Serial Position Effect Markers in Alzheimer's Disease: SPE-Primacy Progression as a Predictor of Conversion from Healthy Controls to Cognitive Impairment

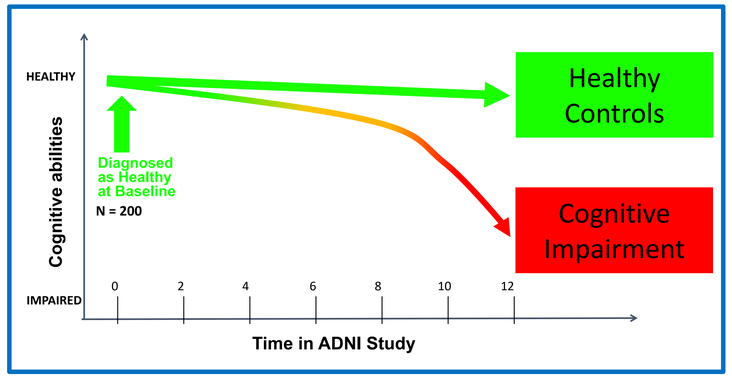
Isabelle K. Avildsen[1], Emnet Z. Gammada[1,4], Aditya Kulkarni[1], Paul K. Crane[3], Laura E. Gibbons[3], and Nancy S. Foldi[1, 2]

[1]The Graduate Center, CUNY; [1,2]Department Of Psychology , Queens College, CUNY

[3] Department of Medicine, School of Medicine, University of Washington; [4] Department of Psychology, University of California Los Angeles

Background

- Serial Position Effects (SPE) of list learning are highly sensitive cognitive markers, which can characterize amnestic mechanisms of encoding, learning, and retrieval. [1-3]
- Primacy position items recruit deep semantic processing; and tracking their accuracy during learning and after short and long delay recall captures both consolidation and retrieval skills.
- We propose that Primacy accuracy over time, i.e. 'primacy progression', may identify individuals at risk of later cognitive impairment.[4]
- Our objective was to compare the SPE-Primacy to Total List scores from the Rey Auditory Verbal Learning Test (RAVLT)[5] as predictors of conversion from Healthy Control (HC) to Cognitive Impairment (either Mild Cognitive Impairment or Alzheimer's Disease).



Aims

AIM 1: To determine whether SPE-Primacy scores are sensitive predictors of Cognitive Impairment in Healthy Controls using RAVLT performance at Learning, Short Delay and Long Delay recall.

- **HYPOTHESIS 1:** We hypothesize that SPE-Primacy at Learning, Short and Long Delay will capture both semantic and episodic encoding/retrieval deficits and thus be predictive of conversion.

AIM 2: To determine whether SPE-Primacy scores are better predictors than the standard Total-List RAVLT scores.

- **HYPOTHESIS 2:** We hypothesize that the SPE-Primacy scores will be better predictors than the Total-List RAVLT scores.

SPE-Primacy Model at Short Delay

	EXP(β)	SE	Z	P VALUE	95% CI
Sex	0.54	.34	-1.78	.07	0.28 – 1.07
Education	0.96	.06	-1.14	.26	0.84– 1.05
Age	1.02	.03	0.90	.36	0.97 – 1.10
ApoE4	4.29	0.36	4.04	<.001***	2.12 – 8.70
Primacy at SD	0.25	0.46	-3.08	.002**	0.10 – 0.60

Primacy SD Model
AIC = 349.36

SPE-Primacy at SD emerged as a a significant protective factor.

With **each unit increase in SPE-Primacy at SD** HC individuals were **75% less** likely to develop Cognitive Impairment.

Total SD Model
AIC = 351.89

Total score at SD also emerged as a significant protective factor.

With **each unit increase in Total-List RAVLT at SD** HC individuals were **11 % less** likely to develop Cognitive Impairment.

