

Modeling Reserve as Residual Cognition

What you don't know can help you!

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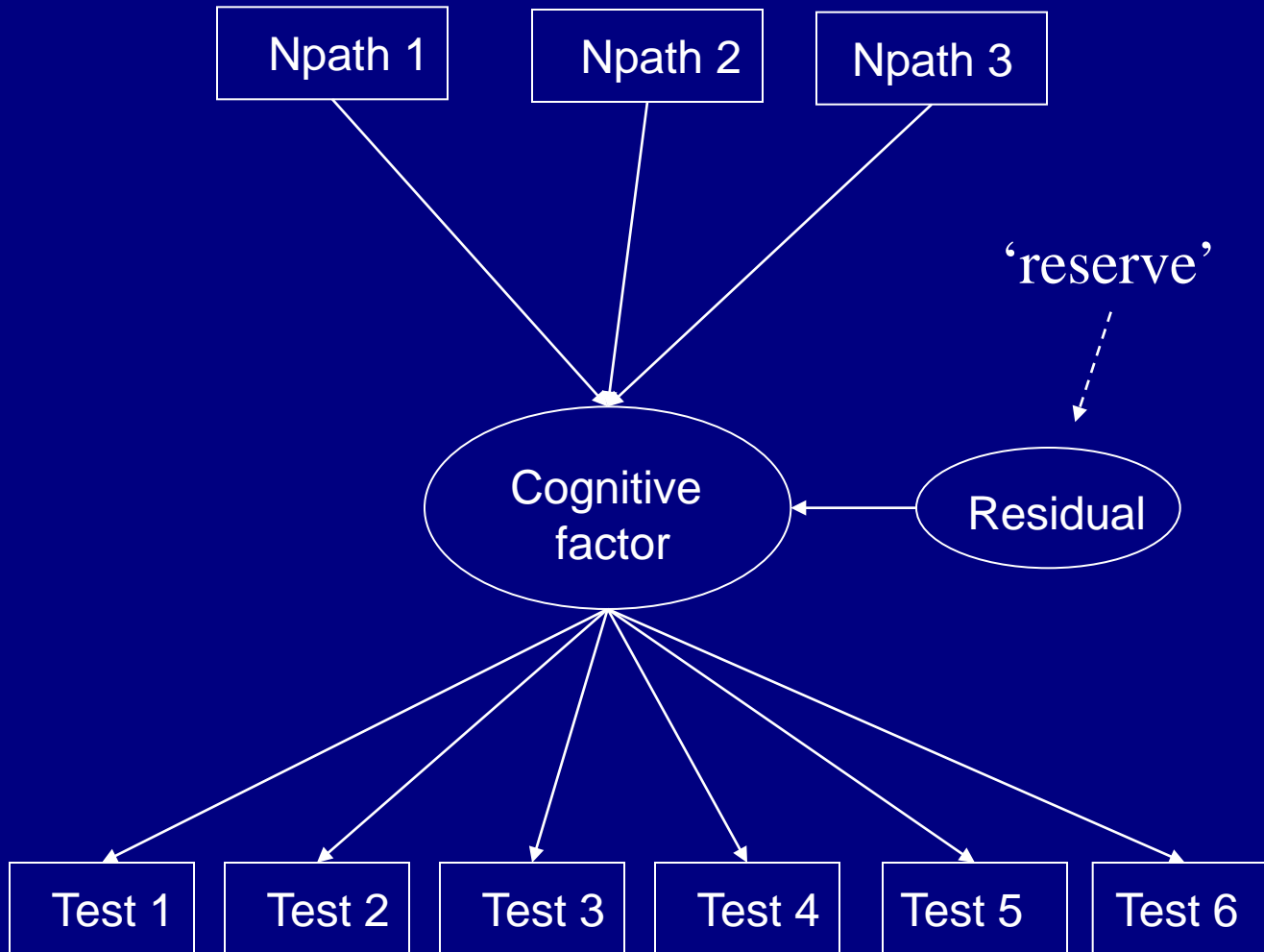
Background

- Brain pathology diminishes cognitive performance; effects are highly variable across individuals
- Cognitive reserve is often used to explain the imperfect correlation between brain pathology and clinical status
- It is a hypothetical construct
- Proxy variables, especially education, are often used in studies of cognitive reserve

Approach

- Conceptually, reserve explains deviations from the level of cognitive performance that would be expected for a given amount of brain pathology
 - High reserve = better than expected performance
- We modeled reserve as residual cognition after accounting for neuropathology

Conceptual Illustration of Approach



Data Sources

- 701 Neuropathology cases
 - Rush Memory Assessment Project (MAP) (n=272)
 - Rush Religious Orders Study (ROS)(n=429)
- All cases had comparable annual neuropsychological assessments
- Potential Reserve Indicators: leisure time cognitive activity (MAP), education, lifetime SES

