Serial Position Profiles May Have Promise as a Cognitive Marker of Preclinical Alzheimer's Disease

Jana E. Jones, PhD[1], Asenath La Rue, PhD[2], Tina Boncyk[2], Bruce P. Hermann, PhD[1], Mark A. Sager, MD[2]

[1]Department of Neurology and [2]Wisconsin Alzheimer's Institute (WAI), University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin

BACKGROUND

In rote list learning, the serial position curve (SPC) provides information regarding relative dependence on primary memory (recency effect) versus secondary memory (primacy and middle region).

Alterations of the SPC are seen in Alzheimer's disease (AD); namely, an exaggerated recency effect.

Abnormal SPC can reflect hippocampal disease, and as a result, it is reasonable to look at SPC as a preclinical AD sign.

The purpose of this investigation was to determine whether asymptomatic persons at increased risk for AD exhibit alterations in the SPC.

METHODS

Subjects included:
- 623 asymptomatic middle-aged individuals with a parent with AD (positive family history, FH+) (median age = 53 years).
- 157 control participants with a negative family history (FH-) of AD whose parents survived to at least age 70 without AD or other memory disorders.

All participants were administered the Rey Auditory Verbal Learning Test which requires learning and recall of 15 unrelated nouns.

PROCEDURES

Percentages of items recalled from primacy, recency, and middle regions of the word list were computed by dividing the number of items recalled from each region by the total number of items presented in that region over the five learning trials.

The primacy region was defined as serial position items number 1 through 4.

The middle region included items 5 through 11.

The recency region was defined as items 12 through 15.

These *regional* scores adjust for the differing numbers of items in different sections of the list.

ACKNOWLEDGEMENTS

RESULTS

TABLE 1. DEMOGRAPHICS

Characteristic	AD Children (n = 623)	Controls (n = 157)
Age (years)	52.37 (6.51)	55.70 (5.86)*
Education (years)	16.00 (2.68)	16.57 (2.89)
Female gender, % (n)	72 (450)	63 (99)
White/Caucasian, % (n)	98 (612)	99 (155)
APOE ε4 allele, % (n)	44 (274)	15 (23)*

TABLE 2. REY AUDITORY VERBAL LEARNING TEST (AVLT) OF AD CHILDREN AND CONTROLS

Cognitive Measure	AD Children (n = 623)	Controls (n = 157)
Standard AVLT Scores		
AVLT learning total (sum of 5 trials)	51.41 (8.08)	51.89 (8.08)
AVLT delayed recall	10.65 (2.93)	10.47 (2.75)
AVLT Serial Position Scores		
Primacy (% recalled)	72.96 (14.63)	74.55 (14.16)*
Middle Region (% recalled)	60.19 (15.24)	61.24 (15.59)
Recency (% recalled)	77.69 (13.01)	76.43 (13.28)
Recency - Primacy (difference in % recalled)	4.73 (19.18)	1.88 (19.31)*
Recency - Middle Region (difference in % recalled)	17.50 (17.65)	15.20 (17.96)*

Note: Values are means (SD) unless noted. Age, education, and gender were covaried in statistical comparisons. *p < .05

FIGURE 1. MEAN DIFFERENCES IN PERCENTAGE OF ITEMS RECALLED FROM DIFFERENT REGIONS OF A WORD LIST

(adjusted for age, education, and gender)
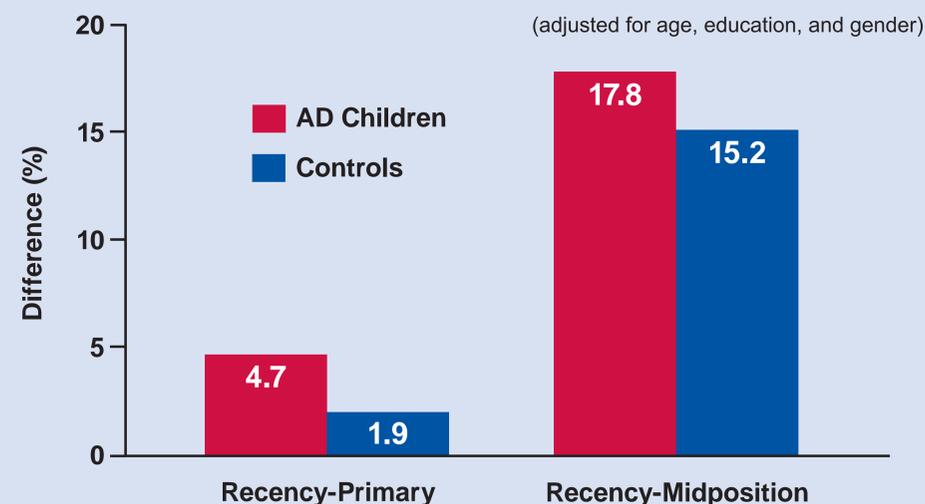
ANALYSES

Demographic variables, APOE allele status, and health and lifestyle variables were compared for AD children and controls by χ2 or univariate *F* tests, using the Bonferroni correction to control for multiple comparisons.

The principal dependent measures were regional serial position scores and difference scores comparing percentages of items recalled from the recency region versus primacy and middle regions.

Standard clinical outcomes from the AVLT (total correct responses across the five learning trials and delayed recall score) were also examined.

RESULTS

There was no significant difference in total words recalled between the FH+ and FH- groups.

Examining SPC effects in FH+ and FH- subjects, the FH+ group showed a significantly greater tendency to recall words from the end (recency) versus beginning (primacy) of the list (4.7% vs. 1.9%, p < .05), as well as the end versus the middle of the list (17.8% vs. 15.2%, p < .05). See Figure 1.

Serial position effects in FH+ subjects were unrelated to APOE, age, gender, and education (all p's > .10).

Additionally, there were no significant associations between serial position scores and depression ratings, blood pressure, or cholesterol levels.

CONCLUSION

Middle-aged asymptomatic individuals at risk for AD do not show a difference in total words recalled compared to controls.

However, individuals with a family history of AD exhibit a distinctly different serial position curve suggesting greater reliance on immediate as opposed to secondary memory.

These findings raise the possibility of subtle hippocampal dysfunction and a potential indicator of disease risk.

Whether alterations in serial position recall, a known correlate of AD, will serve as a promising marker of preclinical AD remains to be determined.

These participants will be studied prospectively following a 4-year test-retest interval.