Total-List RAVLT Model at Short Delay

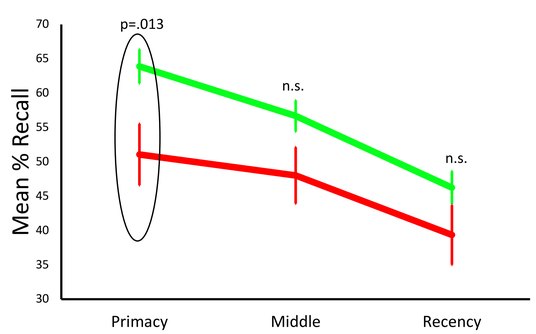
	EXP(β)	SE	Z	P VALUE	95% CI
Sex	0.65	.34	-1.22	.22	0.73 – 1.29
Education	0.94	.06	-1.01	.31	0.85– 1.06
Age	1.03	.03	1.00	.32	0.97 – 1.10
ApoE4	3.97	0.35	3.92	<.001***	1.99 – 7.91
Total-RAVLT SD	0.89	0.04	-2.60	.009**	0.82 – 0.97

* p<.05, ** p<.01, *** p<.001

Short Delay emerged as an area of sensitivity for predicting conversion from Healthy Control to Cognitive Impairment. SPE-Primacy at SD best predicted conversion indicating that important variability may be missed by interpreting total scores alone.

SPE at Short Delay: % Accuracy of Conversion Status by SPE Position at Short Delay

- Baseline SD-recall accuracy comparing individuals who remained HC versus those who converted to CI by SPE position (ANCOVA covarying for Age, Sex, Education, APOE-ε4 allele status).
- Error bars +/- 1 SE.
- The only SPE position that significantly differentiated converters from non-converters at SD recall was the Primacy position (p = .01).



Methods

- Participants from the Alzheimer's Disease Neuroimaging Initiative were diagnosed as HC at baseline (N = 200) and followed longitudinally for up to 12 years.
- SPE-Primacy measures at Learning, short delay (SD), and long delay (LD) recall were compared to Total-List RAVLT scores.
- Six Cox regression analyses, controlling for Age, Sex, Education, and *APOE*-ε4 status, evaluated conversion from HC to Cognitive Impairment.

Results

- The Primacy-SD model best predicted disease conversion (AIC = 349.36, *HR* = 0.25 [0.10, 0.60], p = 0.002).
- Total-List RAVLT scores also predicted conversion at Learning (AIC = 354.25, *HR* = 0.96 [0.93,1.00], p = 0.04) and SD (AIC = 351.89, *HR* = 0.89 [0.82,0.97], p = 0.009).

Discussion

- The SPE-Primacy at SD model as well as two Total-RAVLT models predicted those HC who converted to Cognitive Impairment.
- The Primacy-SD model demonstrated the best model fit (AIC) compared to the significant Total-List RAVLT at Learning or SD.
- We propose that the accuracy of Primacy item recall by short delay represents a progression from initial learning to early-stage consolidation. Primacy items depend not only on semantic processing ability, but also capture valuable variability early in disease, that may be missed by using only total list RAVLT scores.

Limitations include

- Categorization of Mild Cognitive Impairment at follow-up
  - Variable prevalence rates and unclear stability of diagnosis[6]
- Range of follow-up data 2-12 years.
- Lack of diversity in ADNI.

References

[1]Foldi et al. (2003), *PsychRes*, 120(1), 74-84
[2]Howieson et al., *JofClin&ExpNeuropsych, 2011*
[3] Egli et al., *Alz&Dem*, 2014
[4]Foldi, N.S., Taylor,K. Monsch, AU, Sollberger, M., Kivisaari, S. (2019), *BioRix*
[5]*Rey Auditory Verbal Learning Test: A Handbook, 1996*
[6] Thomas et al. (2019) *Alz & Dement, 15, 561-569*

Funding

- **Funding Sources to Nancy S. Foldi:** NIH NIGMS – SCGM12172110; PSC-CUNY #TRADA-60090-00-48; and PSC-CUNY #TRADB-64535-00 42.
- **Isabelle Avildsen:** Doctoral Student Research Grant (2019-2020)

Principal Investigator: N.S. Foldi, PhD
IRB Approval at Queens College – CUNY #2016-0630.