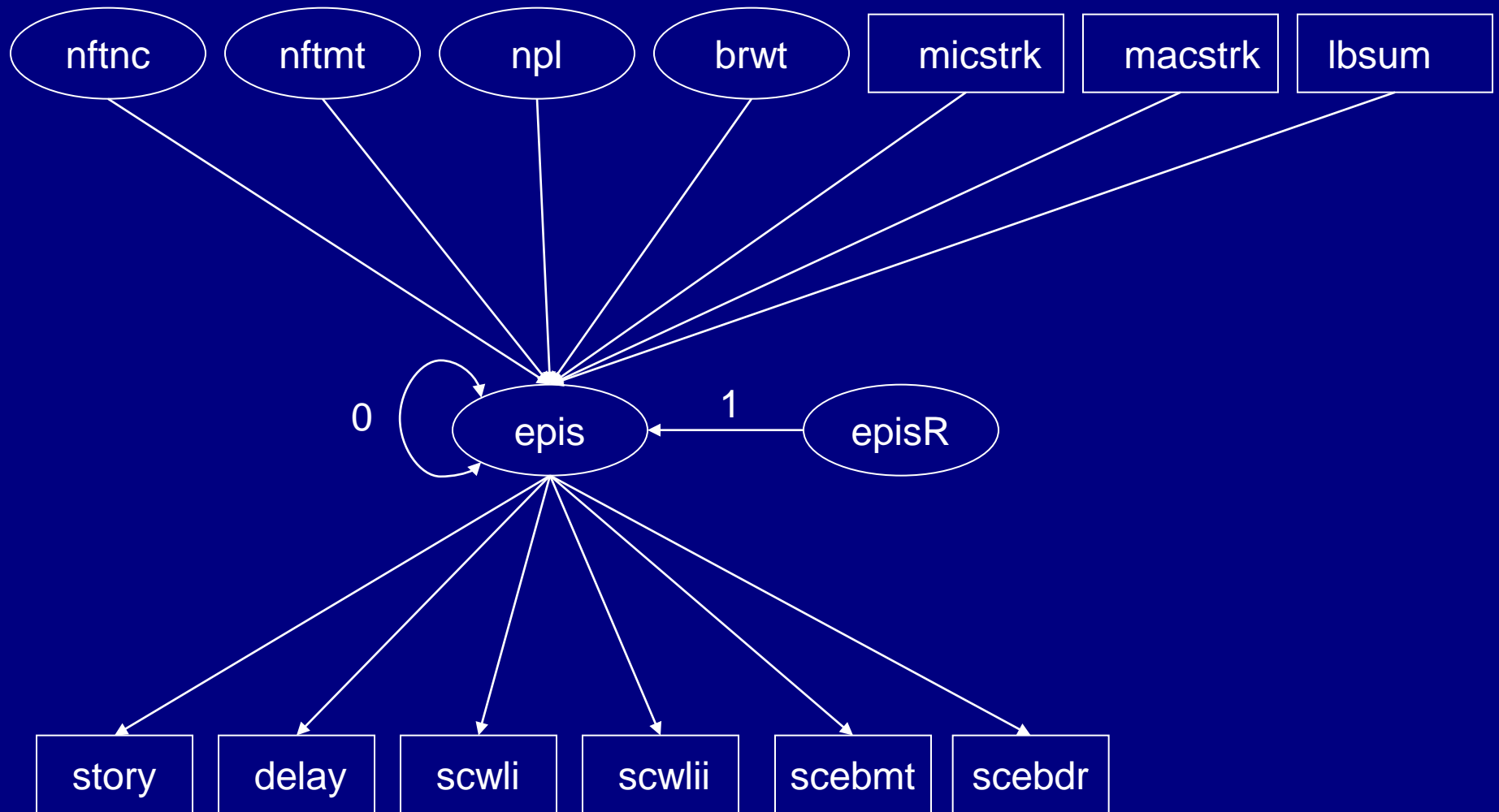
Model-building Steps

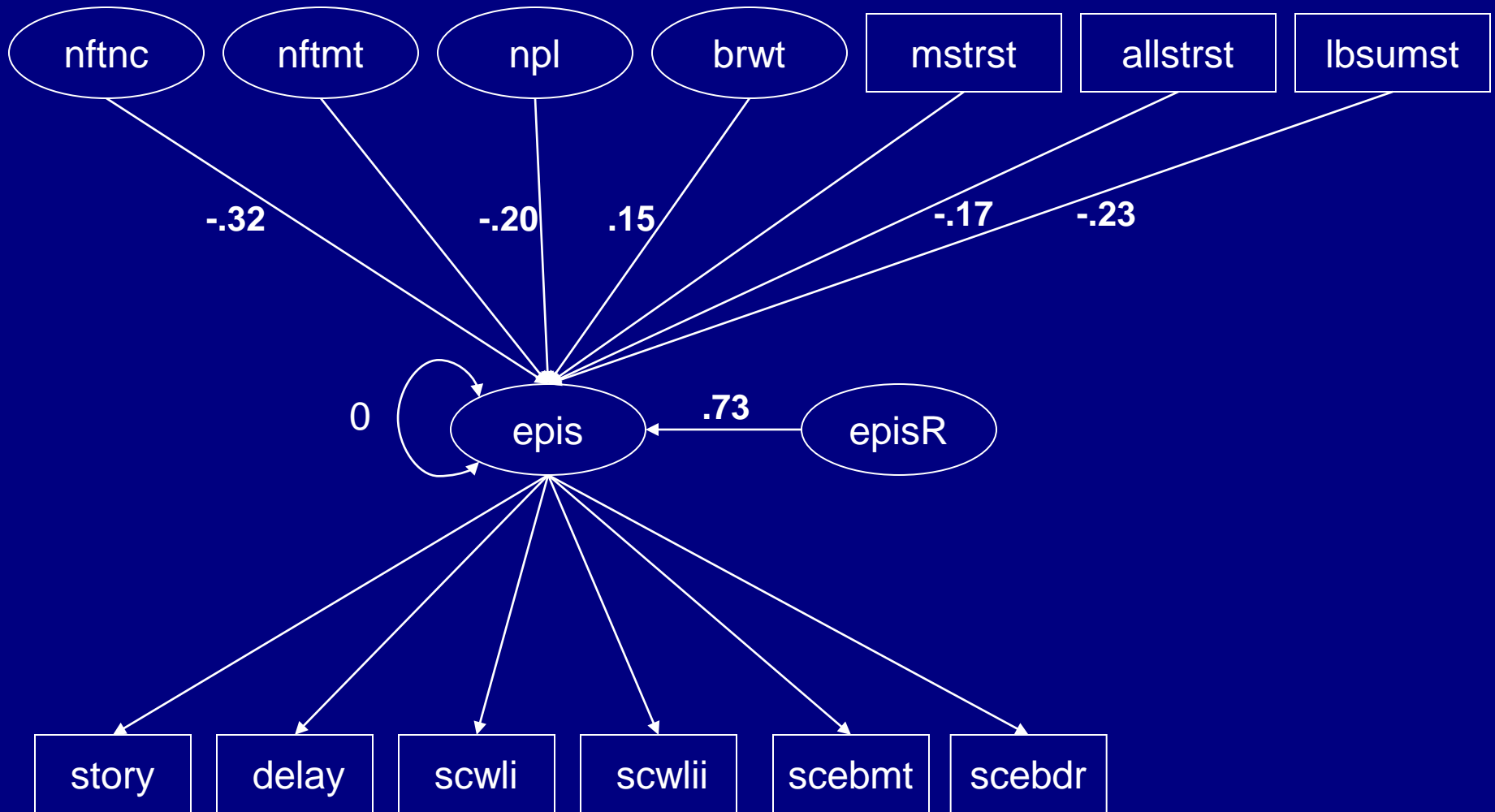
(Mplus code available upon request)

