

Supplementary Material

Stages of Objective Memory Impairment Predict Alzheimer's Disease Neuropathology: Comparison with the Clinical Dementia Rating Scale–Sum of Boxes

Ordinal logistic regression (proportional odds) was used to predict the Braak stage using SOMI and CDR-SB stage in separate models and then combined in a single model [1]. Each analysis modeled the logit transformations of the ordered Braak probabilities using simultaneous linear equations sharing the same slope coefficients.

$$\text{logit}(\Pr(Y > j)) = \log\left(\frac{\Pr(Y > j)}{\Pr(Y \leq j)}\right) = \eta_j + \sum_k \beta_k x_k, j = 1, \dots, J - 1$$

where Y is the value of a Braak stage, J is the number of possible Braak stages, η_j is the intercept for the j^{th} stage, x_k is the k^{th} predictor or covariate (age, time from last assessment to death, education, *APOE* $\epsilon 4$ genotype, and sex) and β_k is the corresponding coefficient. Ordinal logit regression is a proportional odds model, where the odds ratio of making response $Y > j$ at $x_k = x_1$ versus $x_k = x_2$ is $\exp(\beta_k(x_1 - x_2))$ which is independent of the choice of category (j). If x_k is a continuous variable, a significantly positive β_k , i.e., $\exp(\beta_k) > 1$, indicates increase in x_k leads to a larger $\Pr(Y > j)$, i.e., associates with a higher stage of Y ; for a categorical variable x_k , a significantly positive β_k means a specific level of x_k associates with a higher stage of Y relative to the reference level of x_k .

We conducted the Brant test [2] for checking the proportional odds assumption of the ordinal logit model for predicting Braak stage using SOMI (Supplementary Table 1, Model 1). The insignificant result ($p=0.088$) supported the proportional odds assumption. The proportional odds assumption initially did not hold for the CDR-SB stage predicting Braak stage based on a

significant Brant test ($p < 0.001$) (Supplementary Table 1, Model 2). After eliminating the two significant covariates with the smallest p-values, age and time to death, the proportional odds assumption held. Accordingly, Model 2 prime is our primary model for CDR-SB stage.

When comparing the incremental explanatory power of CDR-SB stage and SOMI, we considered the full model with SOMI and CDR-SB stage as predictors and *APOE4* genotype which was the only significant covariate in earlier models that satisfied the assumption of proportionality. The full model passed the Brant test (Supplementary Table 1, Model 3).

REFERENCES

- [1] McFadden D (1973) Conditional logit analysis of qualitative choice behavior. In *Frontiers in Econometrics*, Zarembke P, ed. Academic Press, New York, pp. 105-142.
- [2] Brant R (1990) Assessing proportionality in the proportional odds model for ordinal logistic regression. *Biometrics* **46**, 1171-1178.

Supplementary Table 1. p-values from the Brant Test for Checking the Proportional Odds Assumption of the Ordinal Logit Model

	Model 1	Model 2	Model 2 prime	Model 3
Omnibus Test	0.088	<0.001	0.142	0.996
SOMI	0.999			0.998
CDR-SB stage		0.510	0.565	0.657
Age	0.147	0.078		
Time from last cognitive assessment to death	0.025	0.025		
Education	0.110	0.213	0.142	
<i>APOE</i> ε4	0.623	0.644	0.729	0.723
Sex	0.180	0.361	0.057	

First row reports p-values for the Omnibus Test assuming the parallel regression assumption holds. The other entries are the type III p-values for each predictor (covariate) given other covariates (covariates and predictor) in the model.