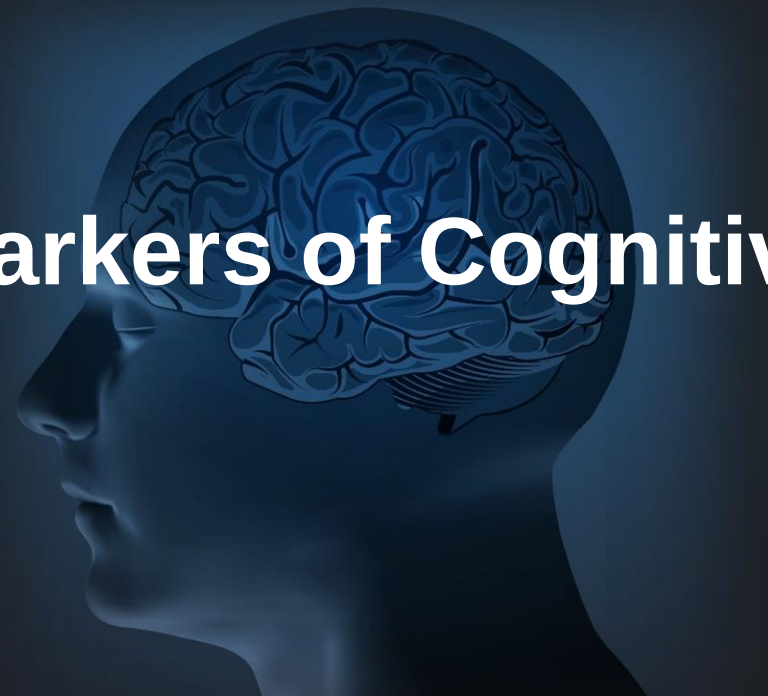

# Behavioral Markers of Cognitive Reserve

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# *DISCLOSURES: supported by National Institute on Aging, Illinois Department of Public Health*