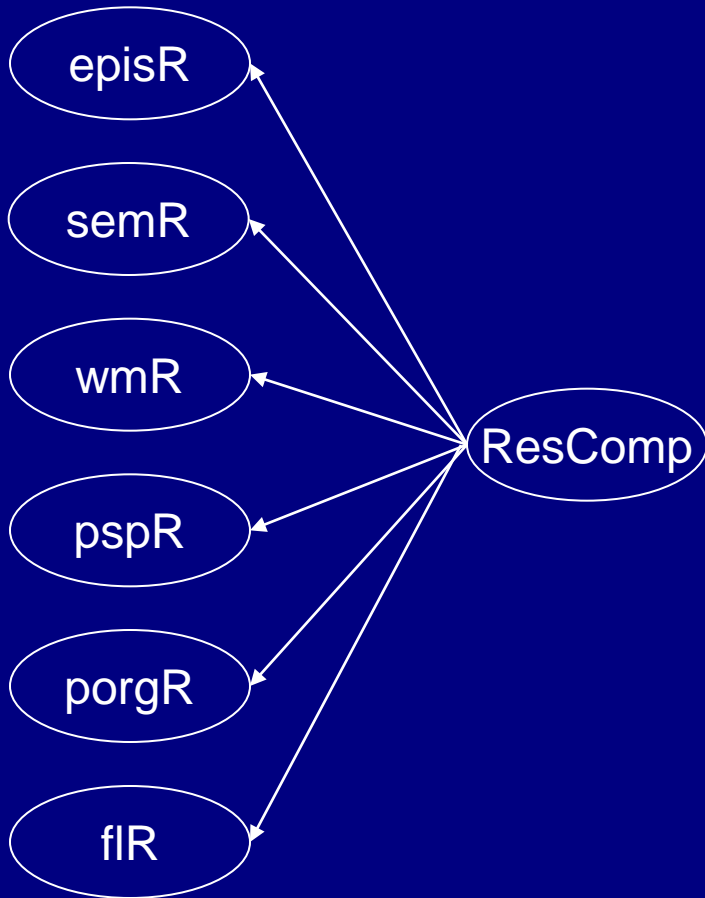
- CFA of AD neuropathology
- CFA of cognitive measures
- Regression of cognitive domains (factors) on neuropathology (AD, VD, LBD)
- Capture residual cognition in latent variables
- Examine dimension structure of residuals across domains; create a second order reserve factor
- Examine independent predictors of reserve

