudinal changes in white matter microstructure were coupled with changes in fluid intelligence (Ritchie et al., 2015, but see Bender et al., 2016)