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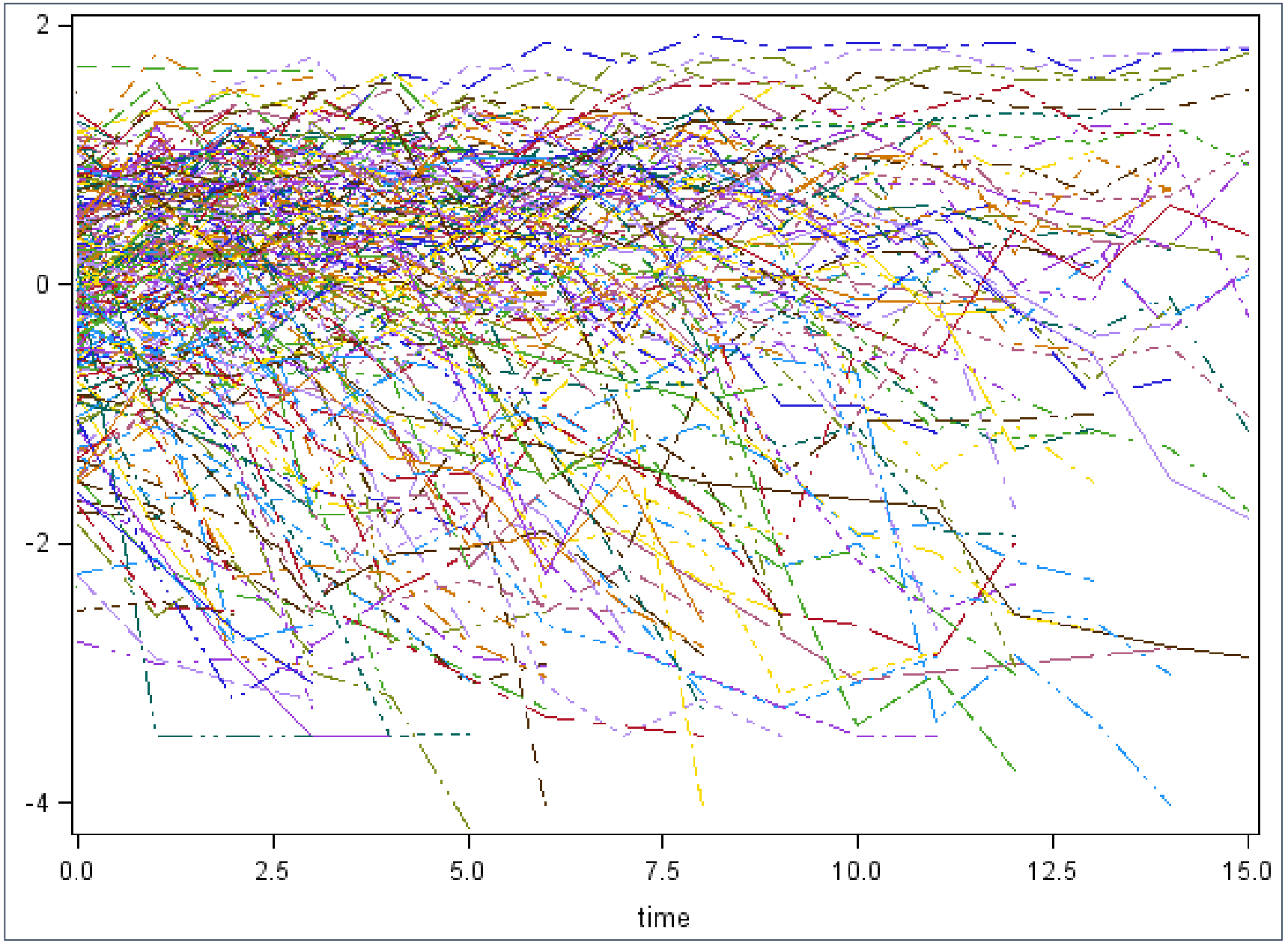
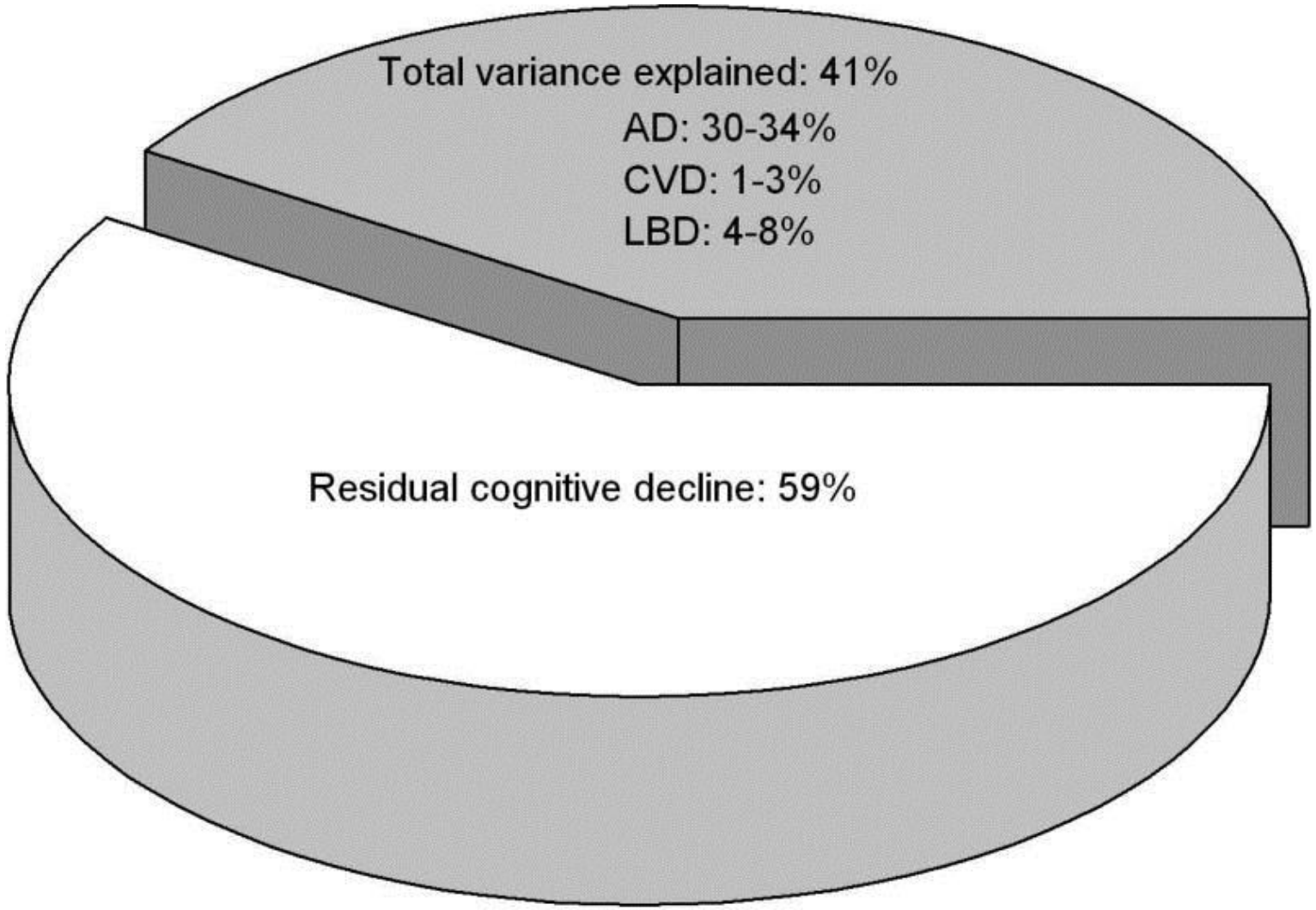
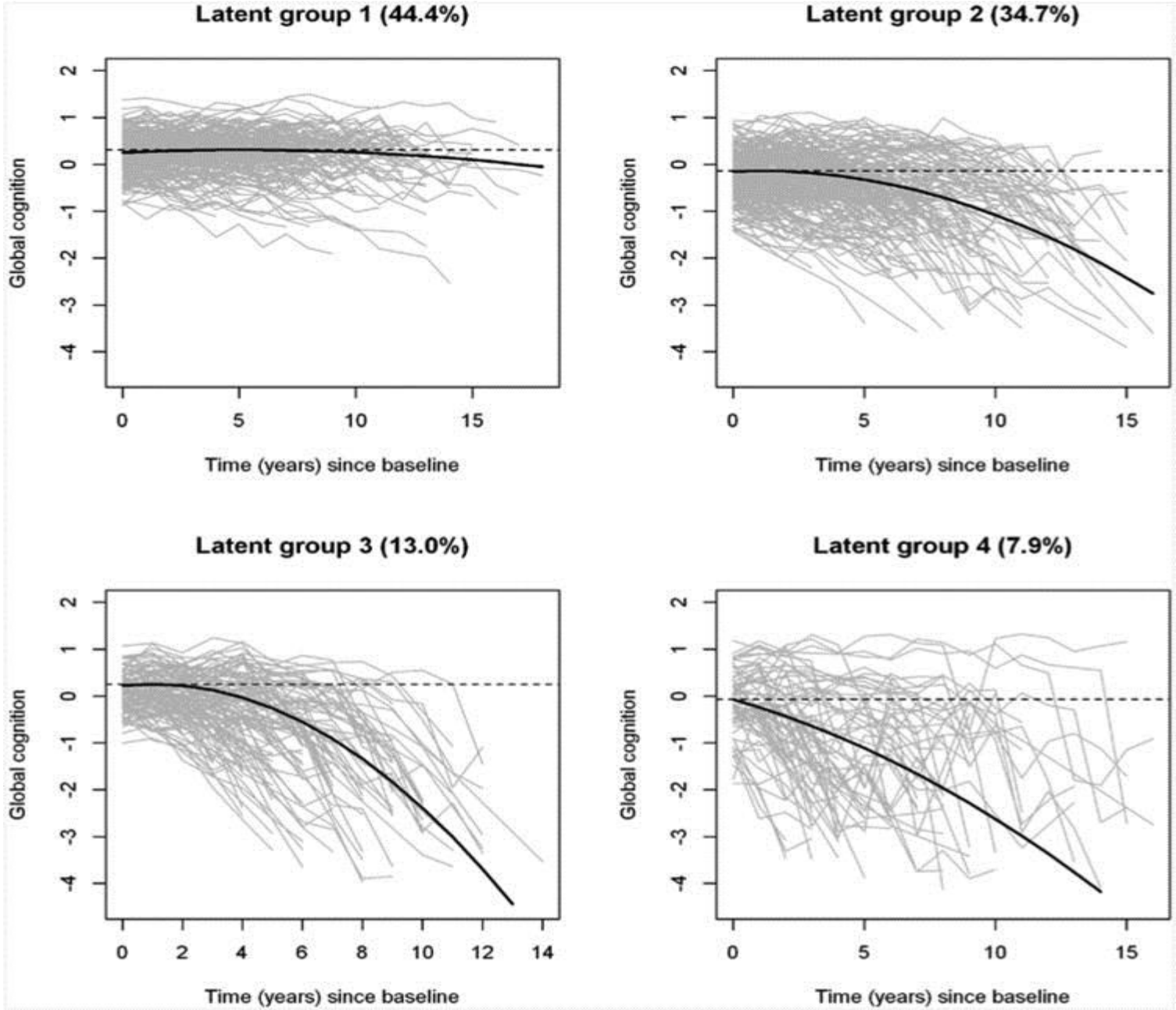
# Objectives

- Clarify association of dementia related pathologies with late-life change in cognitive function
- Identify potentially modifiable behaviors associated with cognitive change not attributable to pathology