Results

Episodic Memory Component of “Residual” Model

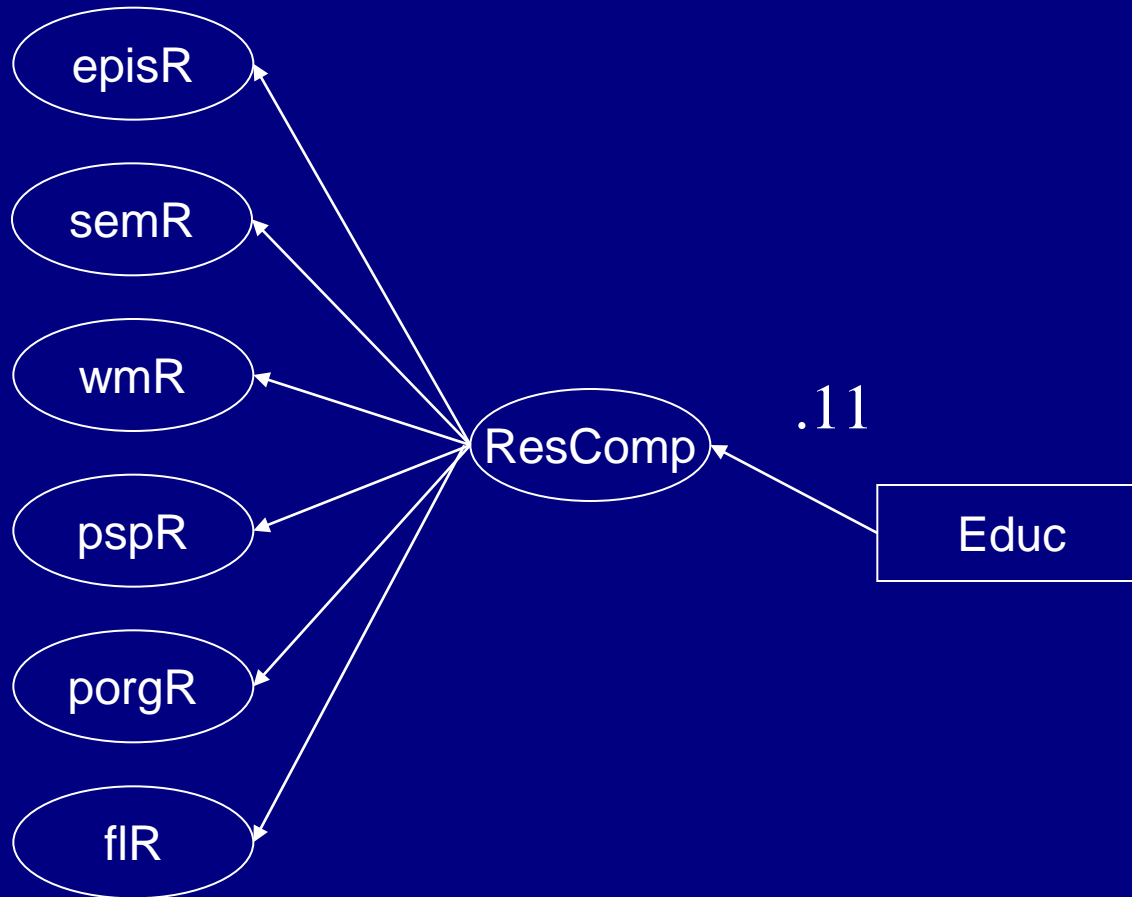


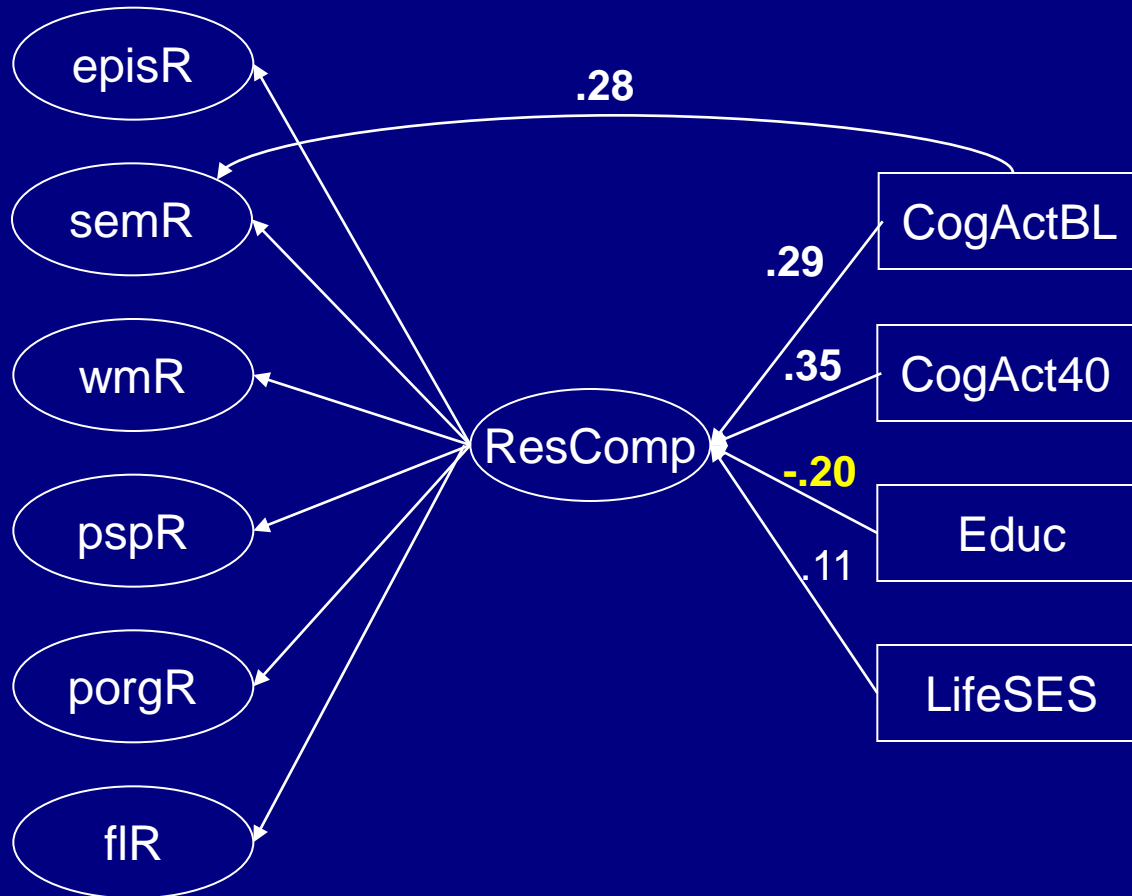




- Model estimated 6 residual terms, 1 for each cognitive domain
- Evaluation of covariance structure showed a single, second order factor accounted for variance in the 6 domains very well

* Each residual estimated simultaneously





Summary

- It is possible to operationally define reserve as residual cognition using latent variable modeling
- Our results consistent with previous studies from the Rush MAP showing that cognitive activity is an important indicator of reserve
- Results are novel in showing that education is not positively related to reserve independent of cognitive activity
- Operationally defining reserve as residual cognition is a useful approach

Reserve as Residual Workgroup

- Eddie Billingslea, Ph.D. - NIA
- Maritza Dowling, Ph.D. - University of Wisconsin
- Dan Mungas, Ph.D. - UC Davis
- Bruce Reed, Ph.D. - UC Davis
- Joshua Sonnen, M.D. - University of Washington
- Milton Strauss, Ph.D. - Case Western Reserve University, Emeritus
- Sarah Tomaszewski Farias, Ph.D. - UC Davis

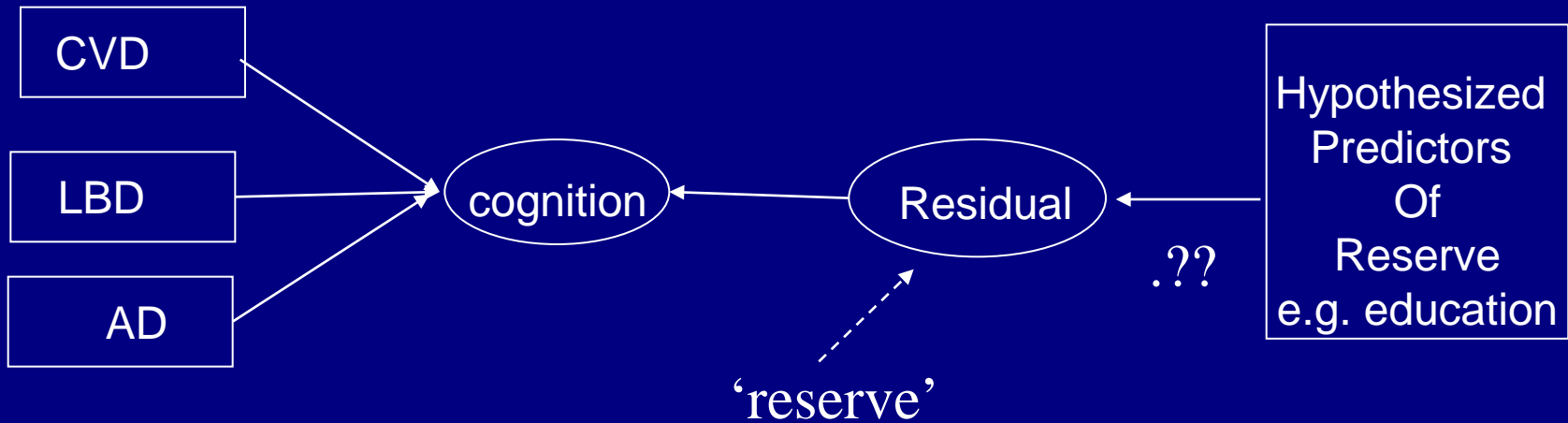
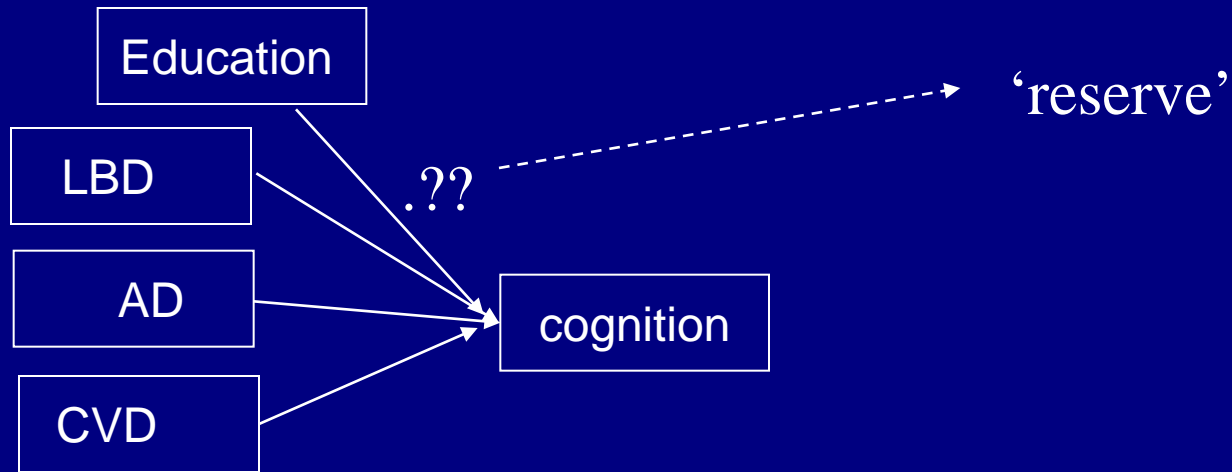
Acknowledgements

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- Advanced Psychometric Methods in Cognitive Aging Research - D Mungas, PI (R13AG030995)
- Brain Pathologies, Reserve and Cognition - B. Reed, PI (R01 AG031563)

Conclusions

- Operationally defining reserve as residual cognition is a useful approach
- Provides a direct, quantitative, individually-specific measure
- Can be used either as a predictor, to study reserve effects, or as a dependent measure in investigations of what determines reserve
- Also enables investigation of how reserve changes over time, and of “domain-specific” reserve
- Quantifying “how much” reserve there serves as a heuristic device; it challenges us to find the determinants of reserve and other factors that explain variability in the effects of pathology on cognitive performance

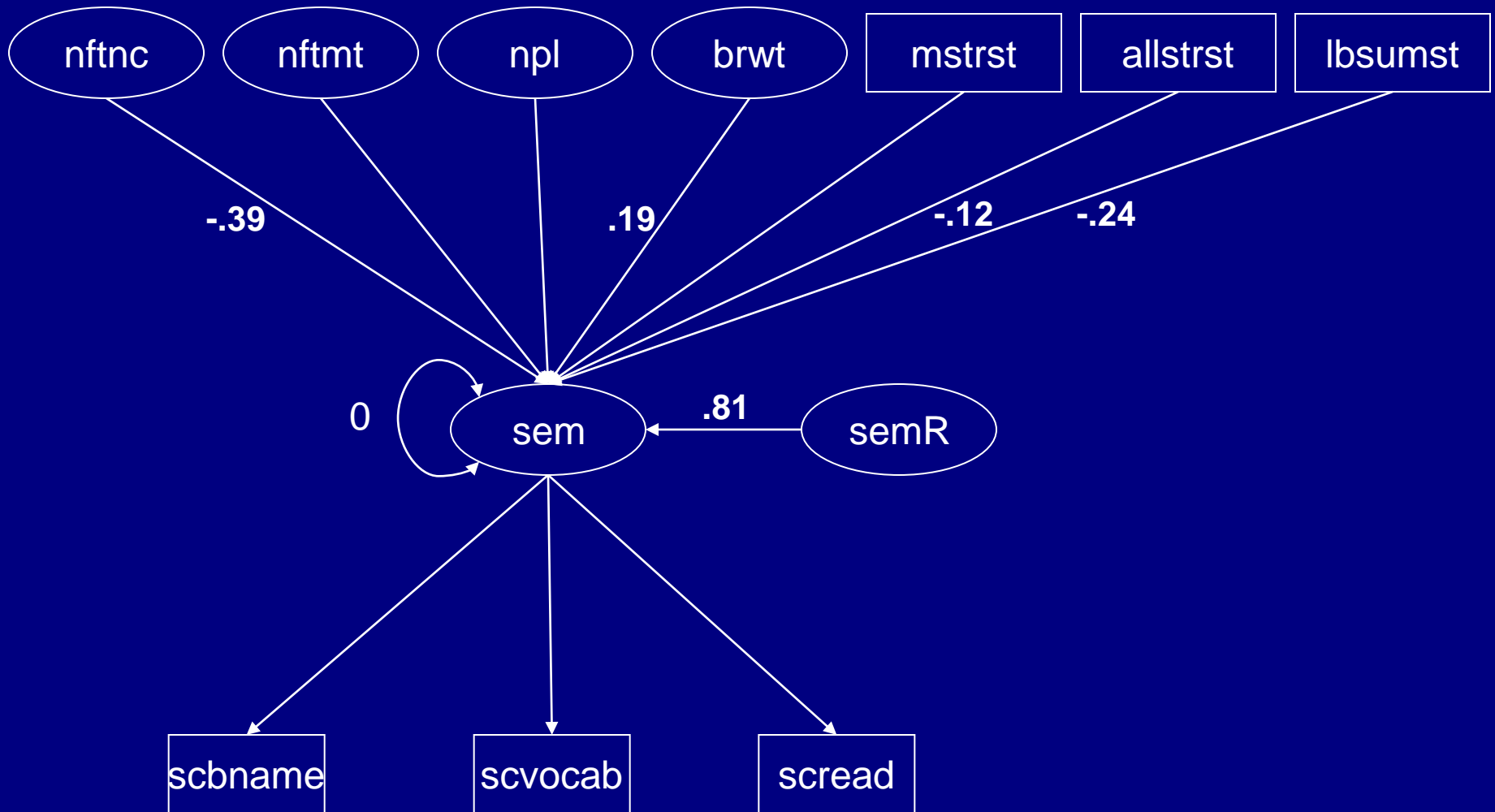
Traditional vs. Residual modeling of reserve