# Heterogeneity of cognitive decline in old age: spaghetti plot

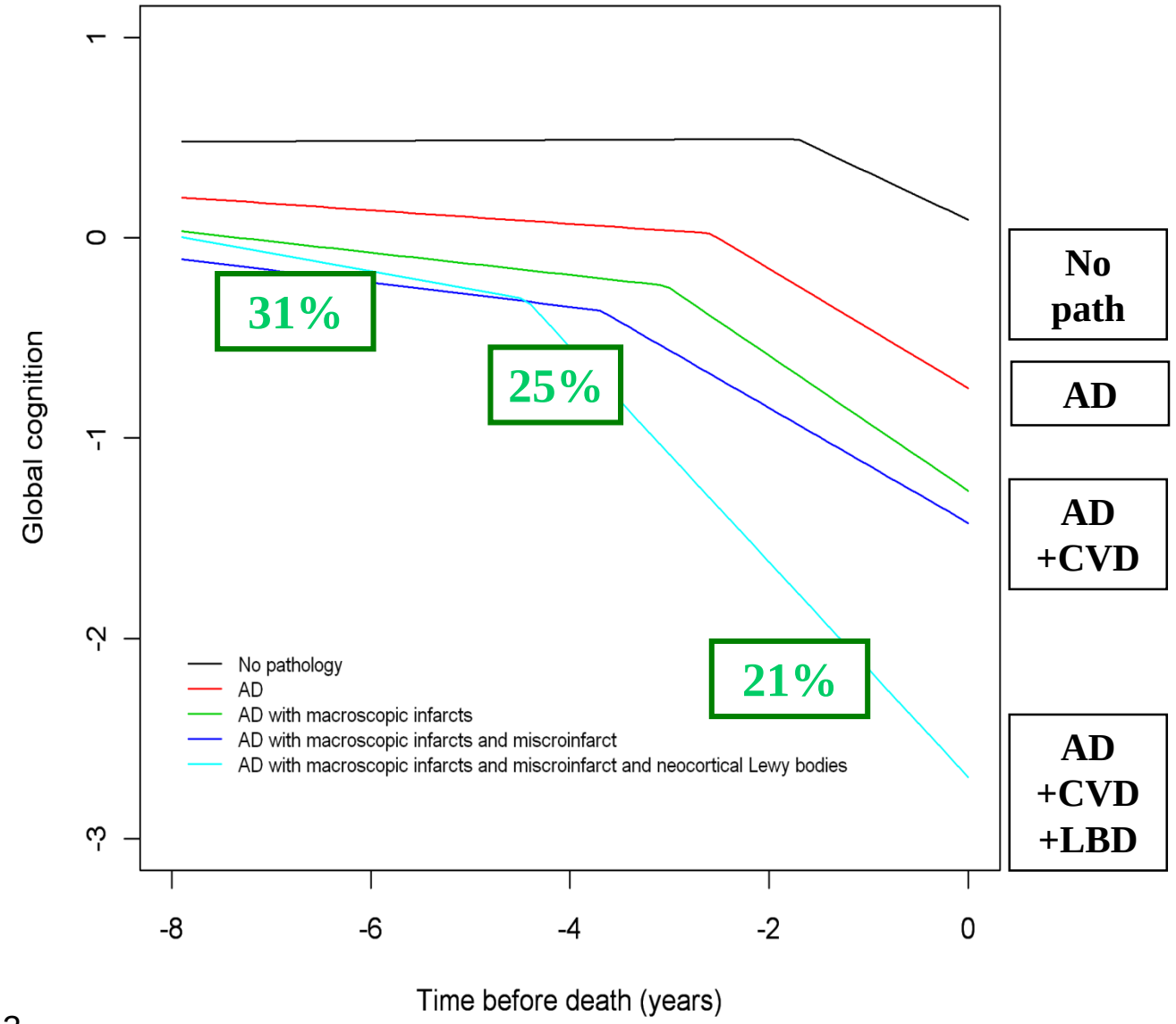



Total variance explained: 41%
AD: 30-34%
CVD: 1-3%
LBD: 4-8%
Residual cognitive decline: 59%

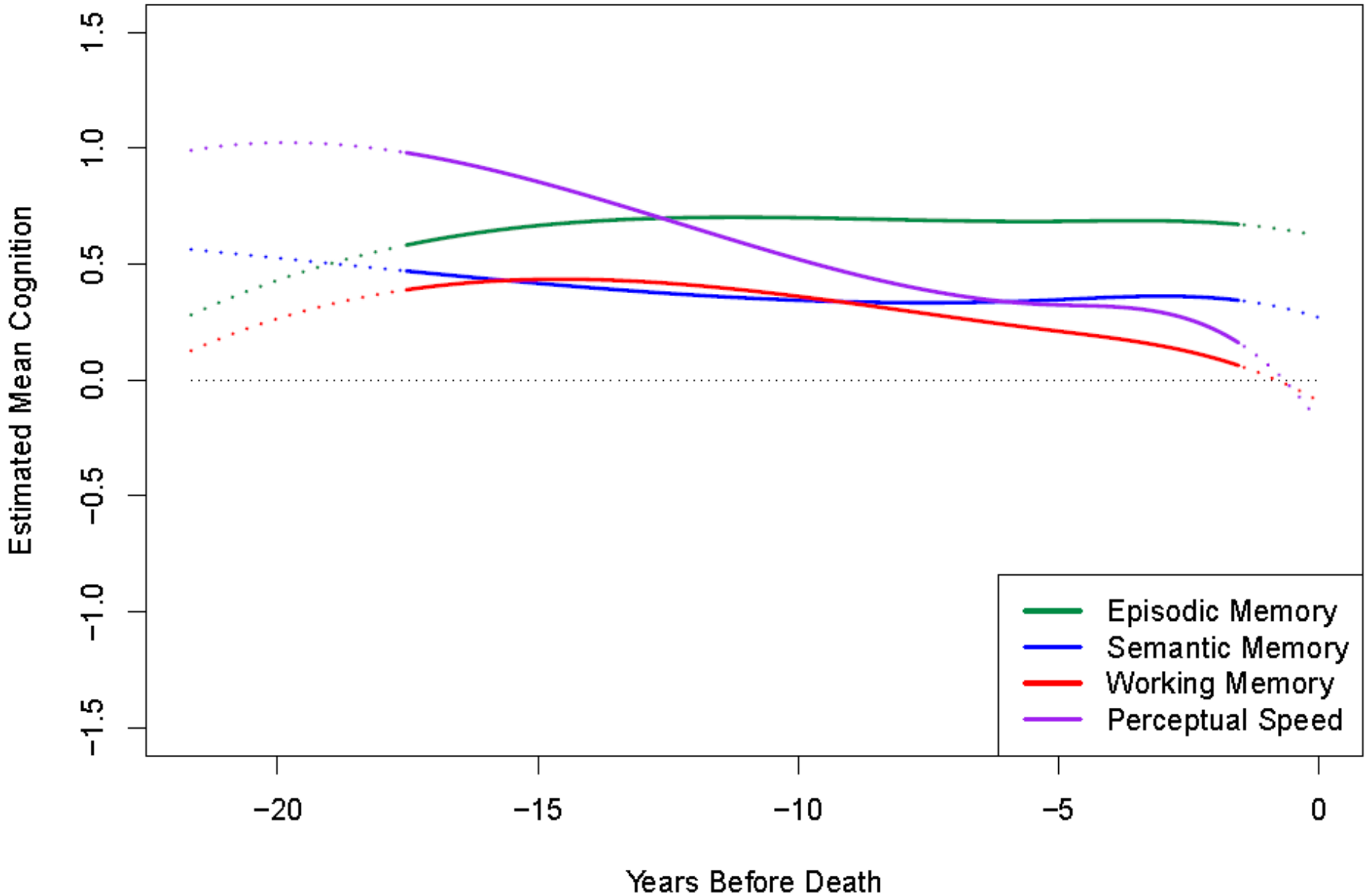

Latent group 1 (44.4%)
Latent group 2 (34.7%)
Latent group 3 (13.0%)
Latent group 4 (7.9%)
Global cognition
Time (years) since baseline