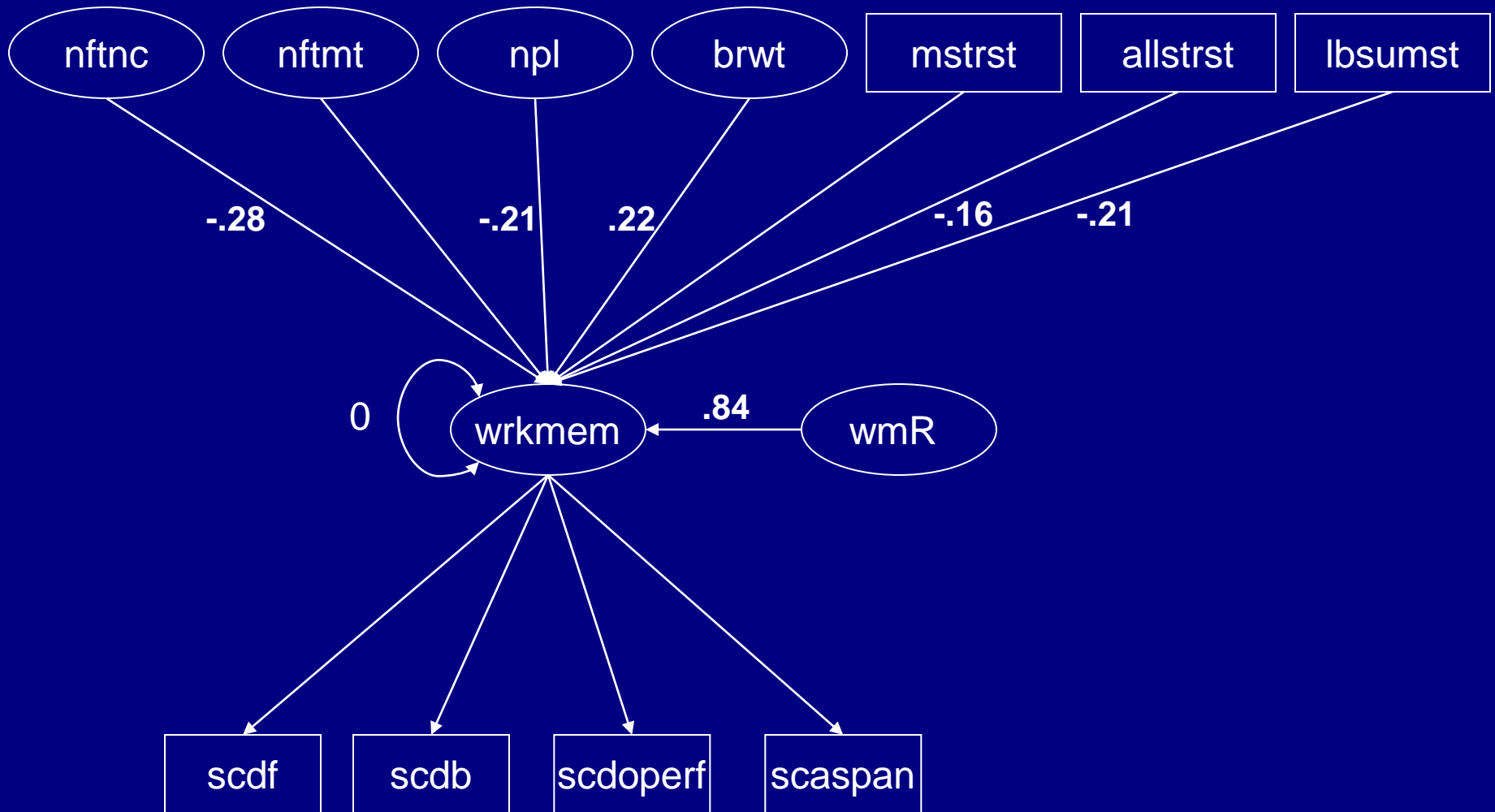


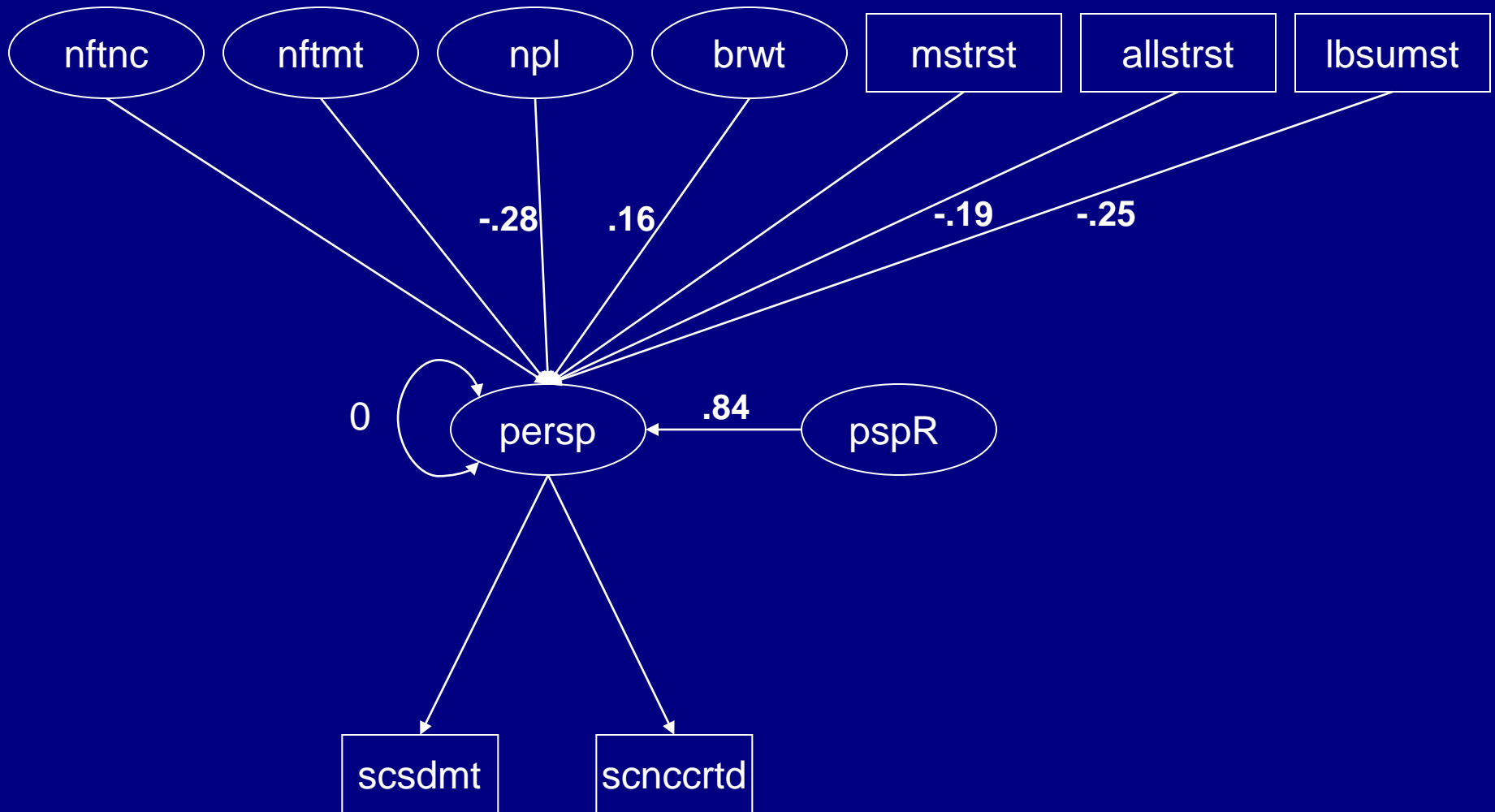
Prior Findings

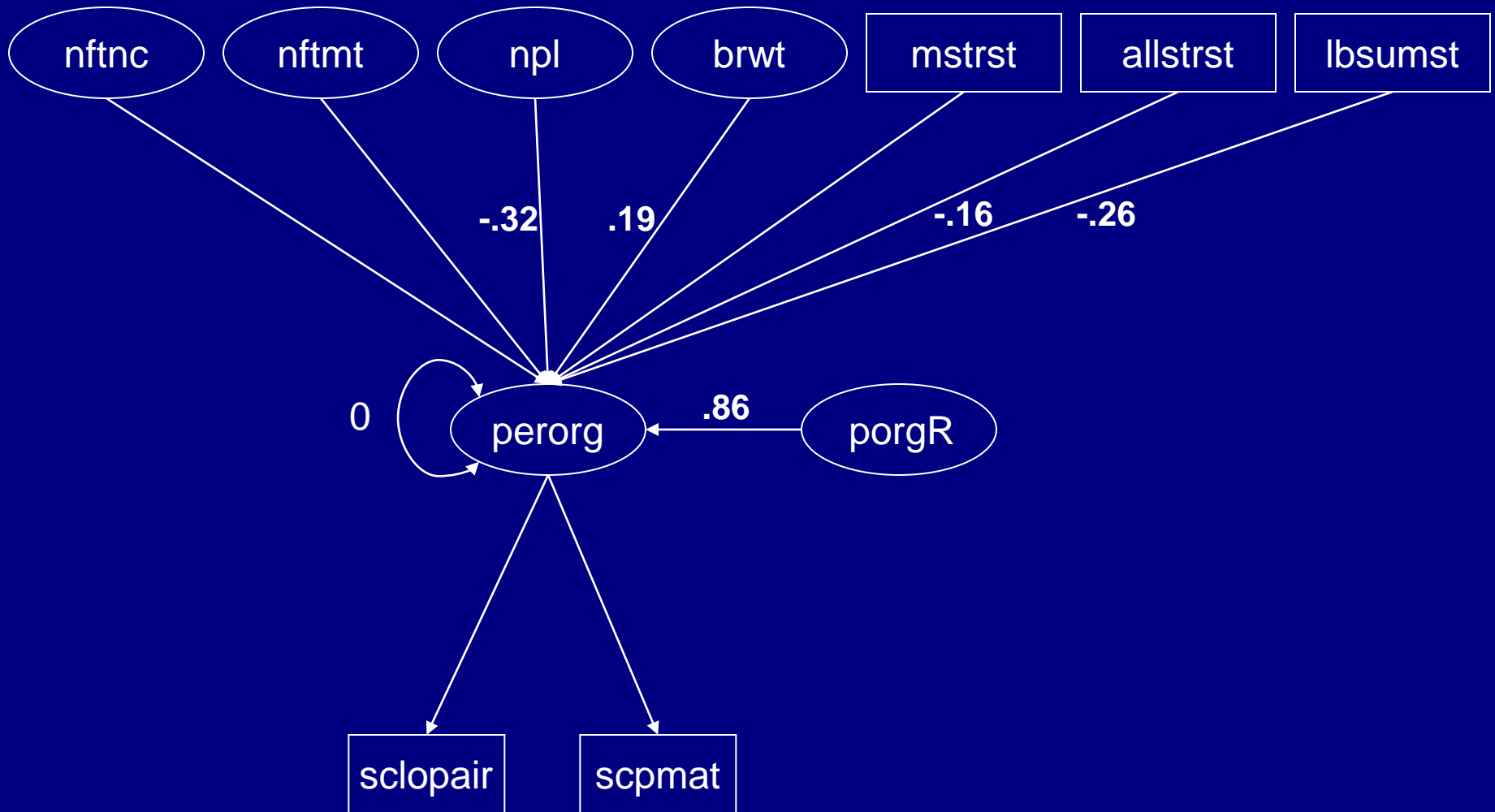
Using our ADC cohort we tested several hypotheses regarding cognitive reserve using the residual of episodic memory on MRI markers of pathology to measure reserve. Results showed:

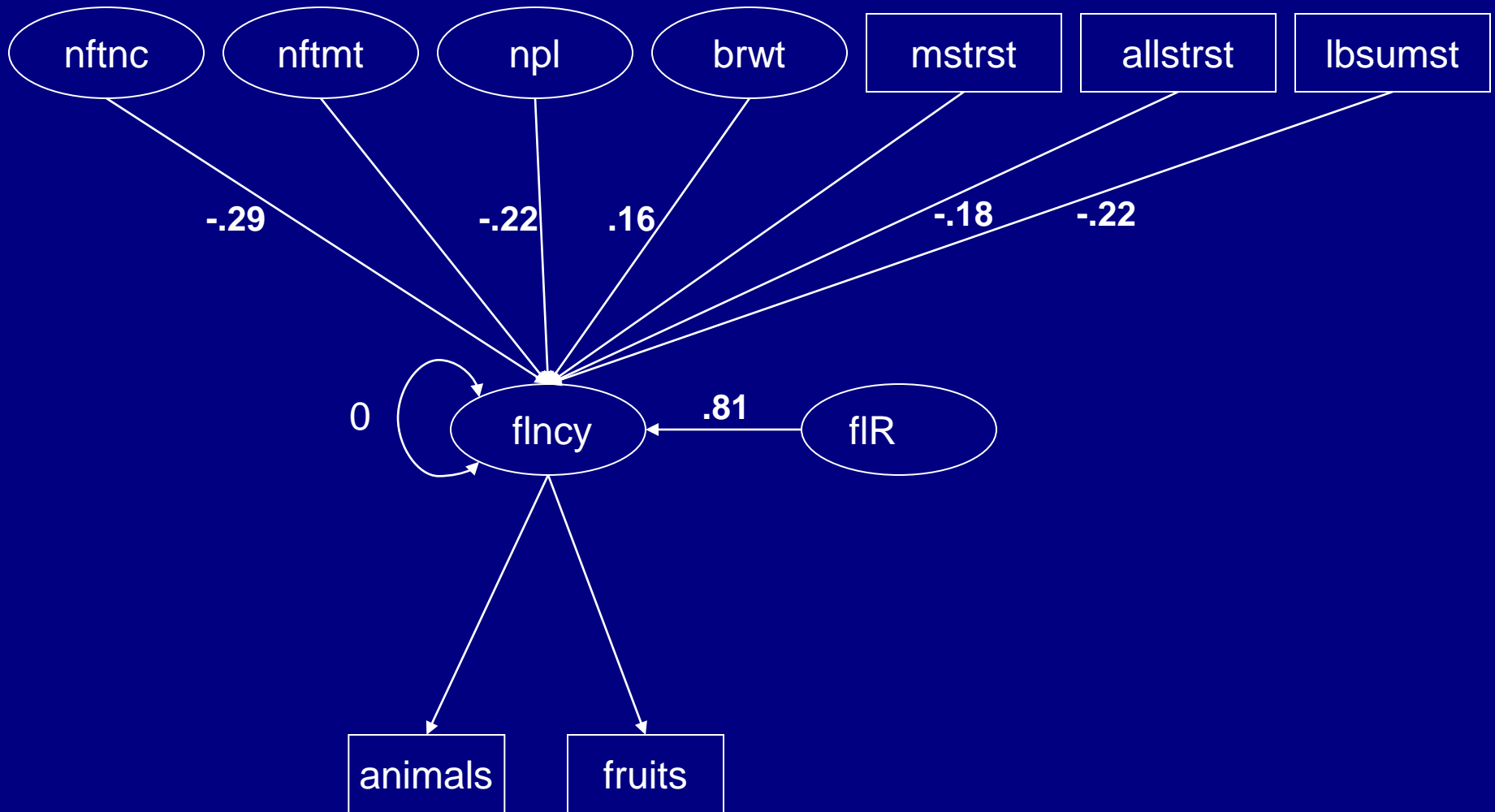
- Higher reserve is associated with slower longitudinal decline in executive function
- Higher reserve reduces the risk of conversion from MCI to dementia
- Brain atrophy has a greater effect on cognitive function in low reserve cases than in high reserve cases.