# Effect of pathology on components of the cognitive trajectory: preterminal and terminal cognitive decline

Pathology mainly affects preterminal slope




Boyle et al. *Annals Neurol* 2013


Estimated Mean Cognition
1.5
1.0
0.5
0.0
−0.5
−1.0
−1.5
−20
−15
−10
−5
0
Years Before Death
Episodic Memory
Semantic Memory
Working Memory
Perceptual Speed

# Prediction of Residual Cognitive Variability

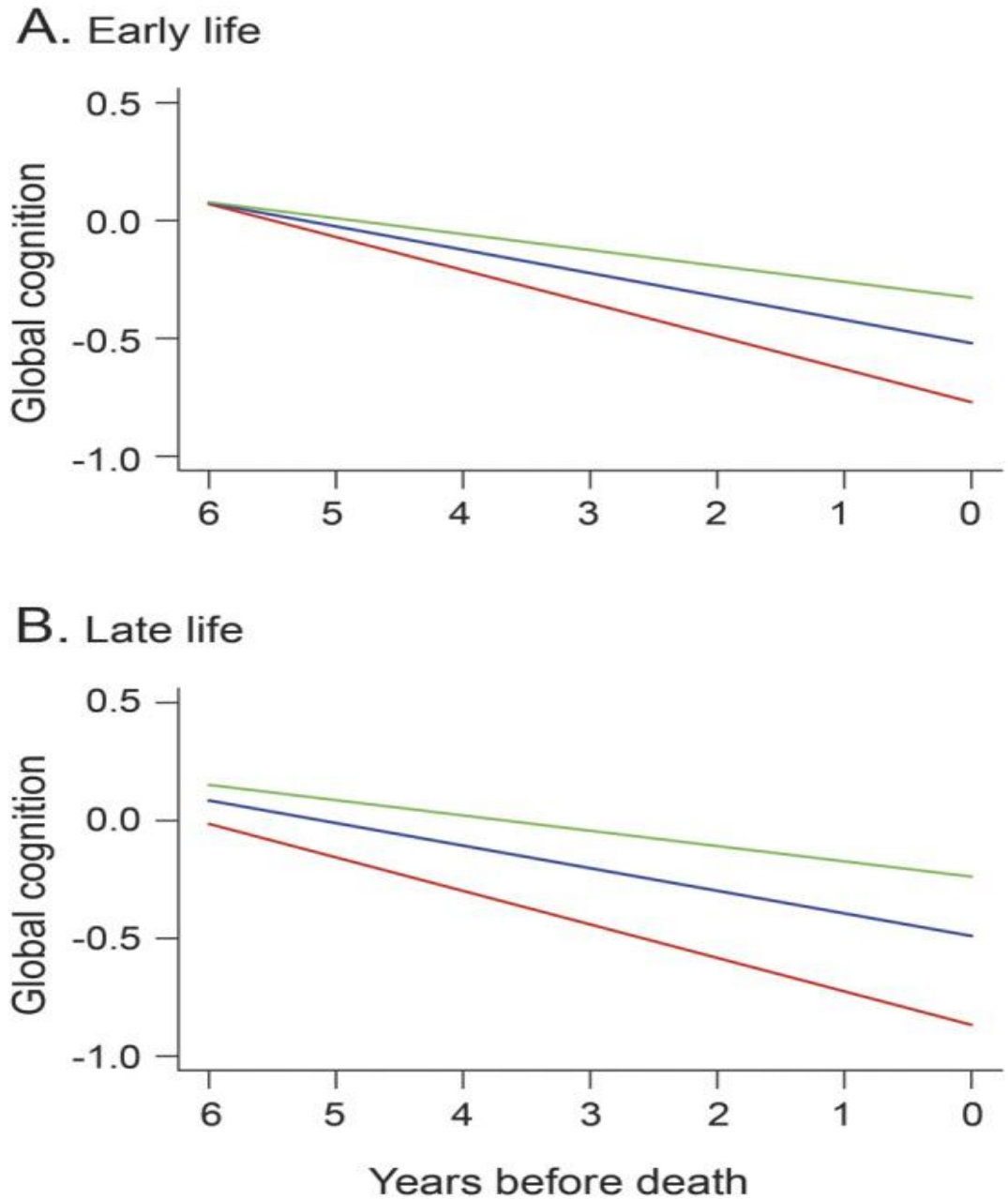
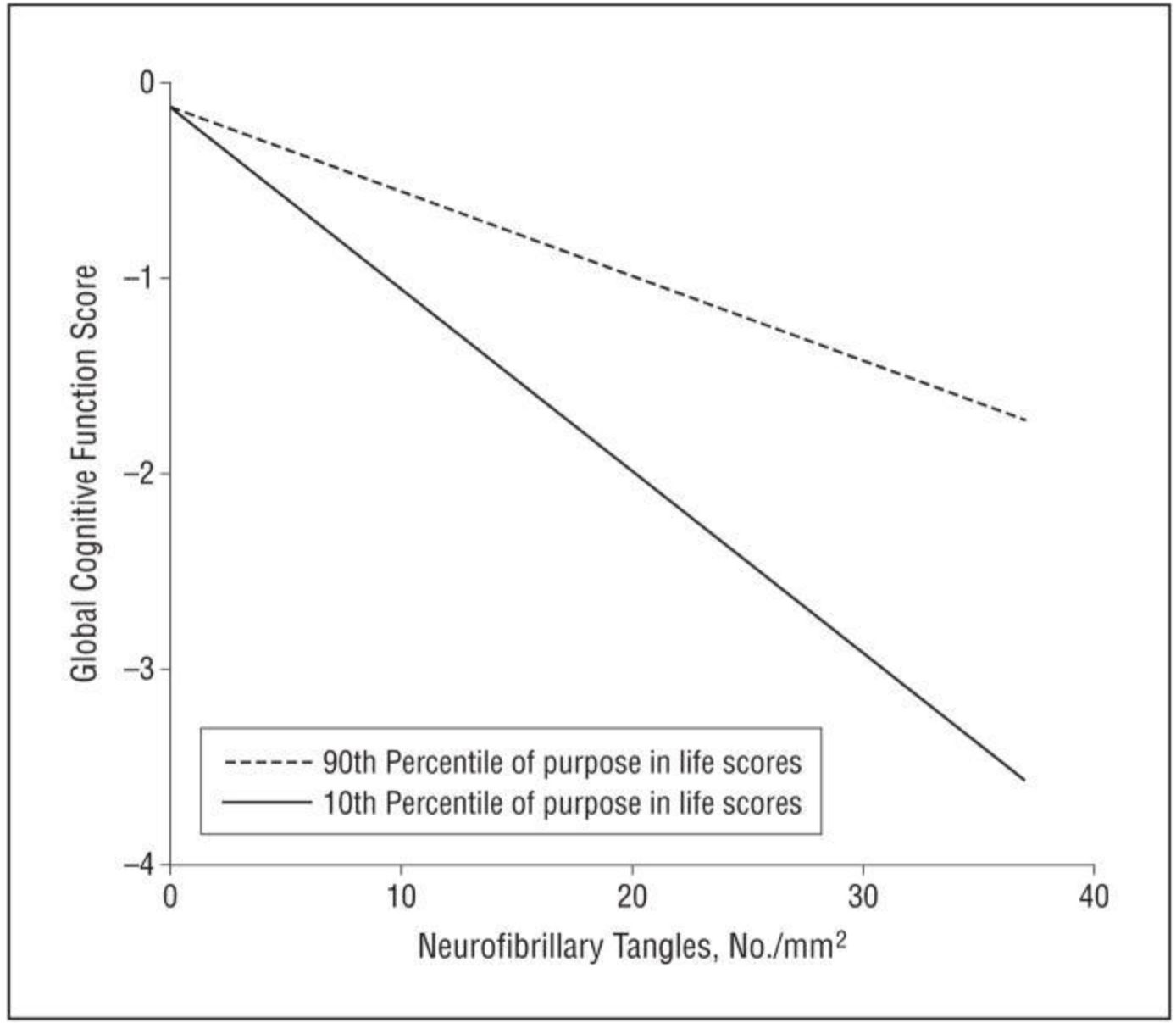
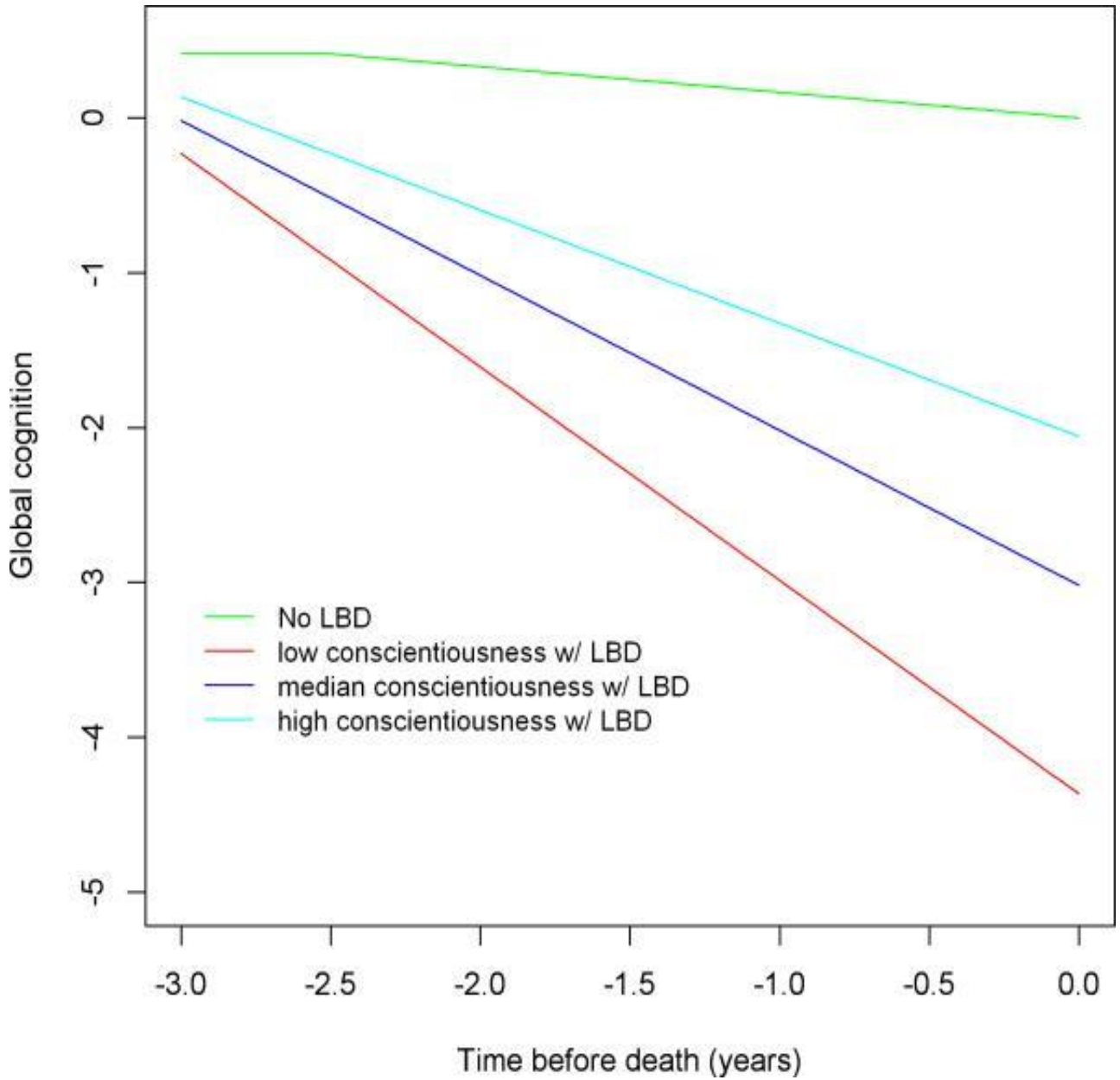

A. Early life
Global cognition
0.5
0.0
-0.5
-1.0
6
5
4
3
2
1
0
B. Late life
Global cognition
0.5
0.0
-0.5
-1.0
6
5
4
3
2
1
0
Years before death

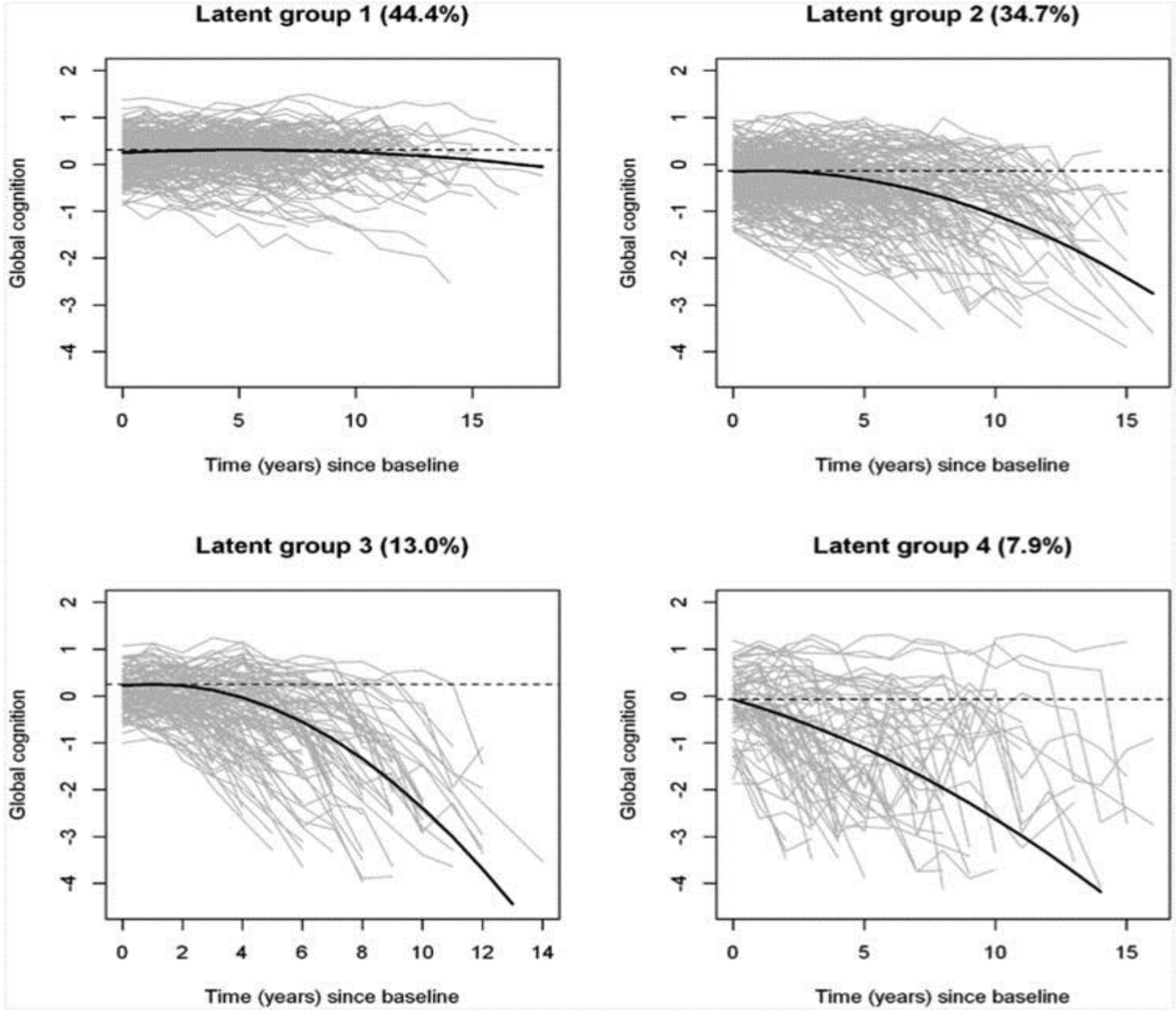
**Table 3** Relation of depressive symptoms and neuropathologic markers to global cognitive decline[a]

| | Model A | | | Model B | | | Model C | | |
|---|---|---|---|---|---|---|---|---|---|
| Model term | Estimate | SE | *p* | Estimate | SE | *p* | Estimate | SE | *p* |
| Time | −0.064 | 0.007 | <0.001 | −0.033 | 0.007 | <0.001 | −0.015 | 0.008 | 0.057 |
| CES-D mean score | −0.113 | 0.030 | <0.001 | | | | −0.104 | 0.026 | <0.001 |
| CES-D mean score × time | −0.014 | 0.003 | <0.001 | | | | −0.013 | 0.003 | <0.001 |
| Amyloid plaques | | | | −0.005 | 0.008 | 0.520 | −0.006 | 0.008 | 0.438 |
| Amyloid plaques × time | | | | −0.001 | 0.001 | 0.369 | −0.001 | 0.001 | 0.307 |
| Tangle density | | | | −0.058 | 0.007 | <0.001 | −0.058 | 0.007 | <0.001 |
| Tangle density × time | | | | −0.006 | 0.001 | <0.001 | −0.006 | 0.001 | <0.001 |
| Gross infarcts | | | | −0.423 | 0.073 | <0.001 | −0.410 | 0.072 | <0.001 |
| Gross infarcts × time | | | | −0.048 | 0.008 | <0.001 | −0.046 | 0.008 | <0.001 |
| Microinfarcts | | | | 0.037 | 0.074 | 0.620 | 0.049 | 0.073 | 0.507 |
| Microinfarcts × time | | | | 0.015 | 0.008 | 0.074 | 0.016 | 0.008 | 0.054 |
| Neocortical LB | | | | −0.617 | 0.103 | <0.001 | −0.591 | 0.101 | <0.001 |
| Neocortical LB × time | | | | −0.072 | 0.011 | <0.001 | −0.069 | 0.011 | <0.001 |
| Hippocampal sclerosis | | | | −0.593 | 0.137 | <0.001 | −0.633 | 0.136 | <0.001 |
| Hippocampal sclerosis × time | | | | −0.048 | 0.014 | <0.001 | −0.053 | 0.014 | <0.001 |

Abbreviations: CES-D = Center for Epidemiological Studies Depression Scale; LB = Lewy bodies; SE = standard error.
[a] Estimated from 3 mixed-effects models adjusted for age at death, sex, and education. In subsequent analyses, there were no interactions between depressive symptoms and neuropathologic markers.


0
−1
−2
−3
−4
Global Cognitive Function Score
90th Percentile of purpose in life scores
10th Percentile of purpose in life scores
0
10
20
30
40
Neurofibrillary Tangles, No./mm2


Global cognition
0
-1
-2
-3
-4
-5
-3.0
-2.5
-2.0
-1.5
-1.0
-0.5
0.0
Time before death (years)
No LBD
low conscientiousness w/ LBD
median conscientiousness w/ LBD
high conscientiousness w/ LBD