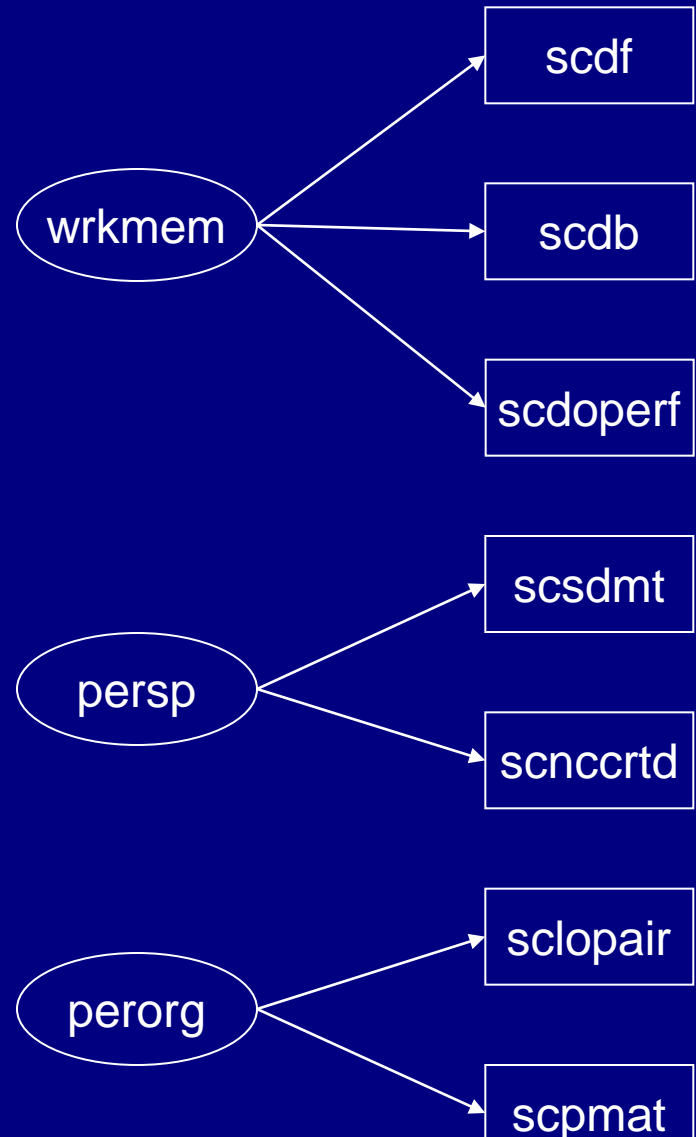
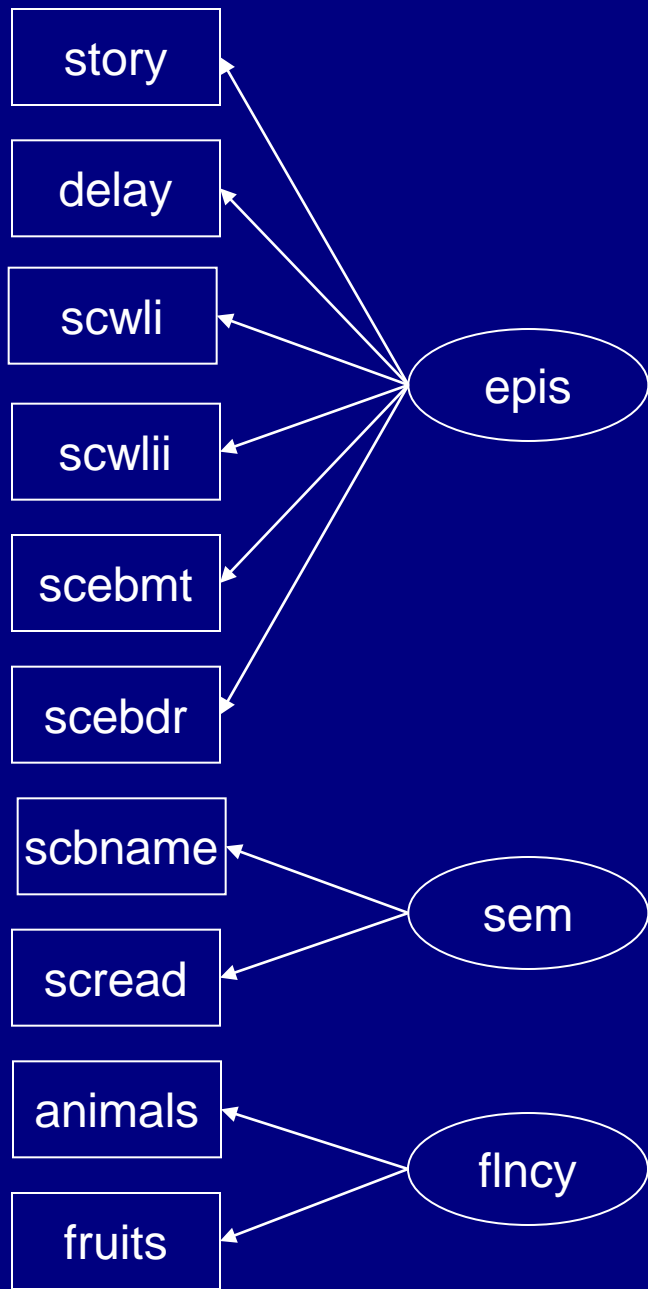












Potential advantages

- ✓ explicitly defined
- ✓ quantitative and individually specific
- ✓ makes no assumptions about what contributes to reserve

Parameterized in this way, it is straightforward to:

- ✓ test potential determinants of reserve
- ✓ Test hypothesized effects of reserve

Disclaimer

- Not a perfect or pure measure: Captures unmeasured systematic variance and sources of random error.
- Whether or not it is a useful measure of reserve can be empirically tested