Latent group 1 (44.4%)
Latent group 2 (34.7%)
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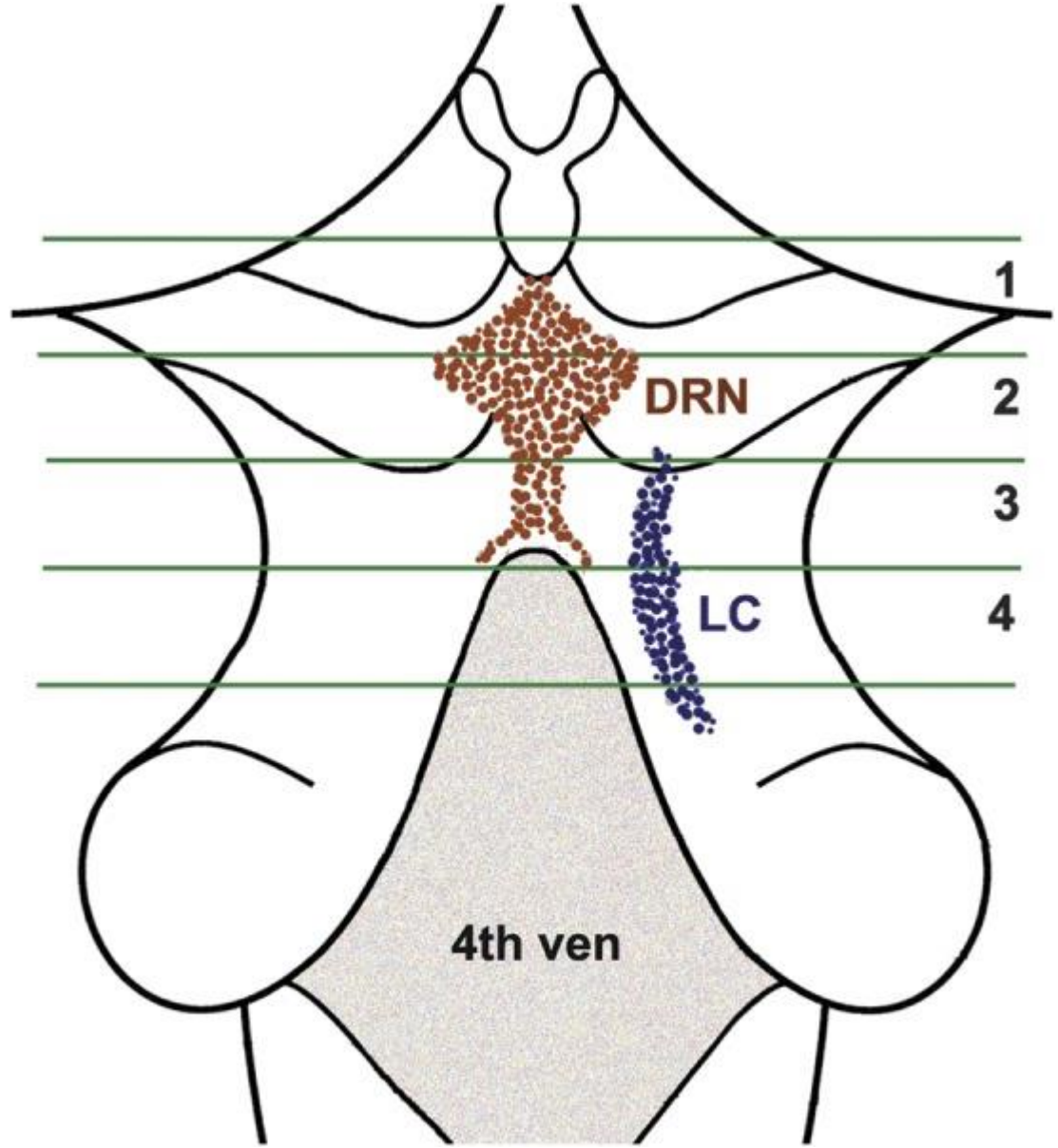
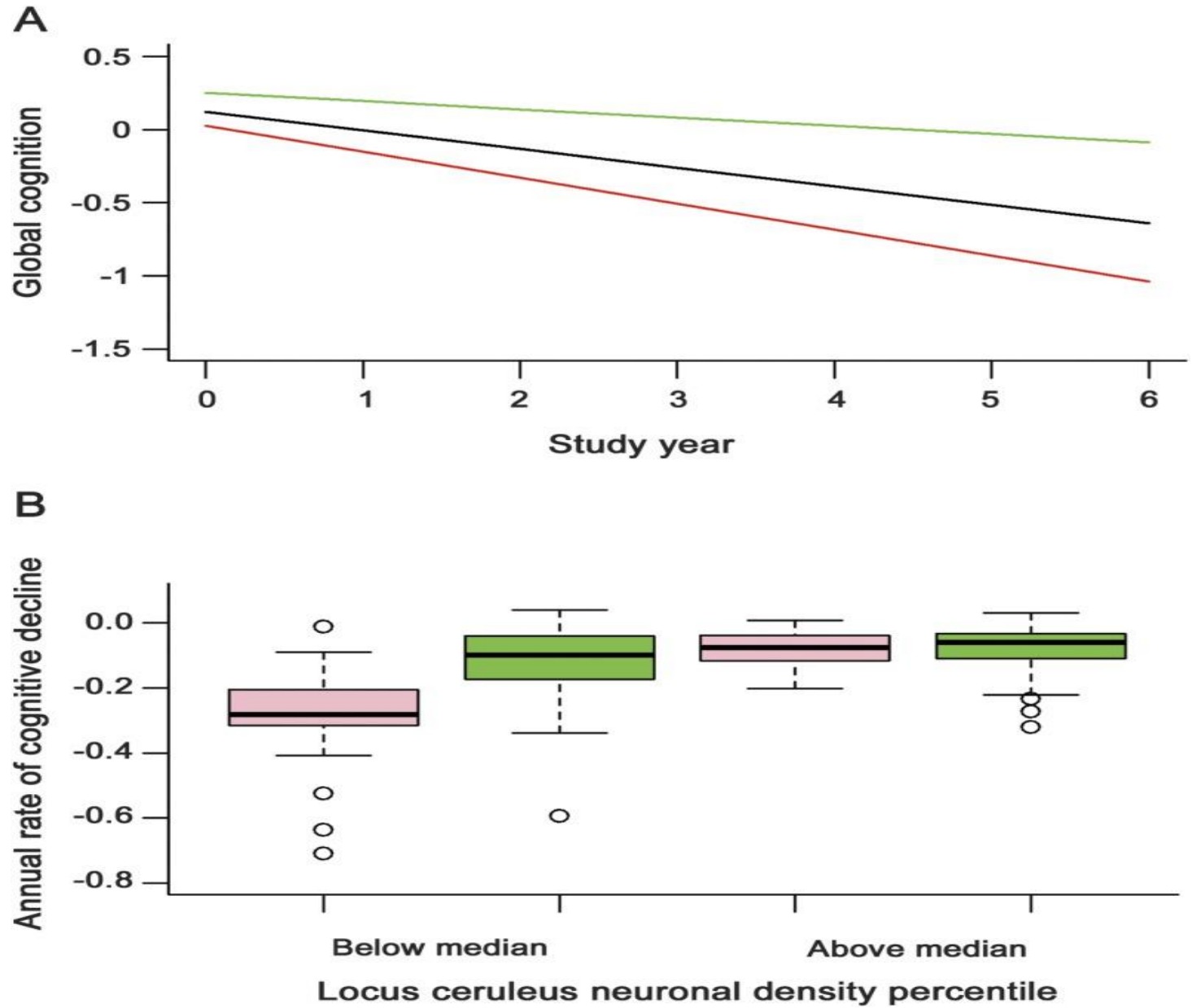
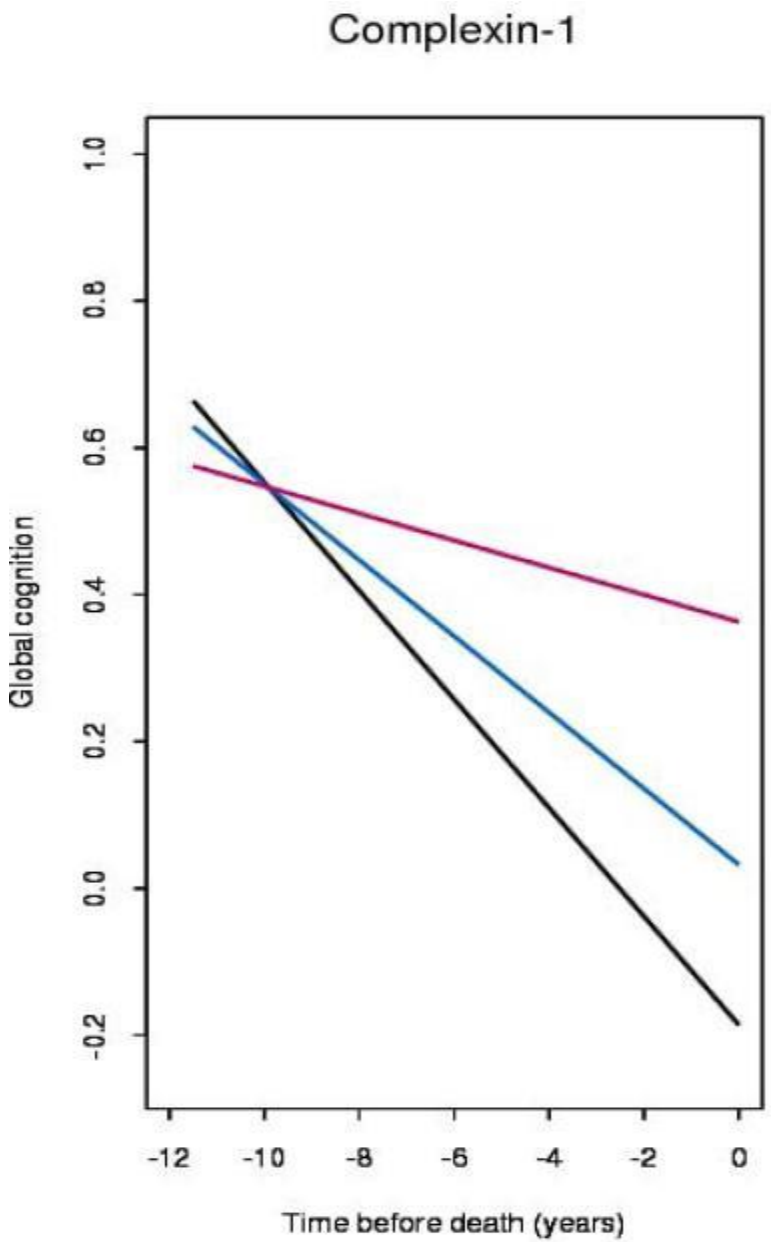
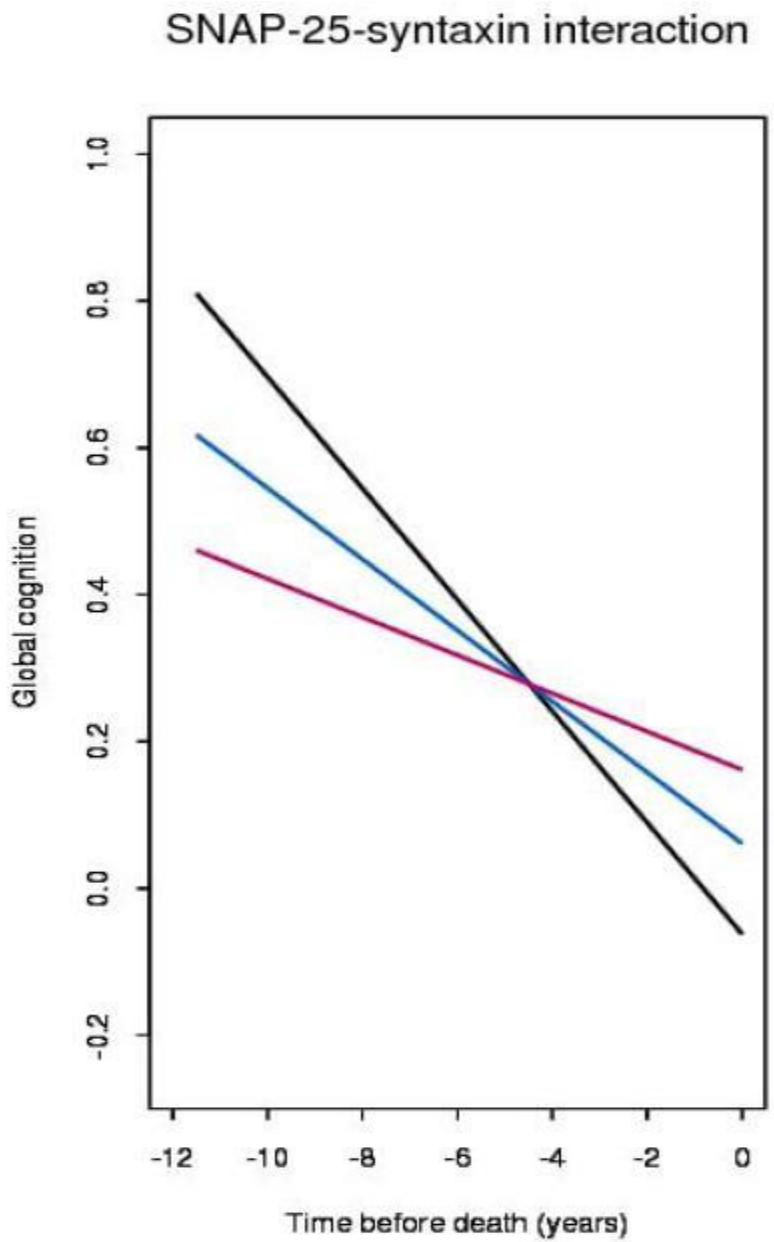
Latent group 4 (7.9%)
Global cognition
Time (years) since baseline


1
2
3
4
DRN
LC
4th ven


A
0.5
0
-0.5
-1
-1.5
Global cognition
0
1
2
3
4
5
6
Study year
B
0.0
-0.2
-0.4
-0.6
-0.8
Annual rate of cognitive decline
Below median
Above median
Locus ceruleus neuronal density percentile


Complexin-1
Global cognition
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
-12
-10
-8
-6
-4
-2
0
Time before death (years)


SNAP-25-syntaxin interaction
Global cognition
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
-12
-10
-8
-6
-4
-2
0
Time before death (years)

# *CONCLUSIONS*

- Much of variability in cognitive aging is not associated with common dementia related pathologies

- This residual cognitive variability is related to individual differences in:
  - Potentially modifiable lifestyle factors
  - Density of neurons and their connections in key brain systems

- Better understanding of how lifestyle influences cognitive reserve may suggest novel strategies for cognitive health maintenance in old age